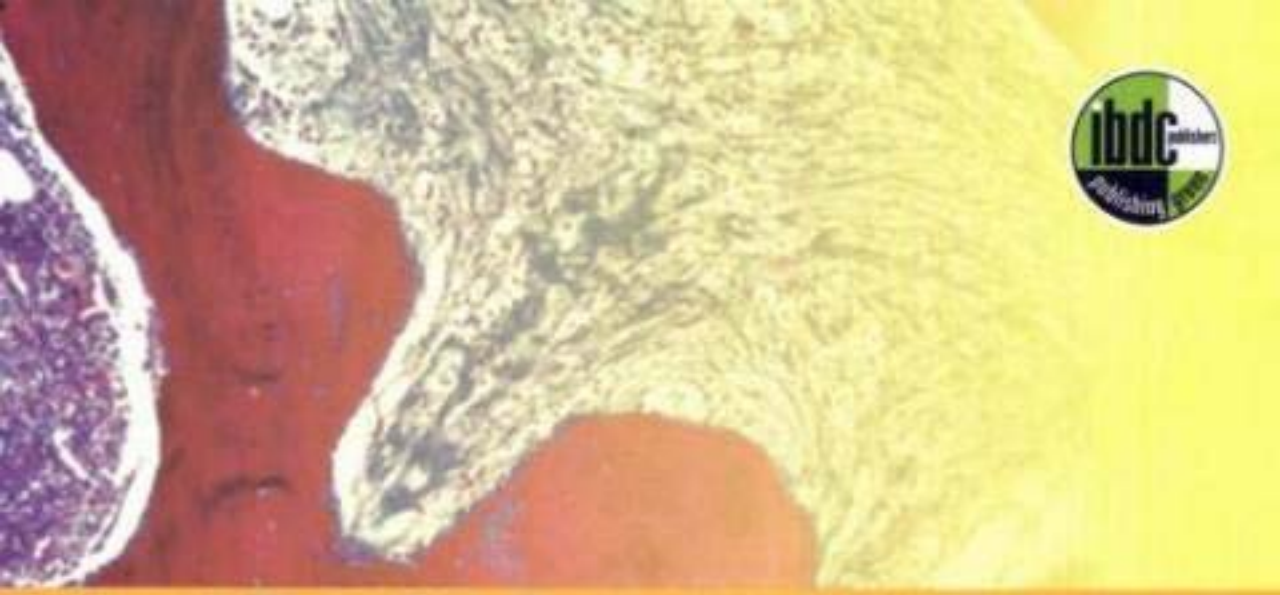
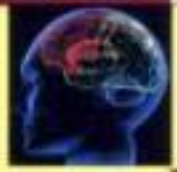


A Text Book on
Systemic Pathology of Domestic Animals



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A Text Book on Systemic Pathology of Domestic Animals

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Postmortem examination

The aim of a gross postmortem examination of the heart is to examine four major areas, the pericardium, the myocardium, the mural and valvular endocardium and the great vessels. It is preferable to commence by examining the heart and blood vessels in situ for abnormalities of size and position. The pericardial sac should also be incised and its contents examined before the thoracic contents are removed. Once removed, the external surface of the heart should be examined, including the pericardium, epicardium and major vessels.

The right ventricle bears responsibility for systemic circulation in the fetus, and in neonatal hearts, Thickness of the wall left and right chambers is about equal; it is not until several months after birth that the mature proportions are attained.

Rigor mortis begins rather earlier in myocardial than in skeletal musculature and reaches its greater development in the powerful left ventricle. Rigor should completely express the blood from the left ventricle; rigor of the right ventricle is less efficient and emptying it's incomplete. The presence of some clotted blood in the right ventricle is normal, whereas if present in the left ventricle after a reasonable postmortem interval, it is indicative of incomplete rigor and therefore of severe myocardial degeneration. Unclotted blood in ventricle is an indication of death due to hypoxia.

Blood usually clots slowly after death and permits RBCs to sediment, where blood is present in volume as in the heart and arterial trunk, this process of sedimentation and subsequent clotting leads to the formation of currant jelly and

chicken fat clots. Currant jelly clot is rich in RBCs hence red in color; chicken fat clot contains WBCs platelets and less RBCs. Chicken fat clot indicates slow death of animal; currant jelly clot indicates rapid death of animal. Chicken fat clot are to be expected in horses, which have rapid ESR. These postmortem clots are to be distinguished from thrombi; postmortem clot if one pulls from the vessels comes away easily, and are not attached to the endocardium or endothelium of blood vessels.

Pericardium: The pericardium is a thin layer that covers the heart. It is double layered pleura. Outer coat is the pericardium and the inner sac completely encircles the pericardium. In between outer and inner coats a potential space with fluid exists that is called pericardial sac. Primary disease confined to the pericardium is rare, but the loose anatomic relationship of the pericardium to the heart, lungs, and pleura sometimes results in the extension of disease processes from the latter organs to the pericardium. The pericardial cavity may communicate with the peritoneal cavity through clefts in diaphragm; the pericardial sac may be absent congenitally without clinical effect. The function of pericardium is to provide automatic compensation and ensures the end diastole trans-mural pressure is the same for all hydrostatic levels of the ventricles. The role of epicardium includes prevention of sudden cardiac dilatation, maintenance of flow of intramural pressures; limitation of right ventricular stroke work, hydrostatic compensation for gravitational or inertia forces; and maintenance of cardiac alignment and streamlined intra-cardiac flow. The heart is attached to the sternum by sterno-pericardial attachment. In that the movements of the heart will be limited to the physiological levels.

Hydro pericardium: The pericardial sac normally contains a very small quantity of clear, serous fluid. Any excess in the volume of fluid is referred to as hydro pericardium. The pericardial fluid is clear or light yellow without floccules, and with low content of protein. Sero-sanguinous fluid is often observed in variety of toxemic and septicaemic diseases. Inflammatory exudates can be differentiated from transudates on the basis of the higher content of protein and cells in exudates and histological evidence of inflammation involving the pericardium and epicardium. Hydro pericardium is often part of generalized anasarca and is seen in most of the cachetic diseases and congestive heart failure cases.

Myocardial necrosis: Saccharated iron compounds by virtue of the capacity of iron to generate free radicals, in ferric\ ferrous translations causes' fatal myocardial necrosis in piglets. Ruminants of early age that is before the rumen is developed and pigs are susceptible to the cardio toxic effects of cotton seed poisoning and the active principles of gossypol. Monensin, ionophore coccidio-stat is toxic in horses and pigs. Myocardial necrosis occurs in dogs ingesting rodenticides that contain thallium. Anichkov cells also known as caterpillar cells have been observed in myocarditis. These cells appear as large mononuclear cells in which the nuclear chromatin is present in and undulating wavy ribbon with slender processes radiating from it. The origin of these cells is disputed. Suggestions include a fibroblastic, pericyte, endothelial, or myocytic origin.

Cardiovascular Pathology

Four sounds of heart are audible in different diseases. First sound ventricular systole occurs -probably due to the closure of auricular-ventricular valves. Second sound is due to the closure of semi lunar valves of aorta and starts with diastole. Third sound is used by rapid filling of ventricle and just occurs after the second sound. Fourth sound is caused by atrial systole and occurs just prior to the standard first heart sound.

The functions of the heart are to maintain sufficient supply of blood to meet the needs of the body tissues. For this, the heart should have sufficient cardiac reserve. Cardiac reserve is defined as the ability of the heart to meet increasing demands that are required under stress.

There are usually three catchwords that are required while reading the heart, viz., cardiac reserve, compensation, decompensation and heart failure. The term heart failure denotes a situation in which the heart is diseased, all compensatory mechanisms have been exhausted and characteristic clinical and pathological signs are exhibited.

The function of the heart is to maintain sufficient supply of blood to meet the needs of body tissues. The cardiac reserve represents the ability of the heart to meet increased demands that arose during physiological conditions like exercise, pregnancy and pathological conditions like anemia, fever etc. The heart is able to adapt itself to varying physiological needs and to pathological abnormalities. This ability is known as compensation. Compensation mechanisms include the cardiac response, namely, dilatation and hypertrophy. Consequent to this, there is systemic response, which includes an increase in heart rate, peripheral resistance, a redistribution of blood flow, vascular contraction and an increase in blood volume. In each case, the compensatory mechanisms are at least temporarily beneficial and are directed toward increasing cardiac output tomeet the metabolic needs of the animal.

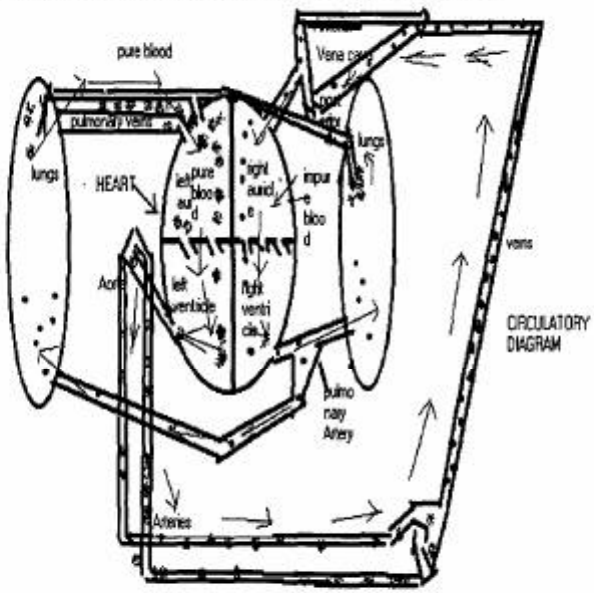
However, in the face of an ever-increasing peripheral resistance together with the increased workload put on the heart. The heart is not able to cope up with the demands and so become fatigued and fails. This state in which the heart is no longer able to compensate is called decompensation. Decompensation is gradual and results in dilatation of the ventricle.

The heart failure stems from two basic pathophysiologic changes, the accumulation of fluid, and tissue or organ ischemia. Fluid accumulation results from the retention of sodium and water. One of the earliest changes following a drop in cardiac output is the redistribution of blood flow within the kidney. The alterations in renal blood flow in heart failure also increase the activity of the renin-angiotensin-aldosterone system, producing more sodium reabsorption from the distal convoluted tubules. There is an increased activity of antidiuretic hormone also.

The fundamental differences between shock and congestive heart failure are that the total blood volume in heart failure is already more than adequate, but the effective blood volume is much diminished because of the poor cardiac output. The factors that lead to cardiac failure are three fold.

1. Alteration in the return of venous blood.
2. Increased resistance to outflow.
3. Impaired cardiac contraction.

Circulatory diagram in an adult mammalian system



If the venous return is inadequate, the heart is not capable of compensation to meet the situation and finally fails. Increased resistance results due to hypertension, narrowing or dilatation of valvular orifices, thrombosis and arteriosclerosis. The heart compensates for the increased resistance to outflow. This is evidence in the form of hypertrophy of heart musculature. However, in time the reserve power of the heart is exhausted and so fails. Any disease that injures the myocardium reduces the contractile power of the heart and so the compensatory mechanism cannot work.

The circulatory failure falls into three general types' namely cardiac syncope, peripheral circulatory failure and congestive heart failure.

The heart is usually attached to the sternum by the steroeopi pericardial attachment. Any heart with pericardium is to be detached first means; the sternopericardial attachment is to be cut and to be separated. Primary diseases confined to the pericardium are rare, but the close anatomic relationship of the

pericardium to heart, lungs and pleura sometimes results in the extension of disease processes from the latter organ to the pericardium. The pericardium is filled with little fluid. The role of pericardium includes prevention of sudden cardiac dilatation, maintenance of low transmural pressure, limitation of light ventricular stroke work, hydrostatic compensation of gravitational forces, maintenance of cardiac alignments and streamlined intracardiac flow.

Three golden rules obtained for the heart necropsy are 1) always weight the heart after removing the post-mortem clots, 2) always inspects before cutting any structure 3) try to preserve any stenotic valve or vessel.

A few special points which may be noted on external examination while doing autopsy suspected for a case of cardiac failure are 1) the extent of any edema as elicited by palpation, 2) any jaundice of skin or conjunctiva any cyanosis and digital clubbing in humans, 4) and any congenital anomalies such as accessory nipple.

Embryology of the heart

Adult heart is a modified blood vessel. Its tunica media is primarily cardiac muscle. The primordial of heart first appears as clusters of angioblast cells between the mesoderm of common-pleural-pericardial cavity and the underlying mesoderm. These primordial referred to as cardiogenic mesoderm. The first change involves the formation of bulbo-ventricular loop. It is formed in that the part of the endothelial tube that comprises the bulbous and the primitive ventricle. While the looping occurs, there is localised expansion of the bulbous and ventricular areas by means of diverticulation. The external sulcus demarcating the constriction of bulbo- ventricular loop is referred as inter-ventricular sulcus. After S-shaped loop is formed The heart undergoes further change in the position. The bulbous shifts to a more ventral and caudal portion while the atrium and sinus venous move cranial. Internal partitioning occurs.

Foetal circulation

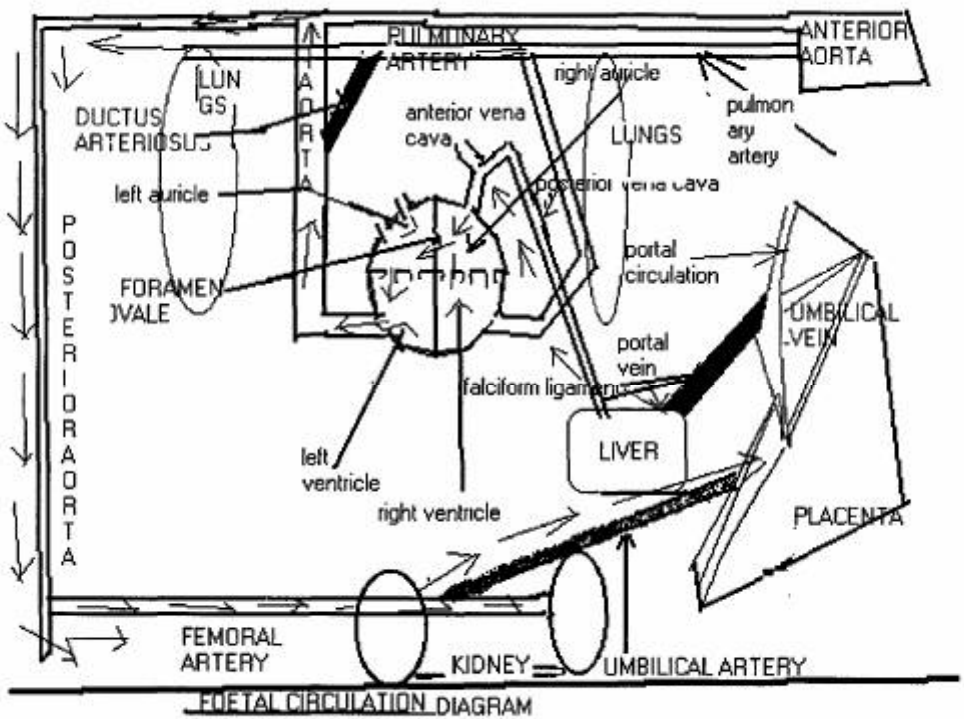
Before discussing the anomalies of heart, it is better to differentiate the changes that occur in foetal circulation and the disappearance of different structures and functions in the adult animal or the prenatal animal.

In the foetus, lungs are not functional. The foetus is a parasite staying in the womb. It is not excreting its secretions to the outside. The mother takes care of the excretions, nutrition and oxygenation of tissues, through the placenta. Placenta is a structure that develops between developing foetus and the uterus of the mother.

Thus, the umbilical arteries of the foetus, the right and left are large vessels, which arise from the internal iliac arteries and pass downward and forward in the umbilical folds of peritoneum on either side of bladder to umbilicus. Here

they are incorporated with the umbilical vein and the urachus in the umbilical cord, ramify in the allantois and end as the capillaries of the foetal placenta. They conduct the impure blood to the placenta. After birth, they are retracted and termed as round ligaments of the bladder.

Umbilical veins, receive the oxygenated blood from the placenta. These enter the falciform ligament of the liver and joins in the portal circulation, so that the blood passes through the capillaries of the liver before entering the posterior vena cava.



FOETAL CIRCULATION DIAGRAM

Ductus venosus is the vessel that is given off within the liver from a venous sinus formed by the confluence of portal and umbilical veins and passes directly to the posterior vena cava. Posterior vena cava and anterior vena cava open into the right auricle.

Foramen ovale is a septum that lies between the left auricle and right auricle. This is patent or in open condition is the foetal life. In the fully matured and born foetus, the foramen ovale is closed and its place there is a deep fossa ovalis in the right artial side.

The right auricle thus contains both pure blood that comes from posterior vena cava and impure blood that comes from the anterior vena cava. Thus, right auricle contains mixed blood (99% pure blood). The pure blood from right auricle enters into the right ventricle and is pumped into the arterial system through pulmonary arteries, by passing lungs for oxygenation. The lungs are devoid of oxygen at this stage, as the foetus is in utero and is sealed from the external environment. Thus, nature has developed a system the pure blood that is in the pulmonary artery is connected to the aorta through a duct known as ductus arteriosus. When the foetus starts breathing, the duct is being closed and forms as ligamentum arteriosum.

The impure blood that comes from right ventricle may have access to the aorta as pulmonary artery is connected with aorta through ductus arteriosus. The heart develops from a S-shaped tube, with various bends. The adult aorta arises out of five pairs of left and right aortic arches, which are present at the beginning. The final aorta arises from the left ventricle. The foetal heart can function without oxygen for longer periods than adult heart because myocardial cells contain relatively large amounts of glycogen throughout-gestation.

Developmental anomalies

These following conditions are recorded in animals and human. Patency of foramen ovale, persistent interventricular foramina, patent ductus arteriosus, persistence of the right aortic arch, coarctation of the aorta, transposition of the aorta, congenital aneurysm of the aorta or pulmonary artery, failure of adequate development of semi lunar valves, valvular stenosis, dysplasia of the tricuspid valve, mitral valvular insufficiency, congenital haematomas, tetralogy of Fallot and endocardial fibroelastosis.

Patency of foramen ovale: Very soon after birth, the foramen ovale, a communication between the right and left auricle, will be closed and the venous blood will be coming into the right ventricle and will be diverted to the pulmonary circulation.

The foramen if it is persisting in the life is called persistent foramen ovale, resulting in mixing of arterial blood and venous blood. Due to circulation of venous blood to arterial side, the efficiency of the individual or animal will be decreased and is exhibited by tiredness and other symptoms of fatigue. In humans, the skin appears to be blue in colour due to the circulation of venous blood to the arterial side, resulting in blue baby condition. This is also known as atrial septal defect. This is compatible with life. Atria septal defects are tolerated well if they are less than 1 cm in diameter. Even larger defects do not constitute serious problems during the first years of life, when the low-pressure flow is from left to right. Persistency in the adult life creates overload in the right auricle, leading to dilatation and failure of heart in due course.

Persistent interventricular foramina: Early in embryonic life the ventricles consists of a single chamber, as in the evolution, the typical example is that of frog, which the student dissects, which eventually divides the ventricle by a septum into a right and a left one, by a growth of interventricular septum. Small openings connecting the two ventricles are of no significance. Large openings if they persist, the functional changes are noticed with this condition. Elevation of pressure in the ventricle and pulmonary artery and hypertrophy of right ventricle is seen. A systolic murmur is herd.

Patent ductus arteriosus: The ductus arteriosus is a channels of communication between the pulmonary artery of the foetus and the aorta. In the foetus, blood does not go to the lungs for oxygenation, and is routed through the ductus arteriosus from the pulmonary artery to the aorta. Within a few days after birth, the lumen of the ductus is closed and later on permanently is sealed.

Patent ductus arteriosus appears to have polygenic inheritance. In crossbred sheep, the author observed due to repeat in breeding by allowing the ram for 2 to 3 generations to sire ewes resulted in patent ductus arteriosus in lambs. When the inbreeding by particular rams had been discontinued, the next generation did not have anomaly of the problems of heart in lambs. In uncomplicated cases, the blood flow from the aorta to the pulmonary artery (left to right shunt) during both systole and diastole. In severe cases, the shunt is reversed, and flow from the pulmonary artery to aorta (right to left course) occurs. If the duct is of sufficient size, there is a volume overload on the left ventricle and a pressure overload on the right ventricle, resulting in compensatory hypertrophy of both. Histologically the media of ductus arteriosus, which is rich in smooth muscle, responds to epinephrine, nor epinephrine, angiotensin, prostaglandin E2 and keeps the ductus in dilated stage. In vivo, oxygen and acetylcholine are probably the most important in causing constriction of the duct.

Persistence of the right aortic arch: This is seen in dogs mainly and in bovine rarely. The oesophagus is encircled and constricted by the ductus arteriosus of the aorta leading to obstruction of oesophagus resulting in dysphagia and then to dilatation of oesophagus proximal to the obstruction. Puppies vomit immediately after taking food.

Coarctation of the aorta: This is narrowing of the lumen of the aorta, most commonly occurring close to the heart or between the origin of the common brachio-cephalic artery and in the ductus arteriosus. This leads to hypertrophy of the left ventricle, as there is hindrance to flow of blood.

Congenital aneurysm of the aorta or pulmonary artery: It denotes the dilatation of the respective vessels.

Failure of adequate development of semi lunar valves: Pulmonic stenosis is a condition where in the pulmonary valves become fused together resulting in

stenosis. Consequent to this, the right ventricle hypertrophies, a pericardial thrill, and harsh systolic murmurs are observed.

This is commonly seen in beagle dogs. There is genetic inheritance in acquiring this condition. The stenosis encompasses three anatomic variations, viz., and supravalvular, valvular and subvalvular or infundibular stenosis.

Valvular stenosis is probably due to the disordered fusion of the valve cushions and their failure to hollow out properly. The valve, which is thin and more or less dome shaped, with an irregular central perforation.

Sub-aortic stenosis: This condition is seen mostly in Alsatian and Boxer dogs. A ring of fibrous tissue immediately below the cusps of aortic valves causes stenosis. This results in hypertrophy of the left ventricle. Clinically, the dog exhibits poor condition, inability to exercise, frequent fainting, tachycardia, poor pulse volume, systolic murmur and cardiac dilatation. There is also evidence that the severity of the disease increases with age.

Dysplasia of the tricuspid valve: This is commonly observed in the cats. There is diffuse thickening of the leaflets, some of which may be absent or short chordia tendinae or papillary muscles, and direct fusion of the affected valves with the ventricular wall. Because of this, the valve is insufficient the right atrium is enlarged, and the right ventricle is eccentrically hypertrophied.

Mitral valvular insufficiency: This is commonly seen in aged cats, there is enlarged annulus, short thick leaflets, short thickened chordae tendinae, upward malformation aortic or hypertrophic papillary muscles, and enlargement of the left atrium and ventricle.

Congenital haematomas (haemocysts): These are present on the margins of the atrio-ventricular valves and are common in calves. These are blood-filled cysts lined by endothelium. These cysts are compatible with the life of the animal. These cysts measure up to 1.0 cm in diameter and are multiple, do not usually persist for more than a few months, but occasional one may enlarge and persist for an year or more, by the time the content is changed to serous fluid.

Tetrology of Fallot: Fallot, a French physician, described a congenital anomaly of heart characterized by four defects. In fact, there are three defects, viz., ventricular septal defect, pulmonic stenosis and in overriding of aorta or dextraposed aorta. These anomalies, accompany by compensatory hypertrophy of the right ventricles, constitute the tetrad.

Affected animals fatigue easily and are usually cyanotic and polycythaemic. This is compatible with life and the animal may die due to complications. Growth rate is usually retarded. The association of the three primary anomalies is the result of a defective development of the conotruncal septum.

Endocardial fibroelastosis: Diffuse endocardial thickening occur when any

chamber of the heart remains dilated for a prolonged period. Thus, one should differentiate the primary endocardial fibro-elastosis and the elastosis due to systemic infections. Primary endocardial fibro-elastosis is characterised by diffuse endocardial thickening by collagen and elastic fibers, and left ventricular hypertrophy and dilatation in the absence of any associated cardiac malformations. The endocardial fibrosis progressively involves Purkinjee fibers, which exhibit some degenerative changes.

Other defects like ectopia cordis, where the heart is found outside the thorax, usually in the neck region or in the abdominal cavity. Acardia where there is complete absence of the heart and diplocardia where there two hearts are incompatible with life. The moment foetus is born; it results in the death of the born foetus.

Diseases of pericardium

Non-inflammatory lesions of the pericardium: As already mentioned, the pericardial sac contains normal amounts of thin serous fluid. Any excess in the volume of the fluid is referred to as hydropericardim. In hydro pericardium, the serosal surface remain smooth and glistening, but if the fluid persists for a long time it may produce slight fibrous thickening and opacity of peri and epicardial surfaces. Hydro pericardium is seen in chronic diseases like congestive heart failure, renal disease, and chronic parasitic infections and in damage to the capillary endothelium that occurs in many infectious diseases due to toxins or anoxic conditions and in anemias. Liver insufficiency as seen in stasis of portal circulation, hypoproteinemia and general oedema as seen with mulberry heart disease in pigs and with tumours that are implanted on pericardium (metastases) and lymphogenous metastases to myocardium and with primary tumours like mesotheliomas of the heart, hydro pericardium occurs.

Haemopericardium: The term haemopericardium is limited to the accumulation of pure blood in the pericardial cavity. If the blood is clotted, it can be assumed that the process is a true haemopericardium. This condition is known as cardiac tamponade. The heart stops usually is diastole. The causes for haemopericardium include trauma, squeal to the direct intracardiac injections that is commonly adopted either in the humans or in animals, when there is tremendous loss of blood or fluid loss, where pulse cannot be perceptible. Blood collections in small animals including chicken, while disturbed during blood collections results in tearing of pericardium, which is rich in blood vessels with resultant haemopericardium. It is seen in horses, in which rupture of the intra-pericardial aorta occurs, in atrial rupture, in endocardiosis and in ulcerative uraemic endocarditis of dogs, following rupture of atrium in coronary artery or aorta. Rupture also occurs in the growing aneurysms of cardiac chamber. The author had seen several cases of rupture of the aorta, due to aneurysms following *Spirocerca lupi* infections in dogs resulting haemopericardium and death.

Pneumopericardium: This is a condition wherein putrefactive change occurs resulting in the gas accumulation. This is invariably due to anaerobic bacterial infections. These have entered into the pericardial sac with a penetrating body consequent to traumatic injury. Gas alsoescapes into the pericardium in traumatic reticulitis. In compound fracture of ribs, air will enter inside the chest cavity and into the pericardial sac.

Pyopericardium: Pus in the pericardium is mostly seen in traumatic pericarditis. It is also found in the tuberculosis infections, consequent to purulent pleuritis, purulent pneumonia due to secondary bacterial infections and due to rupture of myocardial abscesses.

Serous atrophy of pericardial fat: In wasting diseases, wherein the animal lost substantial body weight, serous atrophy of fat is seen. In these conditions, there is progressive mobilisation of depot fat, which accumulates around the heart. As the lipid, vacuoles are reduced in size, and re-replaced by proteinaceous fluid and is called as myxomatous degeneration. The fat depots are converted into grey coloured gelatinous masses. On squeezing the myxomatous tissue, abundant water will be oozed out.

Haemorrhages on the pericardium: Peticheal and eccyhomitc haemorrhages are common in shock, toxaemia and hypoxemia. Most common causes are the toxins of bacteria and viruses of the various diseases of animals. Purpural haemorrhages of horses is common condition in which petichae of the pericardium is common. These haemorrhages are also common sweet clover and cyanide poisoning.

Inflammatory conditions of the pericardium

1) Traumatic pericarditis (as pericardial layer is fully laid with vasculature any injury to the pericardium results in accumulation of blood in pericardial sac results in haemopericardium with resultant stoppage of heart is called as cardiac tamponade. 2) Fibrinous pericarditis also results in variety of infectious diseases like haemorrhagic septicaemia caused by *Pasteurella multocida* organisms in cattle and buffaloes, and in Mycoplasma infections in cattle in contagious bovine pleuropneumonia and in contagious caprine pleuropneumonia in goats, in coli-salmonella infections in poultry and in fresh cases of traumatic pericarditis cases in bovines. The fibrin layer appears to be white in colour and the pericardium will be attached to the adherent lungs so tightly, considerable manual force is to be applied to pull the heart from thoracic attachments. Cor-rugosum or roughness of the heart with thickened pericardial sac is common in these conditions. The adhesions of pericardium with epicardium, makes the myocardial contraction in a difficult manner, resulting in development of congestive heart failure and resultant stoppage of heart. This is also called as shaggy heart. The fibrin in fresh cases, if removed appears to be bread and butter pulling with fine strings in between the two layers.

Pyopericardium with resultant fibrinous pericarditis makes the heart to enlarge to such an extent it is really makes a bovine heart, Cor- bovinum.

In poultry white chalky deposits are found on the pericardium of heart in uric acid pericarditis.

Diseases due to heart musculature

Dilatation of the heart: Concentric or eccentric dilatation of the heart musculature is very common. If the lumens of the chambers are narrowed, it is called concentric hypertrophy and the hypertrophy accompanied by dilatation is called eccentric hypertrophy. Hypertrophy of the right side increases the width of the base, while the left sided hypertrophy increases the length of the heart. However, bilateral hypertrophy causes the heart to be rounder. The increased size of the cardiac muscle needs more nutrition, which may not be adequately supplied to every muscle fiber by the coronary vessels. Because of inadequate blood, supply metabolites formed in and around the fibers are not removed and so accumulate. Due to these factors, the muscle fibers get degenerated and in face of continued work of the heart under the circumstances that were originally responsible for the hypertrophy, atrophy of the muscle fibers results. Consequently, the compensatory heart fails and is not longer able to meet the demands and so decompensation of heart occurs and ultimately leading to heart failure. The left ventricle forms the tip of the heart. The left ventricular musculature is usually thickened, whereas the right ventricle musculature is thin. Dilatation of the heart as the name implies, this is pathological enlargementof one or more of the cardiac chambers, most frequently the right ventricle. The left ventricle because of its thick wall offers more resistance to the dilative force; the auricle expands less noticeably and less extensively because the absence of an intake valve prevents the development of any great internal pressure. Cardiac dilatation is recognised by a rounded bulging of one or both ventricles; the line from the auriculo-ventricular level to the apex, which normally is almost straight, assumes an outward curvature that is often very noticeable. Rarely a weakened sac like aneurysm develops. The author had seen several cases with traumatic pericarditis wherein the needle sticks to the heart musculature with resultant development of aneurysm.

Acute dilatation arises suddenly and leads to death in a few hours or a few days. It is usually the terminal breakdown, which brings the end in some of the acute febrile diseases. Chronic dilatation develops over a period of one or many months and is seen by hypertrophy of the musculature. This involves usually left ventricle.

The cause of cardiac hypertrophy may lie within the heart itself in the form of stenosis or insufficiency of the valve through which the ejected blood must pass or it may be found in leakage of valve through which the blood enters. In the valvular in sufficiency when functionally compensated, there is dilatation of the ventricle. The right ventricular hypertrophy occurs when there is obstructive

processes in the lungs such as fibrosis of lung parenchyma after the after math of pneumonic infections, as well fibrosis of lungs due to variety of infectious cases like tuberculosis as well due to pneumoconiosis like siderosis and byssinosis. This is also common in chronic alveolar emphysema that is commonly encountered in heaves in horses and in a variety of allergic conditions in cows and dogs. It may be due to pulmonary stenosis that occurs in sheep and cattle due to congenital anomalies. Hypertrophy of left ventricle results from aortic stenosis, and atrial hypertension is due to damaged kidney. Very great dilatation of the heart of man is called cor-bovinum. Dilatation leads to congestive heart failure. Large dilatation of heart is seen as cor- pulmonlae in human beings due to severe pneumonic cases, as well in cattle in brisket disease.

Myocardial exhaustion is often called as toxic myocarditis, or myocardial failure. This occurs in many infectious diseases as well in many poisoning cases. This is also seen in potassium, thiamine deficiency or vitamin E-selenium deficiencies in poultry and livestock.

Several degenerative changes are seen in the myocardium. Zenker's degeneration is seen consequent to typhoid infections in humans and consequent to foot and mouth disease infections in cattle especially in calves and consequent to vitamin E and selenium deficiency in calves and lambs. The dead muscle or myocardium appears as white in colour. Fatty infiltration of endocardium results speckled appearance to endocardium gives a tiger appearance, which is popularly called as thrush breast appearance. Histologically minute droplets of fat, detected with special stains are seen in muscle fibers.

Cardiac failure: Decompensation of the heart leads to heart failure. Failure of the heart of one side of the heart ultimately leads to strains to the other side.

The most common causes of the heart failure are hypertension in human beings, aortic valvular disease, mitral valvular disease in animals and human beings, congenital heart diseases in human beings, myocarditis, myocardial degenerations, adhesive pericarditis especially that arises due to traumatic and fibrinous pericarditis in animals, nephritis in dogs.

The right sided heart failure is mainly due to consequence of left sided heart failure. Congestion of the pulmonary vessels occurs consequent to left sided heart failure leads to right sided heart failure. Myocarditis, myocardial infarction and degeneration of heart muscles also lead to heart failure. Other causes to heat failure are increased resistance for the flow of blood in the lungs as seen in heaves in horses and chronic interstitial pneumonia or allergic penumonitis in cattle, constrictive pericarditis and hydro pericardium. Diseases of the heart that lead to failure are those that impose sustained pressure overload on one or both ventricles, impose sustained volume overload on one or both ventricles, depress or alter normal contractility of myocardial fibers or lead to loss or replacement of cardiac muscle and significantly alter the heart's normal rate and rhythm.

The contractile force of the heart can be modified by altering the end diastolic volume, which within certain limits results in an increase in stroke volume. It is a response to an increase work loading both physiologic and pathologic states. The consequent increased stretching of the myofibers increases contractile force. This is known as the Frank-Starling phenomenon. Continued stretch increases contractile force to a limit after which increased stretch will result in a decreased tension development. The limit in most species appears to be macromere length of 2.2 to 2.4 microns. The same phenomenon is seen in those disease states that produce an increase in diastolic work load on the heart, such as arteriovenous shunts, and in atrioventircular and semilunar valvular insufficiencies.

The physical consequences of dilatation are derived from the principle that the pressure developed by a particular level of wall of tension is inversely proportional to the radius of the chamber. As a chamber dilates, the expenditure of energy necessary to develop tension in the wall for the required development of intraventricular pressure is increased.

Acute volume overload of a chamber is expected to lead to dilatation; chronic volume overload is one stimulus to the development of cardiac hypertrophy. In the cardiac hypertrophy, there is increase in heart mass. Hypertrophy of myocardium is associated with reduced contractility of myocardial fibers. Concentric hypertrophy an increase in mass of ventricle without accompanying an increase in end diastolic volume, characterizes increased systolic loads such as aortic stenosis, pulmonic stenosis, and pulmonary hypertension in patent ductus arteriosus. An increase in diastolic load typically produced by atrioventircular or semilunar valvular insufficiency or by arteriovenous shunts, results in eccentric hypertrophy, which is defined as an increase in myocardial mass accompanied by an increased end-diastolic volume. In concentric hypertrophy, there is increased thickens other wall of the affected chamber and a remarkable increase in the size of the papillary muscles and the trabaculae carnie. Extreme hypertrophy of one chamber may encroach on the diastolic capacity of the opposite chamber. In eccentric hypertrophy and dilatation, the heart tends to be globose in shape and the wall usually thin. Papillary muscles are also attenuated.

Lesions: Liver: Shrunken and congested liver. Histologically Cardiac cirrhosis-Nut Meg appearance of liver, hepatic cells surrounding the central veins is necrosed and shows fatty degeneration.

Spleen: Spleenomegaly enlarged spleenic pulp. Haemorrhages may be present liberating haemosiderin. Metaplasia of reticular tissue to fibrous tissue leads to hardening of the organ.

Gastrointestinal tract: Due to congestion of the portal vessels, stomach and intestines may manifest venous stasis leading to digestive troubles and diarrhoea.

In right sided heart failure, the primary disturbance is damming back of blood in

the systemic and portal venous circulation, with consequent decreased flow of blood into the left auricle from the lungs. Anoxia that is caused thereby produces renal pathology in which there is retention of salt and water increasing the blood volume, leading to oedema. On horse and ox, oedema is seen subcutaneously, while in the dog, ascitis is manifested and pleurisy is seen in cat.

Infarction of heart is relatively uncommon. This condition is due to occlusion of the coronary artery by a thrombus, atheroma or arteriosclerosis. Rarely emboli arising from cardiac vegetations especially in swine may give rise to infarction. The sudden occlusion of a large artery may cause necrosis and death. However, gradual obstruction of smaller branches will cause atrophy and replacement fibrosis, which being weak, is a place for dilatation to occur. With this cardiac aneurysm develops.

Mulberry heart disease

Mulberry heart disease in pigs is a dietetic micro-angiopathy and is characterised by sudden death due to heart failure, hydro-pericardium and typical linear haemorrhages on heart giving it an appearance of a bunch of mulberries. This occurs in 3 to 4 month old pigs. Selenium and vitamin E deficiency has been attributed for this cause.

Furthermore, the disease is characterised by oedema and emphysema of lungs, hydro-pericardium, hydrothorax, ascites, hyperemia of gastrointestinal tract, malacic lesions of cerebral gyri. Histological changes in the myocardium is characterised by necrosis of heart musculature, hyperemia and inter-muscular changes.

Manchester wasting disease of cattle

(Synonyms: enteque seco, Pasteur disease, Naalehu, Calcinosis, Calcific arteriosclerosis)

The disease is characterised by progressive wasting, stiffness of fore legs and back and calcification of media of arteries, heart muscle, lungs (inter-alveolar septa) and kidneys (arterioles of cortex and medulla). The disease affects both sheep and cattle.

The affected animals waste away progressively; the joints of the limbs become stiff and fore limbs are often affected. As the disease advances, the animal is disinclined to move and stands with arched back for long periods. On exercise, animals appear to be distressed. Hypercalcemia is noticed.

This is usually attributed by taking plants or its leaves containing vitamin D_3 like principles. These plants belong to the species of *solanum malacoxylon, cisturn diufman, and Trisetum flavescens.*

Myocarditis

Inflammation of the myocardium is called myocarditis. However, myocarditis is common in many systemic diseases primary condition is rare. Myocarditis could be classified as non-suppurative and suppurative.

Non-suppurative myocarditis is found with haematogenous infections like septicaemias, toxaemias and bacteraemia.

In cattle: pasteurellosis, foot and mouth disease infections, tuberculous myocarditis as an extension from pleura and lungs.

In dogs: extension from valvulitis; extension of infections from streptococcus, coli forms, and leptospirosis.

In horses: Equine infections anaemia viral infections.

Suppurative myocarditis: This is found in pyaemia that occurs in mastitis, metritis and joint ill infections. The spread is by way of coronary arteries, direct extension from purulent pericarditis, endocarditis, pleura, lungs and bronchial lymph glands. Infection may also occur through a foreign body penetrating myocardium through the reticulum.

Histologically, the typical appearance of an abscess with neutrophilic infiltration. Healing may occur by organisation and formation. Squeal may be calcification of the lesions.

Parasites of myocardium:

1. Heart worms- stays in the right ventricles of dogs— *Dirofilaria immitis*
2. Heart musculature- *cysts of Sarcocystis tenella* and variety of Sarcocystis spp. Rainey's corpuscles or Meischer's tubules are found in the intermediate hosts like cattle, sheep, goat, buffaloes, and poultry and even in human beings. The main hosts are either a dog or cat, and here it leads a coccidian life cycle mainly infecting intestines. Oocysts that come out from faeces infect the intermediate hosts and form a type of replicating forms merozoites within the sarcocysts. Life cycle will be completed only in the definitive host like cats and dogs and these get infection by ingestion of these sarcocysts.
3. As pseudo cysts in a variety of organs like heart musculature, brain and other internal visceral organs- *Toxoplasma gondii*-Humans and variety of domestic animals act as intermediate hosts. If these cysts rupture, a focal myocarditis develops. The lesion consists of necrosed centre surrounded by inflammatory cells- neutrophils, histiocytes and lymphocytes. Sometimes, the necrosed tissue is calcified. Definite hosts are again cat. Toxoplasmosis infection is set in cats by ingestion of pseudo cysts from intermediate hosts. A coccidian type of life cycle takes place in the intestines, liberating oocysts in the faeces. Intermediate hosts get the infection by ingestion of oocysts from cat faeces. These oocysts develop in the intermediate hosts as pseudo cysts containing the infective merozoites.

4. As cysts or bladder worms in the musculature of heart and skeletal muscles of bovine- Cysticercus bovis-(measly beef) - bovines act as intermediate hosts for the tapeworms. When definite hosts like humans ingest these bladder worms, tapeworms of *Taenia saginata* develop in the intestines of humans who act as definitive hosts, for these bladder worms. Eggs of tapeworm are excreted in the faeces and infection of the intermediate hosts take place by ingestion of the contaminated material containing the fecal matter of humans.
5. As cysts of bladder worms- Cysticercus cellulose (measly pork) – present in the heart musculature and skeletal muscles of pigs, pigs act as intermediate host for the tapeworm of *Taenia solium*. The adult worm stays in the intestines of human beings and the eggs are excreted through faeces. On ingestion of contaminated human faeces, pigs get the infection and these bladder worms coming from eggs stay in the musculature of pigs and cause inflammatory response.
6. As cysts of bladder worm, *cysticerus ovis* are present in the heart musculature and skeletal musculature of sheep. The adult parasite is the tapeworm, *Taenia ovis* and stays in the intestines of dog and fox. Sheep gets the infection by ingestion of contaminated eggs through the contamination of faeces of dogs and foxes.
7. Hydatid cysts of *Echinococcus granulosus* stays in the heart musculature and in every part of the body including, liver, spleen, brain and cause pressure atrophy lesions. These cysts vary from lemon size to a basketball. These stay even in the endocardium. The adult host is the dog and these tape worms stay in the intestines of dog. The infective stage is the egg that contains hexacanth embryo. Intermediate hosts like cattle, sheep, goats and humans get the infection by ingestion of the eggs, through faecal contamination.

Endocarditis

Inflammation of the endocardium is common in animals. The valvular endocardium is commonly affected. From here, the inflammation extends to the mural endocardium. Among animals, swine and cattle are more frequently affected. Endocardium is a constant lesion seen in chronic septicaemic diseases, in which circulating bacteria infect the endocardium.

Species of the animal	Name of the bacteria that affects the Endocardium
Horse	*Streptococcusequi(strangles),Shigellaequirulis,Actinobacilus equili*
Cattle	*Corynebacterium, Pyogenes, Streptococci, Embolic bacteria that originating from traumatic reticulitis, suppurative metritis and mastitis.*
Dog	*Streptococcal infections that cause tonsillitis, gingivitis and pharyngitis. Leptospiral infections.*
Pig	*Erysipelothrix-rhusipathae, Corynebacterium-pygoenes, Streptococci.*

The valves are most often affected because these are exposed to the circulating bacteria and to the forces of blood during systole. Bacteria that are present in the blood are implanted on the valvular endocardium. The surface of the valve that has been facing the force of valve is affected mostly. The auricular surface is usually affected because of the force the auricle is contracting and letting out the blood into the ventricle. Besides, it is the edge of the valves, which are most exposed to stress and trauma and so are more often affected. The implanted organisms grow on the injured endocardium. The toxic metabolic materials released by these bacteria damage the local cells, with the liberation of thrmoboplastin, which converts fibrinogen into fibrin. Fibrin is a good medium for the bacteria to grow and so more and more of fibrin is formed due tdiberation of greater quantities of thrmoboplastin by the cells that are increasingly destroyed by the growing organisms. Thus, a thrombus is formed. The enlarged valve with the thrombus injures the adjacent surface during the movement and during this motion; the thrombi may break off and form emboli.

The lesion being chronic, the thrombus is formed slowly but progressively. This is friable, resembles the head of cauliflower, and so is called vegetation. Endocarditis in which these vegetations are present is called vegetative endocarditis. From the basal areas of the valve granulation tissue invade the thrombus, which is thus organized in the deeper layer. However, so long as the organism is alive, complete organisation and healing is not possible.

In swine, excessive vegetations are common. However, in cattle due to *Corynebacterium, pyogenes* excessive fibrin is not common but fibrosis is frequently seen. Extension of infection from the tricuspid and bicuspid valves do the chordae tendinae makes them weak and degenerated, resulting in their rupture. Mural endocarditis is only an extension of the inflammatory process from the valves. In cattle infected with black quarter, the wall of the left auricle is usually affected showing roughened endothelium. In dogs with uremia and leptospspirosis, ulcerative endocarditis is common. Greenish ulcers are present in the left auricle and ventricle, pulmonary artery and aorta.

Histologically, the lesion is a thrombus in the centre of which bacteria are seen. Leukocytes are present in the intima. In chronic cases, fibrosis and the features of granulomatous lesions with capillary abundance is present.

Effects of endocarditis: The vegetations are formed at the point of contact of the cusps of the valve and prevent theclosure of the valves. These obstruct the lumen, thereby hindering free passage of blood through the lumen. These conditions thus give rise to valvular insufficiency or stenosis. The effect of these conditions is to cause accumulation of blood in the chambers just preceding the lesion.

With tricuspid valve involvement dilatation of the right auricle, general venous congestion and hypertrophy of the right auricle occurs. If pulmonary valves are

involved dilatation of the right ventricle, chronic general venous congestion and hypertrophy of the right ventricle occurs.

If mitral valves are involved dilatation of the left auricle, pulmonary congestion, oedema with resultant pneumonia, hypertrophy of the left auricle, hypertrophy of the right ventricle.

If the aortic semi-lunar valves are affected dilatation of the left ventricle, results. This leads to hypertrophy and later general venous congestion results. The final outcome of the lesion is heart failure.Fragments of the thrombus may be detached to form emboli. If the emboli are contaminated with pyogenic organisms, abscesses will be found in the kidneys, spleen and liver; pulmonary abscesses occur from emboli arising from the right auricuoventircular vegetations and myocardial abscesses from emboli from coronary vessels. If the embolus is bland and sterile, infarction will be caused in kidney and spleen. Emboli arising from the right auriculo-ventricular vegetations cause pulmonary thrombosis and from left side myocardial infarction occurs if emboli enters coronary circulation.

Endothelial cell properties and functions: Vascular endothelial cells, as well as forming the thrombo-resistant monolayer lining of the vascular system, mechanically insulate the circulating blood volume from the highly thrombogenic sub-endothelial materials. The thrombo resistance of the endothelium is normally maintained by a balance between anti-thrombotic and thrombotic factors.

Endothelial cell properties and functions:

1) Maintenance of permeability barrier
2) Elaboration of anticoagulant and antithrombotic molecules: Prostacycline, thrombomodulin, plasminogen activator, heparin-like molecules, adenosine production
3) Elaboration of prothrombotic molecules:Von-Wile brand factor (factor VIIIa), tissue factor, plasminogen activator, collagen, fibronectin
4) Modulation of blood flow and vascular reactivity: Endothelium derived relaxation factor, nitric oxide, endothelium derived hyperpolarisation factor, endothelium derived contraction factors, endothelium, angiotensin-derived contraction factor, prostacyclin, peptidoleukotriene
5) Regulation of inflammation and immunity: Interleukin-1, and adhesion molecules
6) Extra-cellular matrix production
7) Regulation of cell growth: Growth stimulators: Platelet derived growth factor, colony stimulating factor, and fibroblast growth factor. Growth inhibitors: heparin, transforming growth factor.

The thrombo resistance of endothelium is normally maintained by a balance between anti-thrombotic and thrombotic factors. Stimulation of excessive pro-

thrombin can lead to clotting and thrombosis, whereas excessive anti-thrombotic factors lead to ineffective-haemostasis, and bleeding. Anti-thrombotic factors is normally accomplished through binding and inhibition of thrombin via activation by thrombo-modulin of protein C and protein S via accentuation of antithormbin-III activity by heparin like molecules, and via the presence of β2 macroglobulin, inhibition of platelet aggregation through elaboration of prostacyclin (PHI2), a potent inhibitor of platelet aggregation and vasodilator, and by Adpase-mediated conversion of pro-aggregating ADP to adenine nucleotide platelet inhibitors; and promotion of fibrinolysis by synthesis of tissue plasminogen activators. Procoagulation activities include, the presence of minute amounts of tissue thrmoboplastin in endothelial cells, further production of which can be stimulated by endotoxin and by cytokines such as interleukin-1, and tumor necrosis factor, synthesis and secretion of von Wile brand factor needed for adherence of platelets to sub endothelial components, and secretion of platelet activating factor, an activator and aggregator of platelets, and inhibition of fibrinolysis through release of plasminogen activator inhibitors.

In addition to their role in haemostasis, endothelial cells participate in modulation of blood flow and vascular reactivity by production of endothelium derived relaxing factor (nitric oxide), endothelin, a vasoconstrictor, angiotensin converting enzyme, which converts angiotensins I to angiotensin II and prostacyclin. Endothelial cells modulate the action of various vasoconstrictors (catecholamines, serotonin, arginine, vasopressin) and vasodilators (histamine, leukotrienes, adenine nucleotides), and in concert with the endothelium derived factors can thereby allow blood vessels to rapidly adapt to changes in haemo-dynamic conditions.

Endothelial cells aid in the regulation of inflammation and immunity through production of interleukin-1, and various adhesion molecules. These moderate adhesion and hence emigration of leukocytes. Endothelial cells also aid in regulation of cell growth by production of growth stimulators (platelet derived growth factors, colony stimulating factor and fibroblast growth factor), and production of growth inhibitors (heparin, transforming growth factor). Endothelial cells produce basement membrane, and are capable of contraction. The endothelium is a semi permeable membrane, which can also transport metabolites including proteins through the cytoplasm via pinocytotic vesicles.

Sub-endothelial connective tissues consist of various types of collagen, elastin, glycosamino-glycans, fibronectin, laminin, and thrombospondin. Of these fibrillar collagen is the most potent stimulus for platelets adhesion and activation. Collagen also activates the intrinsic pathway of coagulation. Fibronectin or molecular glue, normally function to stabilize cell to cell and cell to substrate attachment, but also become cross linked to fibrin and helps to anchor hameostatic plugs.

Mild endothelial injury, as occurs in the course of inflammation, may be apparent

histologically as hypertrophy of endothelialcells, reactive cells. Increased vascular in inflammation leads to transudation of plasma proteins, including fibrinogens with H& E sections forms as vascular hyalinosis like appearance. Necrosis of endothelium, which maybe caused by a wide variety of agents, leads to exposure of sub-endothelial collagen, a potent inducer of coagulation and platelet aggregation and hence thrombosis. Severe micro vascular damage, as occurs because of lipo-peroxidation of endothelial membranes in vitamin E-selenium deficiency in pigs, can result in hemorrhage and organ failure.

Vascular smooth muscle cells are important both as effectors of vasoconstriction and dilation, and as cells capable of synthesizing basement membrane, collagen, elastin, and proteolglycans of the extracellular space. In response to growth factors derived from platelets and monocytes, macrophages, smooth muscle cells, of the media migrate through fenestrae of the internal elastic lamina to the sub-endothelial area where as myointimal cells; they proliferate and are responsible for organisation of collagenisation of deposits including thrombi. Along with other components of the vessel wall, smooth muscle cells may be involved in degenerative and inflammatory changes.

Arteriosclerosis: Arteriosclerosis means hardening of arteries. In this condition, there is thickening of the walls and narrowing of the lumina of small arteries and arterioles. This condition is characterised by intimal thickening, following proliferation of connective tissue, hyaline degeneration, infiltration of lipoids and fatty calcification (Atherosclerosis).

Two types are recognised, hyaline arteriosclerosis and hyperplasic arteriosclerosis. In human beings, these results due to hypertension but in animals in certain viral diseases and autoimmune diseases, these types of changes are observed.

Hyaline arterio-sclerosis occurs in a slowly developing hypertension while the hyperplasic variety is seen in more acute conditions (essential hypertension), developing due to sudden elevation of blood pressure.

In hyaline arteriosclerosis, which is seen in essential hypertension in human beings, there is homogenous pink collagenous fibrous tissue and thickening of the walls of the arterioles. The cellular details of these arteries are completely lost. In hyperplasic arteriosclerosis, an onion skin appearance is found due to proliferation of smooth muscle cells around the endothelial cells, sub-intimal fibrosis. It is common in human beings and with this, small arterioles and their smooth muscles show proliferation. The arteries of kidney, spleen, pancreas, adrenal and intestines are affected.

Atherosclerosis: This is thickening of large elastic arteries. Athere means in Greek a soft, mushy gruel like substance, is adhering to the intima and thereby causing thickening of the intima and the arteries themselves.

The aorta and primary branches are affected. Cerebral and coronary branches are much more affected.

Animals could be categorised as atherosensitive and atheroresistant animals. Human is an atherosensitive species. Rabbit, chicken and pigs are atherosensitive species. Dogs, cats, cattle, goats and rats are atheroresistant species.

Variety of causes in human beings has been attributed. Senility or ageing process, in which there is progressive degeneration of the walls of arteries leading to fatty degeneration of tissue in which lipids accumulate, high blood cholesterol and lipid contents, hypertension, intramural haemorrhages, endocrine deficiency, heredity, obesity, stress, physical activity and smoking habits may be contributory factors.

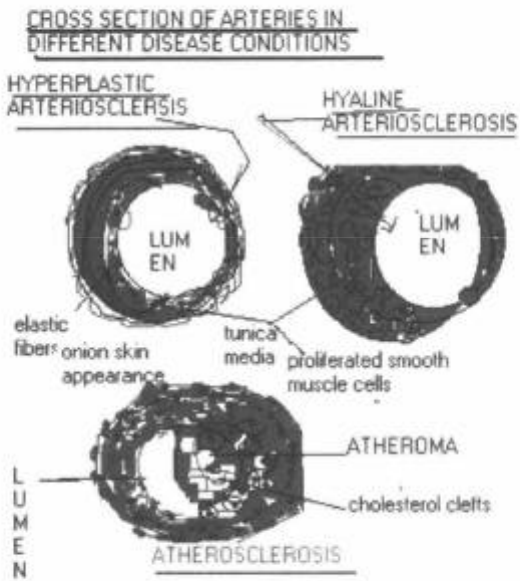
Pathogenesis: The lesion commences as a focal degenerative change in the sub endothelial tissue. The mucinous ground substance of the intima is increased and in these foci fine fat droplets appears. These fatty deposits consist of cholesterol, neutral fats, fatty acids and cholesterol ester. Elastic fibers disintegrate.

In atherosclerosis, reactive O_2 intermediates such as super oxide anion or H_2O_2 may lead to lipid per oxidation. Per oxidation of cell membrane, lipids may alter membrane function or induce injury, where oxidative modification of lipoproteins leads to thrombus formation.

Foam cells that macrophages filed with lipids are found in the atheromatous foci in the intima. These macrophages cluster in the sub endothelial area. Subsequently macrophages die, disintegrate and liberates the fats into the tissue spaces. The fats. i.e., cholesterol crystals stimulate the proliferation of the connective tissue around these foci, especially towards the luminal side. This is a plaque with a central debris consists of granular lipoid rich material and crystals of cholesterol. Haemorrhages and haemosiderin granules are also seen.

A well-formed plaque is supplied with numerous capillaries, whichare the source of haemorrhage. A few lymphocytes may be found around the lesion. This stimulates fibrous tissue proliferation and with further deposition of lipids, atheroma enlarges in size and reaches the endothelial layer, which may be pushed inside the lumen. Along with the changes in the intima, degenerative changes are also noticed in the media. Oedema occurs separating the muscles and the elastic fibres. In these foci, fibrosis occurs and the elastic fibers degenerate.

The fate of atheromatous plaque is important. It may be converted into a dense inflammatory scar containing cholesterol clefts, or it may be calcified, or islands of heterotopic bone may be formed, or thin endothelium may be necrosed due to subendothelial accumulation in formation of ulcer. A thrombus may form subsequently on the ulcer.



Activated macrophages present in the plaque site synthesise many neutral and acid hydrolases, which may modify the components of arterial walls. They also secrete a mitogen, macrophage derived growth factor which may regulate smooth muscle cells and endothelial cell proliferation. It is of little practical importance in domestic animals, but is primarily of interest for the development of animal models of the human disease. The atherosclerotic susceptibility of animals varies; rabbit's chickens and pigs are atherosenstive, whereas dogs, cats, cattle, goats and rats are atheroresistant.

In human beings, atherosclerosis and its complications of myocardial infarction, stroke, and peripheral vascular disease are major causes of morbidity and mortality in the world. Atherosclerosis affects large elastic arteries. (aorta and iliac) the essential lesion is the atheroma or fibro fatty plaque, which is a focal raised intimal plaque with a core of lipid and contains cholesterol and its esters largely covered by a fibrous cap. Complications of plaque include mienralisation, ulceration, superimposed thrombosis, intraplaque hemorrhage age, and aneuyrismal dialtation. The streaks which are soft, smooth, nonelevated lesions ranging from pinpoint size to several square centimeters, are rarely visible grossly unless the aorta is stained with fatal stain such as sudan IV, which stains the lesions as birght orange. Mulitple pathogenesis influences can contribute to the development of plaques. The various theories influence the injury hypothesis. Endothelial injury or dysfunction occurs as a result of hyperlipedemia with cholesterol present in low density and very low density lipoproteins seen as primary culprit. Additional risk factors are hypertension, smoking, obesity, inactivity, and diabetes mellitus.

Immunological mechanisms toxins and viruses are also damage endothelium. endothelial cells injury leads to platelet adhesion, monocyte adhesion and proliferation of endothelial cells. The lipid laden foam cells that are characteristic of both fatty streaks and atheromatous plaques may be either altered macrophages or smooth muscle cells; macrophages predominate in streaks, whereas smooth muscle cells predominate in fibrous cup plaques. Endothelia cell dysfunction is emerging as an endocrinopathy that may contribute to the effects atherosclerosis through impaired ability of endothelial cells to produce endothelial derived relaxing factor and through increased production of endothelin.

Atherosclerosis develops commonly only in pigs among domestic animals. Fatty streaks, and atheromatous plaques develop in aorta, extramural coronary arteries, cerebral and iliac arteries as in humans and the plaques cause considerable stenos is of vessels in swine 8 to 12 years old. The extent of lipid deposition can be influenced by feeding extraordinary diets containing much lipid including cholesterol but the atheromas reach rarely the degree of development seen in humans and they do not lead to occlusive thrombus formation. This apparently requires softening and ulceration of atheromatous plaques. The initial deposits occurs in the proliferated smooth muscle cells which show signs of degeneration and which may become foam cells. Macrophages also appear containing lipid and far may be demonstrable extra cellular presumably released by degenerated cells. Deposits of cholesterol and mineral may be associated with softening of larger atheromatous plaques.

Of the domestic animals, the deposition of cholesterol occurs in dogs alone. This is always associated with hypothyroidism or diabetes mellitus. The deposition of lipids begins in the middle and outer layers of the media and occurs more extensive. If present aortic lesions occur as intimal plaques. The veins are normal. The media may be greatly increased in thickness by the accumulation of lipid most of which is in foam cells, but some is present in identifiable muscle cells of the media or freeing the interstitium as droplets or crystals. The deposition of lipid in the internal layers of the media leads to disruption of the internal elastic lamina and involvement of the intima. The amount of lipid deposited is very great and lead to eccentric enlargement of the vessel. Associated with lipidosis, there is progressive proliferation of connective tissue. The connective tissue become hyaline and relatively acellular and may be heavily impregnated with slats of calcium and iron.

The morphology of atherosclerosis differs in dogs and in humans; lipid is present in the intima but primarily in the media and adventetitia of atherosclerotic canine arteries, but is present primarily in the intima in humans.

Arteriosclerosis describes a heterogeneous group of arteriolar lesions that maybe predominantly hyaline or predominantly hyperplasic. The major causes of these changes in vessels in humans in hypertension but the pathogenesis of the lesions

in domestic animals is often not understood.

Systemic hypertension or persistently elevated systemic blood pressure is an important disease of humans and occurs as primary or essential hypertension and secondary hypertension. Hypertension is self perpetuating as medial hypertrophy and hyalinization of renal arteries lead to more nephrosclerosis, more hypertension and more pressure induced vascular damage.

Hypertension which would be classed as secondary is said to occur in more than 60% of dogs with chronic renal disease and may also occur in association with pheochromocytoma, hyperadrenocorticism, hypo and hyper thyroidism and diabetes mellitus.

The arterial lesions of acute renal insufficiency consist of sub-endothelial deposition of fibrin, disruption of the internal elastic lamina necrosis of medial smooth muscle mineralization, and sometimes a neutrophilic reaction. These lesions may be segmental or circumferential in l in the vessel wall. This arterial reaction is primary degenerative and resembles to hyaline arteriosclerosis. In chronic renal lesions the changes are more to the medial hypertrophy and adventitial fibrosis produce thickening and whirling of renal interlobular and intralobular arteries and resembles to the human hyperplasic arteriosclerosis.

Monckberg's medial sclerosis: This is usually seen in human beings. Genetic and racial tendency is there. In this condition, the medium sized muscular arteries are affected. The muscular tissue undergoes hyaline and fatty degeneration followed by necrosis and calcification. The disorder is related to prolonged vasotonic influences due to epinephrine and nicotine. Hypervitaminosis D also produces this type of lesions. This has seen in Manchester wasting disease of cattle and in dogs with chronic interstitial nephritis.

Arthritis: Inflammation of the wall of the arteries is called arthritis. This may be an acute or chronic arteritis.

Acute arteritis is caused by parasites, bacteria, viruses or fungi. The route of infections is from the outside of the vessel, extending through the wall or through the vasa vasorum or through the lumen of the vessel. Extension of inflammation from adjacent tissues is common as seen in pneumonia, metritis and mastitis. Infection may also occur due to pyogenic bacteria. In such cases, pulmonary vessels are the favored places where emboli lodge and produce inflammation. Inflammation of the intima results in the production of a thrombus at the site resulting in thromboendarteritis.

Arteritis may be further classified as periarteritis or polyarteritis depending on the distribution of inflammatory cells.

Equine viral arteritis is a primary viral arteritis and is due to a RNA viral infection. Grossly petichaeal haemorrhages are seen in all the serous membranes, in the

lungs and on gastric mucosa. Histologically the lesions are found on the media of small arteries, where degenerative changes of smooth muscles with accumulation of fibrinoid material and infiltration of adventetia with fibrinous and inflammatory cells predominantly of lymphocytes.

Chronic arteritis is seen with invasion of larvae of Strongylus vulgaris. The artery is dilated fibrosed and the wall loses its silency resulting in aneurysm formation. The intimal surface is roughened where a thrombus forms. Sometimes these aneurysms ruptures results in fatal rupture.

Polyartertitis nodosa (Periarteritis nodosa) there is inflammation involving all the layers of the arterial wall. Immunologicla mechanisms involving, type II, III hypersensitivity reactions have been attributed for this. Variety of viral antigens, bacterial antigens, drugs and certain chemicals are responsible in inducing inflammatory response consequent to this, the inflammatory cells are present in different layers of the blood vessels.

The term heart failure denotes a situation in which the heart is diseased all compensatory mechanisms have been exhausted, and characteristic clinical and pathological sings are present. Circulatory failure or shock, is a term used to describe a state which may or may not be the result of the heart failure. Diseases of the heart that lead to failure are those that impose sustained pressure overload on one or both ventricles, impose sustained volume overload on one or both ventricles, depress or alter normal contractility of myocardial fibers or lead to loss or replacement of cardiac muscle and significantly alter the heart's normal rate and rhythm.

The contractile force of the heart can be modified by altering the end diastolic volume, which within certain limits results in an increase in stroke volume. It is a response to an increase work load in both physiologic and pathologic states. The consequent increased stretching of the myofibers increases contractile force. This is known as the Frank-Starling phenomenon. Continued stretach increases contractile force to a limit after which increased stretch will result in a decreased tension development. The limit in most species appears to be sarcomere length of 2.2 to 2.4 μ. The same phenomenon is seen in those disease states that produce an increase in diastolic work load on the heart, such as arteriovenous shunts, and in atrioventircular and semilunar valvular insufficiencies.

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Acute volume overload of a chamber is expected to lead to dialtation, chronic volume overload is one stimulus to the development of cardiac hypertrophy. In

the cardiac hypertrophy there is increase in heart mass. Hypertraphy of myocardium is associated with reduced contractility of myocardial fibers. Concentric hypertrophy an increase in mass of ventrile without accompanying an increase in end diastolic volume, characterises increased systolic loads such as aortic stenosis, pulmoni stenosis, and pulmonary hypertension in patent ductus arteriosus. An increase in diastolic load typically produced by atrioventircular or semilunar valvular in sufficients or by arteriovenous shunts, results in eccentric hypertrophy, which is defined as an increase in myocardial mass accompanied by an increased end-diastolic voume. In concentric hypertophy there is increased thickness of the wall of three affected chamber and a remarkable increase in the size of the paillary muscles and the trabaculae carneae. Extreme hypertrophy of one chamber may encroach on the diastolic capacity of the opposite chamber. In eccentrichypertrophy and dilatation, the heart tends to be globose in shape and the wall usually thin. Papillary msucles are also attenuated.

The extracardiac clinical signs and gross and microscopic feature of heart failure stem from two basic pathophysiologic changes, the accumulatin of fluid and tissue or organ ischemia. The sodium and water accumulation primarily involves the kidneys. It also involves the hormone, atrial natriuretic factor, released from heart. The influence of the fialing heart on the kidney stems from its inability to supply them with adequate flow of blood.

The kidney receive approximately 20% of the output of the left ventricle, almost all of which flows through the renal cortices. One of the earliest change following a drop in cardiac output is a redistribution of blood flow within the kidney.There is reduced flow through the outer renal cortex and an increased flow within the outer renal medulla. This results in a readjustment of the fitati factor. As a consequence there is more sodium moves through the glomerual a filter, leading to proportion more sodium being delivered on the proximal convoluted tubules. Because the rate of sodium resorption remains constant, a greater number of sodium ions are reabsorbed. The incrased blood flow seen in heart failure also increase the activity of reninangiotensin-aldosterone system, producing more sodium resorption from the distal convoluted tubules. There is also evidence for increased activity for the water retaining activity of anti-diuretic hormone. The expansion of blood volume has both a beneficial and a detrimental effect. By increasing blood volume venous return is enhanced and in turn cardiac output is improved. However, this is to the detirement of the balance between capillary hydrostatic pressure and plasma osmotic pressure. This leads to an increase into the amount of fluid in the interstital space and body cavities.

Aneurysms

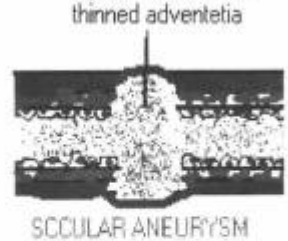
An aneurysm is a localized dilatation of an artery, vein or cardiac chamber. The main factor involved in the causation of the aneurysm is weakening of the wall. The weakening arises due to the damage to the media. The various causes that

weaken the wall are infected bacterial embolus that causes suppuration and destruction of the media, trauma, parasites, and congenital weakness of the walls. Rupture of artery as a result of physical trauma is common. The aortic lesions produced by *Spirocerca lupi* in dogs occasionally lead to rupture. Rupture of uterine artery is a cause of fatal haemorrhage in aged mares at parturition, mycotic ulceration of the internal carotid artery or maxillary artery in horses can lead to fatal guttural pouch hemorrhage. Rupture of internal iliac artery with weakened strongylus vulgaris parasites larvae.

On the basis of their gross appearance aneurysms may be classified as berry, saccular, fusiform, or dissecting. Aneurysms may also be true or false. True aneurysms are composed of all, or most, of the layers of the vessel wall. Dilatation of the cranial mesentric artery occur in the course of verminous enteritis I horses, the arterial wall is often greatly thickened. False aneurysm results from rupture of the artery or aneurysm and are essentially haematomas communicating with an arterial lumen; their walls are formed by the surrounding fibrous tissue.

A fusiform aneurysm is one in which a long segment of the vessel is uniformly dilated around the whole circumference. This is mostly seen in aorta and its branches. Saccular aneurysm is the formation of a pouch on one side of the wall. Dissecting aneurysm strictly speaking is not a true aneurysm since there is not dilatation of the wall. In the aorta, a hemorrhage occurs between the layers of media and blood circulates around within this space, dissecting the wall. Fatal hemorrhages may supervene. The condition is due to a degenerative lesion in the media. Cirsoid aneurysm is a mass of dilated, pulsating and intercommunicating arteries and veins usually subcutaneous in location and most are congenital and a few maybe due to trauma. Arteriovenous aneurysms are abnormal acquired between an artery and a vein due to simultaneous injury to both. There is pulsation in the vein since blood passes directly into it. Mycotic aneurysms are due to infection by bacteria which weaken the wall and small aneurysms developing thereby. This is usually associated with vegetative endocarditis. Miliary aneurysms are aneurysms of small arteries and are seen in cranium known as berry aneurysm. This is a small saccualr dilatation. Parasitic aneurysm is occurring in horses with the anterior mesenteric artery infection by strongylus vulgaris.

The squeal of aneurysms are pressure atrophy of the structures around an expanding aneurysm, rupture of aneurysm leads to fatal results, in the horse colic is common with aneurysm of anterior mesenteric artery, inflammation from the anterior mesenteric artery may spread to the neighboring autonomic ganglia causing intestinal stasis resulting in colic.



Thrombangitis obliterans or Buerger's disease: This is seen in human beings especially in Jewish population affecting mostly the femoral arteries of legs wherein thrombosis of the vessels are seen. There is acute inflammatory reaction involving all the layers of the arteries, results in inflammatory thrombosis. Organization of thrombus and subsequent canalization also may occur.

Vasculitis: Vasculitis denotes inflammation of vessels and is characterized by the presence of inflammatory cells within and around blood vessel walls, with concomitant vessel wall damage, as indicated by fibrin deposition and necrosis of endothelilal and smooth muscles.

Causes of vasculitis: Infections:

Viral: Equine viral arteritis, Equine infectious anaemia, African Horse Sickness in horses; Bovine ephemeral fever, Rinderpest in cattle; Blue tongue, Maedi-Visna in sheep: Hog cholera in pigs, Ranikhet disease and IBD and Marek's diseases in poultry.

Chlaymidal infections: sporadic bovine encephalomyelitis in bovines and chlamydiosis of poultry.

Rickettsial infections *like Ehrilichia canis* in dogs.

Bacterial infections like *Salmonella spp, Erysipelothrix, Haemophilus, Actinobacillus, Corynebacterium pseudotuberculosis,* Pateurella *hameolytic, and Mycoplasma gallisepticum* in domestic animals.

Mycoitc infections like *Mucormycosis, Aspergillus fumigatus, Histoplasma farciminousm* and *Sporothrix infections.*

Protozoal infections like Babesiosis, theilerosis in bovines and encephilotozoon cuniculi in rabbits. Helminthes with their migrating larvae cause vasculitis changes in animals. These are strongylus vulgaris, Dirofilaria immitis, Spirocerca lupi, Onchoerca spp, schistosoma spp. Vasculitis is also caused by non infections like immune mediated disease that occur in systemic infections, staphylococcal hypersensitivity, serum sickness reactions, all hypersensitive reactions of type II and III with foreign proteins.

Non-immune mediated infections due to uremia conditions in animals especially in dogs.

Diseases of veins

Veins are termed small, medium, or large or alternately, as venules, collecting veins and great veins; all have large lumina in relation to their wall thickness. Classification of veins by wall characteristic is difficult because the layers in their walls may be absent or difficult to distinguish. Venules of greater than 30 μ diameter have an incomplete muscular media and thin adventitia. Venular endothelium is normally more permeable than that of capillaries and is also more

sensitive to vasoactive amines the action of which can cause leakage. In the lymph node paracortex, postcapiallary venules, which are non muscular venules with prominent endothelium, are important sites of lymphocytic traffic. The media of increasing thickness in medium and large veins, whereas the media predominates in arteries. Back flow of blood in veins is prevented by the presence of semilunar valves, which are invagination of the intima into the venous lumen. Venous valves are not present in vane cavae or hepatic portal vein. Paucity of valves in veins of the head and face may contribute to incidental venous congestion in these areas and to retrograde spread of infection.

Phlebitis is the inflammation of the veins and is usually septic in character. Phlebitis is seen in animal in the following conditions.

In the new born animals, umbilicus is usually infected resulting in omphalophhlebitis. The usual organism is *Shiglela equirulis* in the foals and *coliforms* in the calves. The infection also extends from the adjacent inflammed area. This is common in lungs in pneumonic cases and metritis cases with uterus and mastitis cases with udder infections. Infection passes through the thin walled veins more easily than through the thicker arterial walls.

Infection occurs through vene puncture. During intravenous injections, if irritant chemicals are injected inadvertantly outside the vein, periphelbitis and phlebitis will be set up. Foreign bodies as seen in traumatic reticulitis and foreign bodies are also cause chronic phlebitis of the veins involved.

Grossly the inflammed vein is enlarged, has a thickened wall with neutrophilic infiltration. Usually thrombosis develops causing thrombo-phlebitis. Infected thrombi will get softened and disintegrated and thus septic emboli may be formed. A bland thrombus may become organized. Sometimes the thrombus gets calcified and is called as phlebolith. The importance of phlebitis lies in the damage of thrombosis with eventual emboli formation, causing pulmonary embolism, pyaemia, septicemia or septic arthritis.

Sundry disease conditions of veins: Varicose veins: Varicose veins are dilated and tortuous veins. These are not common as in animals as in man. In animals, it is seen with supra-mammary veins of udderin cows as well scrotal veins in bulls. In humans, leg veins and as well veins of anal region (haemorrhoids) are most commonly affected. Stagnation of blood in the dilated vessels causes pain.

The exciting causes are those of increase in the pressure of blood in the veins and these are found in these following conditions. Whenever there is hindrance to the return of venous blood as seen in mitral stenosis, pulmonary emphysema and cirrhosis of liver. Pressure on veins by tumors, pregnant uterus, increased abdominal pressure as in straining. Standing for a long time and other causes like muscular exertion as seen in athletes, ageing, post- inflammatory weakness of the vessel wall.

Diseases of lymph vessels:

Lymphangitis: Inflammation of lymph vessels.

Lymph adenitis: Inflammation of lymph glands.

Except in poultry all domestic animals have well developed lymphatic system. Lymphatic capillaries originate in loose connective tissue and consist of very permeable walls and endothelial cells which may lack, or have discontinuous, basal lamina. In larger lymphatics, valves are present, the basal lamina is continuous, and walls consist of three ill-defined layers, an internal elastic lamina is usually absent. The thin walled veins and lymphatic are more susceptible to compression and occlusion, are more often involved by inflammation in adjacent tissue, and are more liable to neoplastic, invasion than are the thicker walled arteries.

Lymph edema is defined as swelling of a part of the body by an increased quantity of lymph due to a lymphatic system disorder. Lymph edema may be classified as primary or secondary. Primary lymph edema is usually congenital, and maybe hereditary due to anomalous development of the lymphatic system. Secondary lymph-edema occurs because of obstruction of previous normal lymphatics due to inflammation neoplasia, surgery, or trauma. Lymhoedema is of significance because may predispose the affected area, usually limb, to secondary bacterial infection and poor wound healing. Prolonged lymph edema leads to fibrosis as seen in elephantiasis cases with human beings in *Wucheria Bancroft*, microfilaria larval infections.

Dilatation of normally developed lymphatic vessels (lymphangiectasis) almost invariably results from some of obstruction and leads to the accumulation of excess interstitial fluid in the drainage area. Causes of such lymphatic obstruction include infiltrating neoplasm, inflammatory thrombosis, and post surgical scarring.

Intestinal lymphangiectasia is the most common cause of protein losing enteorpathy in dogs, John's disease of cows. Dilated lacteals in intestinal villi rupture or leak the contents into intestinal lumen and severe hypoproteinemia results.

Chylothorax is the result of leakage or rupture of the thoracic duct occurs infrequently in dogs and cats.

Chylous ascites results from rupture of the cisterna chili.

Lymphangitis is seen in bone farcy a chronic granulomatous disease of cattle in the tropics caused by Nocardia farcinica or due to Mycobacterium smegmatense.

Sporadic lymphangitis causing hind legs of horses caused by Malleomyces mallei or cutaneous glanders of horses.

Ulcerative lyamahgntis is a chronic progressive inflammation of the subcutaneous lymphatics of horses. The causative agent's the *Corynebacterium pseudotuberculosis*

(ovis is the cause of the classic condition. Two biotype of *Corynebacterium pseudotuberculosis* are recognized. One is nitrate negative group isolated from sheep and goats and the other one nitrate positive one isolated from horses and cattle. The bacteria produce a potent phospholipase exotoxin which attacks the sphingomyelin of vascular endothelial cells, and may be important in aiding the spread of bacteria by acting as permeability factor. Ulcerative lymphangitis typically begins about the fetlocks of the hind limbs. As a result of lymphangitis, there is diffuse swelling in the leg soon followed by development of dermal noduels. These are abscesses and ulcerate with discharge of thick creamy pus. Only small areas of skin are sloughed off. The ulcers heal and leave small areas of depilated, depigmented skin. As primary ulcers heal, new nodules form in adjacent skin, suppurate, ulcerate and cicatrize and in this way the disease progresses slowly. As the new nodules develop, the lymphatics between them become carded much and as much as 1- 2 cm thick and fresh abscesses develop along the inflamed area. In uncontrolled infections, over a course of many months, much of the skin of the body and neck as well as the limbs may be affected and this leads to death of animal.

Epizootic lymphangitis: A pseudo-farcy caused by *Histoplasma farciminousm* seen in horses. The initial cutaneous lesions or focus of infection in a wound has a tendency to ulcerate or it may under go alternating periods of discharge and closure of some weeks before healing and scarifying. The infection may resolve but often spreads centripetally in the adjacent tissues and along the lymphatics. In the adjacent tissues which are swollen, small nodules develop which is about 1 cm in diameter and in the course of few days these ulcers to discharge at first a viscid gray exudates and later pus. The initial lesions are intradermal and freely movable over the subcutaneous tissue. Spread of the infection is slowly via lymphatics and these convey the organisms into subcutaneous tissues and into the deeper tissues. The inflammed lymphatics are thickened and hard and along the course new nodules forms and ulcerate, discharge and eventually heal with scarification.

Parasitic lymphangitis: Filarid worms of the genus *Wuchereria bancrofti* in humans and related species parasitise the lymphatic system of dogs and in cats in tropical areas. *Brugi malayi* (*Wuchereria*) parasitise the cats and primates in India. Cats may be reservoir hosts for human infections. These are transmitted by mosquitoes and their life cycles are similar to those of other filarial worms. Infective larvae enter peripheral lymphatics, migrate to nearest lymph nodes and develop for 2 weeks before migrating down afferent lymphatics, where they mature and produce granulomatous lymphangitis, lymphadenitis and usually cause lymph-oedema and elephantiasis as occur in humans. The microfilaria should be differentiated from *Dirofilaria immitis.*

Tumors; tumors of endothelial origin are classified as benign or malignant. These are angiomas or angio-sarcomas. Haemangiomas are benign tumors of endothelial

cells and may be classified as capillary or cavernous based on the size of the vascular channel formed. Haemangiomas are usually single ovoid, red black masses of 0.5 to 3 cm in diameter which ooze blood when cut. Histologically blood- filled vascular spaces are lined by a single layer of well differentiated endothelium. The vascular spaces are separated by variable amounts of connective tissue stroma. Haemangiomas are not encapsulated and not invasive. Bovine cutaneous angiomatosis in adult diary cows are nodular dermal vascular proliferation occur anywhere in the skin. Lesions resembling haemangiomas occasionally develop in the skin of the scrotum or perineum of boars, or the vulva, mammary gland or ovaries of sows.

Haemangiosarcomas are malignant tumors of endothelial cells, occur more frequently in dogs. The tumors arise in any part of the body. These are common primary cardiac tumors of dogs. These are having grey hemorrhagic areas and may reach a diameter of 30 cm in spleen.

Lymphangioma is rare, benign tumor which consists of lymph channels forming capillary, cavernous, or cystic tumors. Lymphangiomas occur as congenital malformation or may develop spontaneously in adults.

Lymphangiosarcoma is an extremely rare tumor in domestic animals. The tumors are histologically similar to Haemangiosarcomas, but the irregular vascular channel contains few red cells. This is diffusely invasive and metastasizes widely. Ultrastructurly, lymphangisarcomas are distinguished from haemangioma sarcomas by the general lack of lamina, few micro-pinocytotic vesicles, few intercellular junctions and a discontinuous endothelial cell layer in lymphangisarcomas.

Purulent lymphangitis is associated with suppurating conditions of the tissue drained. There is intense infiltration by leukocytes of the wall of the vessels together with thrombosis.

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Chapter 2

Diseases of Haemopoieitc System

Summary; The haematopoietic system- introduction; The pluripotential cells of bone marrow; The haematopoietic bone marrow; Extramedullary haemopoiesis; Bone marrow cells- Primitive cells; Neutrophils, Eosinophils, basophils, lymphocytes, monocytes, Rubriblast; Erythrocytes-RBCs; Leukopoesis, Myeloblast, Eosinophilic Myelocyte, Band cell; Lymphocyte Series; Monoblasts; Megakaryoblasts; Myeloid and erythroid ratio;Aplasia-Quantity of hemoglobin in the cell, Diameter of RBCs, Leptocytes,Target cell , Acanthocytes, Reticulocytes -Anemia's in animals -Types of Anemia's in animals and their causes; Aplastic anemia: Myelophthesic anemia: Hemorrhagic anemia; Hemolytic anemia -Total leukocyte values for various species of domestic animals; Factors affect leukocyte count: Leukocytosis. Neutrophilia, Basophilia; lymphocyte - B-cells or cell mediated immune response (T-cells). Leukemia. Acute leukemia's, Acute lymphatic leukemia, Chronic lymphocyte leukemia of large granular lymphocyte type: Low grade lymphomas of diffuse type: Acute leukemia's: Acute myeloblastic leukemia without maturation; monocytic leukemia; Diseases of spleen; Hyperspleenism

Haematopoietic system

The haematopoietic system includes blood, bone marrow spleen, lymph nodes and other lymphoid tissues. Haematopoietic or haemopoiesis; Bone marrow is for making blood. The blood constitutes the liquid component, mostly of water with dissolved salts and number of other constituents and the solid component composes of proteins and cells.

The haematopoietic system is widely distributed and includes organs having functions other than contributing to blood formation. In addition, Haemopoietic system also provides a microenvironment that attracts appropriate circulating cells and enables them to multiply or differentiate into the cells of particular lineage.

The haemotopoiesis takes place in the adult usually in association with reticulo-endothelial system, in the bone marrow. Thus the close relationship between bone, reticulo-endothelialsystem and haematopoiesis exists in mammals and birds.

The bone marrow maintains an embryonic function of division of cells of blood elements throughout life, because it has to constantly renew cells of blood.

Below mentioned table depicts the tissues or organs and their functions in haemopoiesis.

Table 1 showing the tissues\organs and their functions in haemopoiesis

Tissue/organs	Functions in haemopoiesis
Bone marrow	Produces RBCs, granulocytes, monocytes and blood platelets. Stores iron, produces special type of lymphocytes to seed lymphoid tissue
Lymph nodes\ follicles	Produces lymphocytes, plasma cells and participate in antibody production
Liver	Stores B_{12}, folic acid and iron. Produce prothrombin, fibrinogen and albumen. Converts bilirubin to bilirubin glucoronodie. Retains embryonic potential for haemopoiesis and produces a precursor of erythropoietin
Spleen	Produces lymphocytes and plasma cells. Stores RBCs and iron. Destroys aged and abnormal RBCs and degrades hemoglobin through its extensive reticulo-endothelial system. Retain the embryonic potential for haemopoiesis.
Stomach and Intestinal mucosa	Stomach produces HCl for release of iron from complex organic molecules. Produces intrinsic factor for B12 absorption by intestinal mucosa.
Reticuloendothelial system	Destroys RBCs and converts hemoglobin to iron, globin and free bilirubin. Stores iron.
Kidney	Involved in the production of erythropoietin or an erythropoietin stimulating factor
Thymus	Produces T-cells and erythroblasts

The pluripotential cells of bone marrow gives rise to myeloid stem cells, from wherein RBCs, WBCs, comprising Neutrophils, Eosinophils, Basophils and Platelets will come. The lymphoid system cells will be lurking both in bone marrow or bursa in birds and in thymus as well in the peripheral lymphoid organs. A large number of humoral factors control differentiation and maturation of blood cells. These pluripotential cells are also being called as haemocytoblasts.

The haematopoietic bone marrow with actively divided cells is red in color, when it elaborates sufficient amount of blood cells, the marrow looses its activity, the cells become atrophied and the marrow turns out to yellow in color. When on demand the fatty marrow is converted to red marrow. Serous atrophy of marrow fat is a late change seen in starvation and in chronic diseases and is a significant lesion.

In the adult of all species the haematopoietic marrow is concentrated in the spine, pelvis, sternum, ribs, pelvis and proximal end of the limb bones. Marrow capillaries serve for transport of blood cells to the systemic circulation via the vein which parallels the nutrient artery. These capillaries are lined by specialized endothelial cells. There are reticular cells which are weakly phagoyctic stay in the marrow.

These cells are hormonally active and essential for the maintenance of growth and differentiation of haematopoietic stem cells.

Haematopoietic system in the embryos: In the embryo at 3 weeks of age the nucleated blood cells arise from the yolk sac. Blood islands in the yolk sac liberate nucleated RBCs and they contain large nucleus and loosechromatin with nucleoli. These contain embryonic hemoglobin.

Haematopoietic system in foetus: From 2nd month of life the primitive blood cells migrate from the blood islands of yolk sac to the thymic anlagen, the primordial lymph nodes, liver (hepatic phase) and spleen. During this period, the primitive stem cells are being capable of differentiation into all blood ceil lines. Even granulocytes being to appear and by 4th month, they are numerous.

Lymphopoiesis: This is seen in lymph nodes at 4th month and continues throughout the life.

Myeloid phase: Fetal and spleenic haemotopoiesis is erythroid. Coincident with the remodeling of fetal bone which provides a marrow cavity, there is colonization of Haemopoieitc stem cells which arises from the blood islands of yolk sac. This begins approximately by the 5th month (if the animal having 9th month gestation). In the beginning granulopoiesis alone occurs but gradually, the bone marrow takes over the function of formation of blood cells.

The nucleated red cells in the fetal blood gradually decrease in number and by 6th month, none are present in the peripheral blood, now contain only nonnucleated cells.

Growth and differentiation: This depends on the provision of suitable microenvironment depending on the growth factors and interleukins. Differentiated or committed stem cells can produce only one or two cell types and have limited proliferative capacity. Growth differentiation and maturation are forced by a high proportion of receptors for the factors acting early in the proliferative cascade on primitive cells and vice versa.

Both embryonated and myeloid stem cells could be recognizable in the bone marrow. The peculiarity of these cells is to divide and aggregate in the form of colonies. The stem cells actively divide and developing cells differentiate and mature. Thus, the reticulocyte and mature RBCs could be recognized in the company of its stem cells (haemocytobalst). This is like a lactating animal with its offspring surrounding it.

Number of substances (chemicals and hormones) i.e., humoral mediators are responsible for the division of stem cells and maturation of the haematopoietic cells. These factors are being called colony stimulating factors. Stem cells that are going to release RBCs, multiply under the control of substances that control the colony forming units of erythroid series. Similarly, stem cells which give rise to

granulocytes give rise to Neutrophils and monocytes from under the control of substances that control forming units of monocytes. Megakaryocites committed colonies arise form stem cells and also under specific mediators. These mediators are interleukins 1, 2, 3, 4, 6 and 7 and a variety of stem cell factors. Tumor necrosis factor that comes from monocytes also stimulates growth factor production which increases marrow cell release.

The blast cells make 1% of marrow cells. 25% of marrow cells are in the proliferative phase and 75% are in the maturation phase.

Below mentioned are the various morphological stages of myeloid and erythroid differentiation of cells.

Erythropoiesis

Rubriblast

↓

Prorubricyte

↓

Basophilic rubricyte

↓

Polychromatic rubricyte

↓

Normochromic rubricyte

↓

Metarubricyte

↓

Reticulocyte

↓

RBC

The development of RBCs takes around 6 days. The first three morphological stages of erythroid and myeloid series are dividing cells and rest of the series of cells is undergoing the nuclear and cytoplasmic maturation. For the Neutrophils to develop and come out it will take 6 days; the monocytes 35 hours and the platelets around 4 days.

Extramedullary haemopoiesis: This denotes formation of blood cells in organs other than the bone marrow. As noted earlier this is common in the fetus. But in adults at the time of needs, in severe hemolytic anemias, the liver and to a slight

degree of the spleen, resumes the Haemopoieitc activity. Because immature cells are developing in these areas, these focal islands of immature cells appear as white spots grossly.

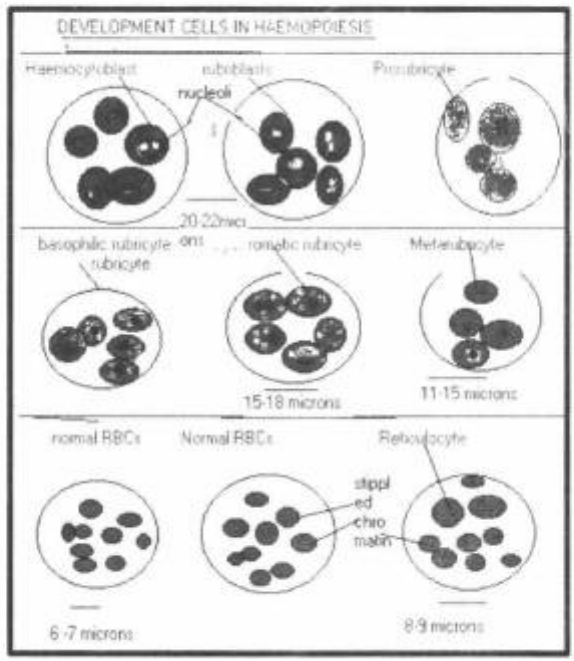
Bone marrow cells: All cells that develop in bone marrow alter morphologically as they progress from primitive to mature type.

Primitive cells are usually larger than mature cells, and the nuclei of these young cells are relatively large in relation to the amount of cytoplasm contained in the cell. As cells develop through various stages of maturation, nuclei become smaller, and in RBCs, they disappear completely. Another nuclear alteration that takes place is a change in shape. In primitive granulocytic cells, nuclei are round or oval or may be have a slight indentation. As granulocytes mature, the nuclei lose their shape, become more deeply indented and eventually are segmented. Color changes in the nucleus also become apparent as the cell matures. In young cells, nuclei are rich in reddish purple tinge. As the nucleus begins to differentiate, it becomes predominantly blue and stains more darkly.

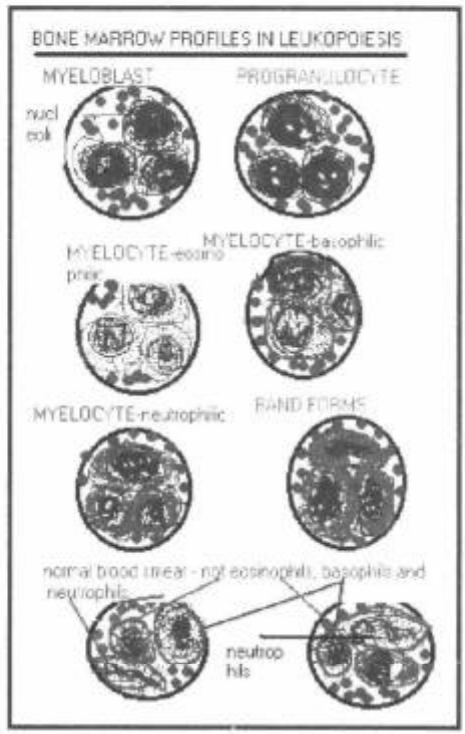
Erythrocyte series

The **developmental stages** from immature to mature erythrocytes are Rubriblast prorubricyte → basophilic rubricyte → polychromatophilic rubricyte → Normochromic rubricyte → Metarubricyte → Reticulocyte → Erythrocyte (mature RBCs).

Rubriblast: Rubriblasts have characteristics of other blast cells. In young Rubriblasts, the cytoplasm stains light blue, but in more mature forms, there is superimposed reddish tinge that gives the cytoplasm a peculiar dark purplish blue color. The nucleus usually contains nucleoli and is round. The chromatin is slightly red colored and delicate. **Prorubricyte:** The prorubricyte is smaller than the rubriblast and the nuclear chromatin is less delicate. **Rubricyte**: the rubricyte is smaller than the prorubricyte and may have a nuclear chromatin arrangement in a pattern suggesting the spokes of a wheel. This nuclear arrangement is due to the appearance of darkly stained portion of nuclear chromatin separated by light streaks. The cytoplasm is bluish red, or polychromic. This variation cytoplasmic staining properties permits the classification of the cells as a basophilic polychromatophilic or Normochromic rubricyte, depending on the degree of haemoglobination. **Metarubricyte:** The cytoplasm in this cell is predominantly red, but there may be a slight residual basophilia. In some cells, the cytoplasm stains the same way as do nonnucleated RBCs. The nucleus of the cell is pyknotic and appears as blue black mass with no distinguishable chromatin strands. **Reticulocyte:** This is a non-nucleated cell of Erythrocyte series but when stained of supravital stain diffuse network of bluish fibrils that is residues of chromatin are present. The reticulocyte is larger than RBCs and is usually polychromatophilic. **Erythrocytes (RBCs):** These are the mature cells of the series and stain as reddish. Crenation and slight irregularities of cells are considered to be normal.



Leucopoiesis
Myeloblastic
↓
Promyelocyte
↓
Myelocyte
↓
Metamyelocyte (Juvenile)
↓
Bands (stabs)
↓
Segmenters
↓
(Neutrophils,
Eosinophils
Basophils)



Alteration in nuclear chromatin also occurs during cell maturation. In immature cells, chromatin strands have a fine, delicate structure. The presence of nucleoli is an indication of cellular immaturity. Nucleoli, which are signs of metabolic activity, are, in all probability, portions of cytoplasm in the process of formation. Nucleoli are usually visible as structure less masses within the nucleus that are light blue with Romanowsky stains. These are composed of RNA. After the cell divides, nucleoli lose their blue color and remain as structure less rings.

In addition to these nuclear changes, the cytoplasm is also altered in the staining characteristics. Since all developmental alterations from one cell type to another do not occur as a single step but as a gradual process, cells may be observed that are morphologically on the borderline between one stage of development and the next. Identification of such cells may prove to be difficult, but the best rule to follow is to name the cells by the company it keeps.

Granulocytic series

The **developmental stages** of the granulocyte series (from immature to mature) are as follows.

Myeloblast → Progranulocyte → Myelocyte → Metamyelocyte → Band cells → Segmented granulocytes.

Myeloblast: This cell has a fine chromatin structure and does not contain cytoplasmic granules. Nucleoli are visible and the cytoplasm is distinctly basophilic.

Progranulocyte: This cell has a nuclear structure denser than that of the blast cell and has darkly stained azurophilic cytoplasmic granules. Nucleoli are usually visible but are fewer in diameter. The cytoplasm stains less intense blue and the nuclear, cytoplasmic ratio is altered, as the cytoplasm is more abundant than in less mature blast forms.

Myelocyte: This cell contains specific granules that are identified by their staining properties as neutrophilic, eosinophilic or basophilic myelocyte. The Myelocyte is distinguished from the Progranulocyte by the presence of their specific granules. The nucleolus is round or oval and the chromatin is coarser than the chromatin of the pro-granulocyte. Nucleoli are not usually visible. Cytoplasm stains faint grayish pink.

The **Eosinophilic Myelocyte** contains granules in cells from the dog where these granules are varying in size and stain lightly. In the cow, the granules are small and round and stain an intense red. Eosinophilic granules of sheep cells are stained red and ovoid. In horse, these granules are large and stain a dull red orange. In the pig, these granules are pale pink-orange and are ovoid.

The Basophilic Myelocyte has the granules in the cytoplasm obliterating the nucleus. These granules stain dark blue to black.

Neutrophilic Myelocyte: Granulation in the Neutrophilic Myelocyte consists of fainter granules of the cytoplasm.

Metamyelocyte: This cell closely resembles the Myelocyte but has a slightly indented nucleus. The nuclear chromatin is coarser than that in younger cells. Cytoplasmic granules are present.

Band cell: This cell of the granulocytic series has a nucleus that resembles a curved or coiled band. The band cell may be differentiated from the Metamyelocyte by the lengthening of the nucleus and a tendency for the sides to become parallel. Typical cytoplasmic granules (eosinophilic, basophilic, or neutrophilic) are present.

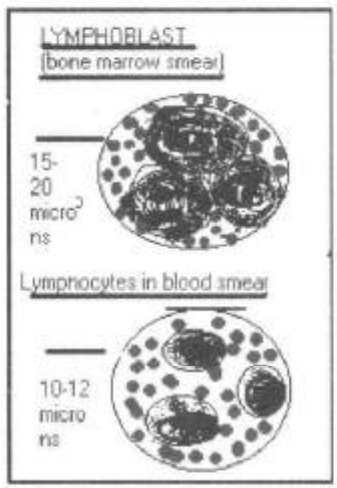
Segmented granulocytes: This cell maybe eosinophilic, neutrophilic or basophilic depending up on the staining properties of the cytoplasmic granules. The nucleus is lobated and the lobes of the nucleus are connected by filaments.

Lymphocyte Series

Lymphoblast: The lymphoblast having abundant cytoplasm with vacuolated nucleus and nucleoli represent. It is difficult to differentiate this cell from other blast forms as it has characteristic similar to those of the myeloblast. These cells could be identified by the law of the company they keep.

Prolymphocyte: the morphological characteristics of the prolymphocyte are intermediate between those of the lymphoblast and those of mature lymphocytes. It has a coarser chromatin structure than the lymphoblast. Nucleus usually contains indistinct nucleoli. The cytoplasm is slightly bluish.

Lymphocyte: the nucleus of mature lymphocyte has a coarser chromatin structure and is usually located eccentrically. Azurophilic granules maybe present in the cytoplasm of lymphocytes, they occur most frequently in the bovine and ovine species. The small quantity of cytoplasm stains slight blue. The nucleus has a slight indentation.



Monocytic series

Monoblasts are difficult to differentiate from other immature cells in marrow. The monoblast is often larger than the corresponding blast cell of the neutrophilic or Erythrocytic series. Nucleoli are usually prominent. The cytoplasm is granular and basophilic.

Mature Monocyte; Nucleus becomes indented and a fine nuclear chromatin pattern is present. The chromatin stains reddish purple. The relatively large nucleus is irregularly shaped and sometimes folded upon itself in the mature monocytes.

Thrombocyte series

Megakaryoblasts: Megakaryoblasts resemble other unidentified cells. The cytoplasm stains light blue and there is a vacuolated zone. The nucleus is relatively large red staining, and round with chromatin pattern and nucleoli. Frequently the cell is binucleated.

Promegakaryocyte: The nucleus of the Promegakaryocyte has a chromatin structure similar to that of immature cell but the nucleus is multilobed or indented. The cytoplasm stains blue and contain a variable number of granules that stain bluish.

Megakaryocyte: This is the largest cell present in the bone marrow often being more than two micron in diameter. The cytoplasm is plentiful and has coarse granules. Some cytoplasmic granules are aggregated as well defined masses or as small, ill defined clumps. The well defined masses are thrombocytes and are most numerous in the cell periphery. The nucleus of immature megakaryocyte is lobulated or indented; no nucleoli are present, and the chromatin pattern is similar to that of any mature cell.

Thrombocytes: The thrombocyte is the non-nucleated fragment of megakaryocyte cytoplasm that contains azurophilic granules similar to those seen in the megakaryocyte.

Myeloid and erythroid ratio: All cell series in normal bone marrow develop in a sequential fashion with the number of mature forms exceeding that of immature cell types. In normal animals, the ratio between myeloid and erythroid elements is approximately 1:1. At least 500 cells should be enumerated and identified.

Hypoplasia: A reduction in the marrow cellularity occurs. This is followed by decrease in the number of cell types in the peripheral blood. There is erythroid hypoplasia and increased myeloid activity is seen in such conditions as chronic renal disease, chronic inflammation, hypothyroidism in the dogs, pan leucopenia in the cat, feline leukemia virus infections and trichstrongyloid parasitism in cattle and sheep. Due to decrease in erythroid elements, the Myeloid and erythroid ratio is usually increased.

Aplasia; the term aplasia suggests complete lack of cell production. In the bone marrow there is complete lack of erythroid and myeloid cells. This condition has been associated with the use of toxic drugs, viral infections, exposure to high doses of radiation and plant toxins.

Hyperplasia: If there is a peripheral demand for erythrocytes accompanying or following anemia, erythroid hyperplasia will prevail. Inflammatory processes result in granulocytic hyperplasia, while thrombocytopenia as seen in injuries and surgical operations followed by megakaryocytic hyperplasia; if tissue destruction has been considerable and a demand exits for tissues macrophages, monocytic hyperplasia may occur. With erythroid hyperplasia an increase occur in nucleated RBCs, which reduce M: E ratio.

Myeloproliferative disorders: A complex of disease conditions that results in proliferation and only partial differentiation of primitive mesenchyma cells of the bone-marrow spleen, lymphnodes and liver is called myelproliferative disease. Included in these disorders in cats are granulocytic leukemia, megakaryocytic leukemia, polycythemia Vera, erythremic myelosis, and erythroleukemia. In erythremic myelosis, almost no cells of the granulocyte series are found in the bone marrow. Clusters of undifferentiated cells having characteristic prorubricyte and basophilic rubricytes predominate.

Recapitulation of RBCs: the major function of red blood cells is to transport hemoglobin, which in turn carries oxygen from the lungs to the tissues. In some lower animals, hemoglobin circulates as free protein in the plasma, not enclosed in red blood cells. The red blood cells have other functions besides simply transport of hemoglobin. They contain large quantities of carbonic anhydrase, which catalyses the reaction between CO_2 and water increasing the rate of this reaction about 250 times. The rapidity of this reaction makes it possible for blood to react with large quantities of CO_2 and thereby transport it from the tissues to the lungs. Hemoglobin within the RBCs acts as an acid base buffer and neutralizes most of The buffering power of blood 5 millions/cmm. The average count in different domestic animals is given in the ensuing table.

Table showing haematological parameters in different species

Spp	RBC	Hb	PCV	MCV	MCH	MCHC	Reti culo-cytes	Myeloid: Erythroid ratio
Dog	6.8	15.0	45	70.0	22.8	33.0	0.8	1.2:1.0
Cat	7.5	12.0	37.0	45.0	15.5	33.2	0.6	1.6:1.0
Cattle	7.0	11.0	35.0	52.0	14.0	31.0	0.0	0.71:1.0
Sheep	12.0	11.5	35.0	34.0	10.0	32.5	0.0	1.1:1.0
Goat	13.0	10.0	35.0	27.0	19.5	31.5	-	0.69:1.0
Pig	6.5	13.0	42.0	60.0	19.0	32.0	0.4	0.52:1.0
Horse	7.5	11.5	35.0	58.5	19.7	38.6	0.5	1.5:1.0
Chicken	3.0	9.07	28.33					
Man	4.5-6.0	14.0-16.0	38-45	82-92	27.31	32-36	0.1	
Woman	4.3-5.5	12.0-16.0	36-47	82-92	27.31	32-36	0.1	

The shape and size of RBCs: Normal RBCs are having biconcave discs, and in humans, having a mean diameter of 8 μ and the thickness at the thickest point is around 2 μ. The average volume of red blood cell is around 83 cubic microns. The shape of RBCs can change as they pass through the capillaries. Concentration of red blood cells in the blood: It varies from species to species.

In the chicken, it is around 2.5 to 3 milions/cmm, whereas in sheep, it is around 10 to 13 millions/cmm, in man it is around 5 to 6 milions/cmm and woman it is around 4 to 5 millions/cmm. The average count in different domestic animals is given in the table.

Quantity of haemoglobin in the cells: Red blood cells have the ability to concentrate haemoglobin in the cell fluid up to approximately 34 grams per 100ml of cells and in human blood the concentration never rises above this value. When the haematocirt (the % of blood cells in blood) in human's 40 to 45% and the quantity of haemoglobin in each respective cell are normal, then the whole blood of men contains 16 grams % of haemoglobin in males and 14 grams % of haemoglobin in females. Each gram of pure haemoglobin is capable of combing

with approximately 1.39 ml of oxygen. Therefore, in normal man over 21 ml of oxygen can be carried in combination with hemoglobin in each 100 ml of blood and in normal woman it is around 19 ml of oxygen can be carried.

Dogs, horse and man are representatives of the more active types, and thus their haemoglobin needs are greater than those of more lethargic animals such as cow, sheep, goat and cat. The smaller the cell the greater the number per unit volume of blood. Roleaux formation is there in horse blood and as a result greater Sedimentation rate is seen. Cow, sheep and goat RBCs do not form Roleaux; hence sedimentation rate has limited value in the study of blood of these animals. Haemoglobin could be calculated by dividing PCV by three.

The average life span of RBC in chicken is around 28 days. This is thought to be due to high body temperature. Red cells with diameter of 7 to 10 μ pass through the capillaries with a diameter of 3 to 5 μ. B_{12} is required for the synthesis of DNA and folic acid is required for the synthesis of RNA in red cells.

Normally around 1% of red cells are replaced daily. Most species of domestic animals have PCV values from 38 to 45%. Lactating dairy cows have a PCV of 32 to 35, chicken 30 to 33. The PCV is approximately three times the haemoglobin concentration. Haemoglobin is expressed in grams per deciliter. Biosynthesis of haemoglobin starts at rubricyte stage.

RBCs contain 62 to 72% of water and 35% solids. In that 95% of haemoglobin is in RBCs.

Mean corpuscular volume: is expressed in μm^3 or femto liters (fl)

$$MCV = \frac{PCV \times 10}{\text{No. of RBCS per } \mu \text{ L of blood } / \times 10^{-6}}$$

MCH(Mean corpuscular haemoglobin)expressed in μμg or pg

$$MCV = \frac{HB \text{ IN } G \setminus DL \times 10}{NO.\ OF\ RBCs \setminus \mu L\ OFBLOOD\ X\ 10^{6}}$$

Mean corpuscular haemoglobin concentration (MCHC). MCHC in g\dL or g%

$$= \frac{Hb \text{ in } g / dl \times 100}{PCV \text{ in } ml / dl}$$

Deciliter=d=10^{-1} (one tenth);Centiliter=c=10^{-2} (one hundredth);Milliliter=m=10^{-3} (one thousandth);Microlitre=μ=10^{-6} (one millionth);Nanolitre=n=10^{-9}(one billionth);Picolitre=p=10^{-12}(one trillionth);Femtolitre =f=10^{-15}(One quadranth)

MCV provides an average cell size in cubic micrometer. Most mammals are born with large RBCs (80 to 90 μm^3) which then decrease to (55 to 65 μm^3) in 8 weeks. MCH expresses average weight of haemoglobin present in RBCs. MCHC gives average% of the MCV which the haemoglobin occupies.

Sedimentation rate: When blood containing anticoagulant is allowed to stand in perpendicular tube, the RBCs sink because they are heavier than the plasma in which they are suspended. The speed with which the RBCs fall in the blood of normal animals is relatively slow, but in animal with inflammatory disease in which there is tissue necrosis and degeneration, speed is increased. This alterations suspension stability probably results from changes that occur in the physico chemical properties of the RBC surfaces and the plasma. Alteration in these properties on the RBC surfaces cause red cells to aggregate and form Roleaux. The larger the aggregation and the more aggregations that occur, the more rapid is the fall RBCS. Increase in plasma fibrinogen is probably responsible for these changes.

Table 2. Normal values for ESR in various species of domestic animals

Species	mm in fall	mm.in fall	mm in fall
	30 minutes	1 hour	24 hours
cattle	0	0	2.25-4.0
sheep	0	0	3.0-8.5
goat	0	0	2.0-2.5
pig	0-6	1-14	More
horse	15-38	more	More
dog	1-6	5-25	More
cat	-	7-23	More
man	-	0-9	More
woman	-	0-2	more

Diphasic sedimentation: occasionally in an ESR determination there is no definite line between the settling of RBCs and the plasma. The plasma is clear except for a stream of red cells that seems to be following along behind the red cell mass much as the tail follows a dog. This phenomenon is the result of the presence of reticulocytes or other young forms RBCs. It may also occur if there are large numbers of abnormally shaped RBCs. This trailing out of RBCs occurs because these cells are larger and do not actively participate in Roleaux formation. Whenever di or biphasic sedimentation occurs, it suggests that the presence of an erythrogenic alteration.

Erythrocyte morphology: the morphology of RBCs is most readily observed by examination of smears, such as those utilized making differential leukocyte counts or wet mounts. Erythrocytes of domestic animals vary in size depending upon the species. The average size of an RBC in various species of domestic animals is presented in table. The diameter of RBC of dog is the largest and that of the goat and sheep is the smallest. A slight variant in size of RBCs are common.

Anisocytosis is the variation size of RBCs. This occurs commonly in blood smears of cattle. Cattle RBCs vary from 3.6 microns to 9.6 micron in diameter. The great differences usually occur in young animals. Anisocytosis is not common in sheep blood. Anisocytosis occurs in animals with a regenerative anemia when macrocytes

are being released into the peripheral circulation.

Table 3. Diameter of RBCs in various species of domestic animals

species	RBC diameter (in μ)
Cattle	4.0-9.5
sheep	3.5-6.0
goat	3.2-4.2
pig	4.0-8.0
horse	5.6-8.0
dog	6.9-7.3
cat	5.4-6.5
man	5.5-8.6

Table 4 Average osmotic fragility of normal RBCs in hypotonic saline solutions

Species	% of saline-minimum resistance	% of saline maximum resistance
cattle	0.59-0.66	0.40-0.50
sheep	0.60-0.76	0.40-0.55
Goat	0.62-0.74	0.48-0.60
Pig	0.70-0.74	0.45
horse	0.42-0.59	0.31-0.45
Dog	0.45-5.0	0.32-0.36
Cat	0.69-0.72	0.46-0.50
chicken	0.41-0.42	0.28-0.32

Abnormalities in shape:

Poikilocytosis is defined as a major deviation from the normal shape of the RBCs. Marked deviations in shape may be a sign of abnormal erythrogenesis. Care must be taken in evaluating poikilocytosis because improperly prepared blood films may contain abnormally shaped RBCs.

Leptocytes are thin RBCs in which surface area is increased but cell volume is not changed. Consequently, it is possible for the cell membrane to fold and become distorted. These cells are usually more resistant to hameolysis in a hypotonic saline solution. Since such cells have a larger diameter, they usually do not participate in Roleaux formation and not clump readily with other cells. Consequently, in ESR determinations they do not always fall readily and may lead to a minus value in a corrected sedimentation rate.

Target cell (codocyte) is a form of leptocyte. The target cell is characterized by a dark staining center section surrounded by a clear, unstained area that is surrounded by a peripheral ring of stained cytoplasm. Target cells are most commonly seen in canine blood. Leptocytes are more commonly found in an animal having a chronic disease process, and this should be considered when evaluating the morphology of RBCs in individuals having a characteristic nonresponding anemia.

Spherocytes are recognized by their morphology and staining characteristics. They are most frequently found in the dog, appear smaller than normal RBCs, stain more intensely, and have no central pallor. Spherocytes have a more rigid membrane and therefore resist deformation. Because of this rigidity the intravascular life span is shortened, as these cells are rapidly removed from the peripheral circulation. Spherocytes occurs in dogs with autoimmune haemeolytic anemia. Stored RBCS tend to become spherical. Dogs transfused with large quantities of stored blood may have a detectable sperocytosis.

Acanthocytes are RBCs with rounded projections .Such cells have been demonstrated in blood from healthy cows and in blood from dogs with liver diseases.

Crenation is the appearance of projections on the RBC surface which is usually not clinically significant, results from delayed drying exposure to lytic agents or the presence of hypertonic solution. Crenation does not take place in dog blood. It happens with cat blood. In smears from pig blood Crenation occurs characterized by sharp points appearing on processes emanating from the cell.

Reticulocytes: These are immature RBCs. They may however be identified in peripheral blood smears by their size and staining characteristics. If present in large numbers, they may increase the MCV. A reticulocyte differs from a mature red cell in that it is more resistant to Crenation, does not participate in the formation of Roleaux, has a lower specific gravity, is a larger cell, and is more resistant to hypotonic saline solutions. Reticulocytes aren't found in the blood of healthy horses, sheep, goats or cows. Reticulocytes mature in the bone marrow of these animals. In the dog and cat as many as 0.5 to 1.0 % reticulated cells may appear in peripheral blood. In the pig there may be up to 2% reticulocytes are present in peripheral blood. Many laboratory animals including the guinea pig, rat, rabbit and mouse have a reticulocyte level between 2 and 4 5.

Reticulocytes take stain by supravital stains like brilliant cresyl blue or new methylene blue. The most commonly used stain is 1.0% solution of brilliant cresyl blue in physiological saline and 0.5% solution of new methylene blue in a 1.6% solution of potassium oxalate. Reticulocytes stained in this manner have a bluish stippling the centre of the cell. The quantity of bluish-staining material in any reticulocyte may vary depending upon the stage of maturation.

Three distinct types of reticulocytes have been demonstrated in cat blood. Those classed as type I are lightly reticulated and have a faint blue stippling with new methylene blue stain. Type II reticulocytes have isolated dark granules and one or two threads of reticulum. Type III is characterized by the appearance of a heavy dark granular network.

Under the influence of increased levels of erythropoietin there may be a premature release of reticulocytes form the bone marrow. These are termed shift or stimulated reticulocytes which are larger and contain more reticulum than do the more mature

reticulocytes.

The degree of reticulocytosis is proportional to erythrpoietic activity, as an increased reticulocyte count indicates increased erythrogenesis. An acute hemorrhage is usually followed by reticulocyte shower, which indicates accelerated erythropoietin. Chronic hemorrhage is usually followed by reticulocytosis, but it is not a high as that occurring in association with acute hemorrhages.

Discovery of a reticulocytosis in an animal may lead to detection of an other wise occult disease such as hidden hemorrhage or unrecognized hameolysis of RBCs, A sudden drop to very low values may indicate impending or existing marrow failure.

Punctuate basophilia or basophilic stippling is characterized by the appearance of punctuate aggregation of basophilic staining material in the form of large number of fine or coarse granules in the RBCs. The number of granules in RBCs varies in inverse ratio to the size of the granules. They stain deep blue with Wright's stain. RBCs containing these granules may stain normally in other respect or they may exhibit polychromatophilia. Basophilic stippling may also be seen in some nucleated red cells. Stippling is generally attributed to degenerative changes in the cytoplasm involving RNA in the young cells. Basophilic stippling of RBCs also occurs in dogs with lead poisoning.

Polychromasia: Diffuse basophilia is characterized by an overall bluish-red colour to the normally red staining RBCs. After the Metarubricyte loses its nucleus, a small amount of basophilic substance remains in the cytoplasm. This remnant of cellular maturations composed of RNA and protoporphyrin, the latter being responsible for the fluorescence of RBCs under u.v. light.

Howell-Jolly bodies: Howell-Jolly bodies are remnants of nuclear material after the nucleus has been extruded. In Wright stained smears Howell-jolly bodies appear as refractile single, and at times double, bluish spherical bodies within RBCs. In the bovines these must be distinguished from Anapalsma marginale. Howell-Jolly bodies may appear within the cell anywhere where Anapalsma are usually uniform in size and are confined to the periphery. Howell-jolly bodies are common in nay severe anemia. These are commonly seen in cat RBCs... As well RBCs of horses.

Heinz bodies: Heinz bodies are small, round to irregularly shaped refractile inclusions that may occur singly or multiply within a single cell. These bodies occur in horses having an anemia resulting from phenothiazine therapy or wild onion poisoning. These bodies are thought to consist of denatured protein and are most commonly associated with hameolytic anemias produced by agents toxic to RBCs. Their presence is indicative of injury to RBCs and may occasionally indicate an unsuspected hemolytic anemia. Heinz bodies appear as blunt projections on the RBCs membrane. In humans appearance of these bodies may follow exposure to chemicals such naphthalene, sodium nitrate, sodium chlorate, sulfanilamide, paraminosalycylic acid, isoniazid, nitorfurantoin, certain anitmalarial

drugs and phenacetin. These bodies are thought to consist of a denature protein and are most commonly associated in hameolytic anemias that are produced by agents of toxic to RBCS. Their presence indicates injury to RBCs and may occasionally indicate unsuspected hameolytic anemias. These occur in cats treated with urinary antiseptics for treatment of cystitis and urolithiasis. Small number of Heinz bodies is seen in dogs treated with prednisonlone. These bodies are thought to consist of a denature protein and are most commonly associated in hameolytic anemias that are produced by agents of toxic to RBCS. Their presence indicates injury to RBCs and may occasionally indicate unsuspected hameolytic anemias. These occur in cats treated with urinary antiseptics for treatment of cystitis and urolithiasis. Small number of Heinzbodies is seen in dogs treated with prednisonlone.

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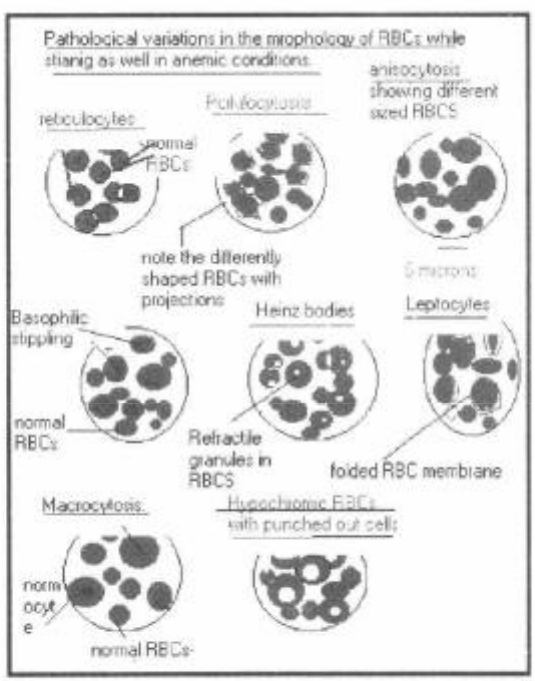
Nucleated RBCs: Nucleated red blood cells do not occur normally in any species of domestic animals in the peripheral blood smear, with the exception of the suckling pigs up to three months of age and occasionally the normal dog. These are usually confined in the bone marrow and are seen in anemias. The presence of these in peripheral blood indicates the current bone marrow response of the animal.



Anemias in animals

Anemia is reduction in the quality and quantity of RBCs in peripheral circulation. Oligocythemia is a term used only for the reduction in the quantity of RBCs.

Anemias could be classified depending on the morphology of RBCs, on the etiology that could reduce the quality and quantity of RBCs.

Thus anemias depending on the etiological agents involved could be classified as dys-haemopoietic anemia, where destruction is normal and production is not there due to lack of vitamins, minerals or the nutrient substances required to incorporate and produce haemoglobin as well RBCs.

Where the production is normal but destruction is more due to a variety of etiologic agents acting and bring down the quantum of RBCs in the body. Here this may be due to hameolytic crisis or due to hemorrhagic crisis.

Depending on the morphology of RBCs that are observed in the blood smears as normocytic normochromic, macrocytic normochromic, macrocytic hypo chromic and microcytic hypo chromic (less spoken). By utilizing MCV, MCVC and MCH these morphological alterations could be judged.

Etiologically anemias as already stated could be classified depending on blood loss, excessive destruction of RBCs, or shortened RBC life span, depression of bone marrow and less release of RBCs in to peripheral circulation, and depression of bone marrow, release of less number of RBCs due to nutritional deficiencies.

Additionally anemias can be classified as responding or nonresponding. In general macrocytic anemias are responding, normocytic anemias are usually non-responding and microcytic anemias can be either responding or nonresponding.

By this, we are saying that every day number of RBCs is being produced in the body and simultaneously number of them is being destroyed.

Thus it is appropriate to discuss here how RBCs are being produced in the body, what are the chemicals that are required for the production of RBCs and how these RBCs are being maintained in the body of or around 120 days and how the old RBCs are destroyed and how RBCs are becoming old or degenerated. That is briefly we are discussing here the physiology of the RBC or production and destruction. The average life span RBC in most of the mammals is around 120 days except in chicken it is 28 days. The rapid destruction in chicken is due to high temperatures present in the body of chicken.

The RBC is specialized coin like structures useful in the carrying out gas transport (oxygen and carbon dioxide) in the mammals and other species 9 avian). The mammalian RBCs are devoid of nucleus, whereas the avian species having the nucleus. In a simplified manner the RBCs can be looked as simple cells with cell membrane surrounding haeme, an important structure in the transportation of gases, globin and some functional enzymes. As there is no nucleus the amount of

enzymes and their life is limited. Thus, when the capacity of enzymes are degrading macromolecular components and sugars are lost, the cell dies. The RBC, membrane is a bilayer of phospholipids (35%) with interposed molecules of unesterifieid cholesterol (15%) and glycoplipids and proteins (50%). The surface proteins make up the receptors and antigens of RBCs. On the inner surface of the integral membrane proteins bind to a fibrillar cytoskeleton, made up of spectrin and actin, which provides membrane shape, flexibility and durability. Cell volume is maintained by control of sodium and potassium levels through the action of ATP-dependent membrane enzymes. The membrane structural proteins are relatively fixed for the life of the cell as already stated including enzymes. The lipid particularly cholesterol is in dynamic interchanges with that in plasma.

The RBCs composed of 60 to 70% of water, 28 to 35 % of haemoglobin and matrix of largely proteins, of which some 95% is haemoglobin and the rest largely the enzyme systems required for glycolysis, production of the haeme and globin and ATP production. As already stated the loss of the nucleus during maturation is accompanied by the loss of RNA and mitochondria. As a consequence, the mature RBCs have lost the enzymes required for a function of tricarboxylic acid cycle and cytochormes essential for electron transport. The mature RBCs are therefore unable to derive phosphate bond energy form the citric acid cycle and are unable to synthesis i.e. further haeme. The remaining source of energy is through the metabolism of glucose to lactic acid to produce a functional level of ATP. The ATP functions to partition glucose from plasma, maintain homeostatic levels of intracellular sodium and potassium, maintain the biconcave shape, indirectly maintain iron in a ferrous state, and protect the integrity of the globin chains. As a consequence of Embden-Meyerhoff pathway, there is production of the intermediate compounds of 2, 3 diphohphoglycerate which competitively binds to haeme, control oxygen affinity and thus off loading. The balance between intracellular synthesis and utilization of glucose is such that glycogen is not formed and therefore RBCs are critically dependent on a constant access to plasma glucose. Haemoglobin consists of 4 haeme molecules and in turn these are attached to the globin molecules. One molecule of haemoglobin contains four iron atoms and can carry four molecules of oxygen. The most important feature of haemoglobin molecule is the the ability to combine loosely and reversibly with oxygen. The primary function of haemoglobin in the body depends upon its ability to combine with oxygen in the lungs and then to release this oxygen readily in the tissue capillaries where the gaseous tension of oxygen is much lower than in the lungs.

Oxygen doesn't it combine with two positive valences of the ferrous iron in the haemoglobin molecule. Instead it binds loosely with one of the six co-ordination of the valence of the iron atom. This is extremely loose bond so that the combination is easily reversible. Furthermore the oxygen does not become ionic oxygen but carried is a molecular oxygen to the tissue where because of the loose, readily reversible combination, it is released into the tissue fluids in the form dissolved molecular oxygen rather than ionic oxygen.

The globin portion of the haemoglobin molecule is composed of our large polypeptide chains. The nature of these chains determines the binding affinity of the haemoglobin for oxygen. Abnormalities of the chain can alter the characteristic of the haemoglobin molecule as well. The author in the cattle has observed by electrophoresis fraction the haemoglobin molecules could be catergoriesd as A, B, AB types. For instance inhuman beings in sickle cell anemia the amino acid valine is substituted for glutamic acid at one point in one of the four chains. When this type of hemoglobin is exposed to low oxygen, it forms enlarged crystals inside the red blood cells that are 15 microns in length. These make it the cells almost impossible pass through the smaller capillaries, and the spiked end of the crystals are very likely to rupture the cell membrane, thus leading to sickle cell anemia.

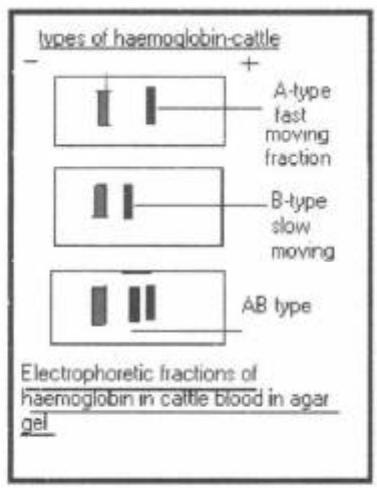


Fig. Electrophoretic fractions of haemoglobin.

Synthesis of haemoglobin begins in the erythroblasts and continues through the normoblast and reticulocyte stages. Even when the reticulocytes leave the bone marrow and pass into the blood stream, they continue to form minute quantities of haemoglobin for another day or so.

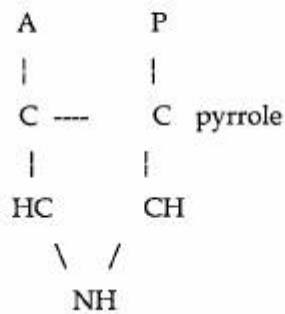
The three essential components for haemoglobin formation are iron, protoporphyrin, and the globin chains. 2/3rds of erythrocyte haemoglobin is synthesized during the rubricyte stage and 1/3 is completed under the direction of messenger RNA and is left in the reticulocyte at enucleating stage. The initial step in haeme synthesis is the intramitochondrial union of glycine and succinyl coenzyme A to form δ-aminolevulenic acid and this step requires B6 help.

Lack of pyridoxine (B6) in the diet of some animals not only decrease the rate of red blood cell formation but also depresses the rate of haemoglobin formation to an even greater extent.

Two molecules of δ-aminolevulenic acid condense to from ringed pyrrole porphobilinogen. This is being taken place in the cytoplasm of Rubriblasts and rubricytes. The formation of a tetrapyrrole that is porphyrin occurs by condensation of 4 monopyrroles derived from phorphobilinogen. These are then transported to mitochondria. Condensation of 3 molecules of porphobilinogen forms tripyrryl methane. Tripyrryl methane condenses to form type I urophorphyrinogen or type III. The uroporhyrinogen and coprophyrinogens which are then transported back into the mitochondria for conversion to protoporphyrin and addition of iron forms haemė.

Important stages in the formation of haemoglobin

I) 2 molecules of α-Ketoglutaric acid + glycine→



II) 4 Pyrrole → Protoporphyrin III

III) Protoporphyrin III+Fe → haeme

IV) 4 haeme + globin → haemoglobin

The primary function of erythrocyte is to serve as a carrier of haemoglobin. Haemoglobin in turn functions as a carrier of oxygen and carbon dioxide and is therefore known as respiratory pigment. In addition, the RBCs contribute to blood volume by means of its mass and consequently affect blood flow dynamics.

The life span RBC varies according to the species of animal. Mean life span of RBCs in cattle is 160 days, in sheep varies from 70 to 153 days and in goat as 125 days, in horse it varies from 140 to 150 days, in pigs 62 days, in dog 110 days and in human 90 to 140 days and in chicken around 28 days. In chicken, the lower life span as already told is due to high body temperature. The red cells with diameter of 7 to 10 μ pass through the capillaries with a diameter of 3 to 5 μ. Normally about 1% of red cells are replaced daily.

The total number of RBCs in 450 Kg. bullocks with a blood volume of 8% is around 300 trillions. About 35 millions are destroyed for every second. Ageing of RBCs may be to exhaustion of enzymes that serve the metabolic function resulting in the accumulation of metabolites leading to loss of maintenance of membrane integrity or it maybe due to exposure of sialic acid groups, which the cells of Reticuloendothelial system recognize and capture them. Thus several

hypotheses have been postulated about the ageing and destruction of RBCs. Fragmentation without the loss of haemoglobin may be one method of RBC destruction. Fragmented portions of cell continue to become smaller until they are only dust like particles, referred to as haemoglobin dust, that are subsequently removed by the Reticuloendelial system.

After erythrocytes are removed from the blood, as discussed in general pathology the Reticuloendothelial system breaks down haemoglobin to iron and globin and protoporphyrin. Iron goes into the storage system of the body and may be reutilized. Globin is degraded, and the polypeptide chains are returned to the amino acid pool. Protoporphyrin is split, converted to bilirubin and excreted.

Diseases of the haemopoieitc system

Polycythemia: It is a condition where there is increase in the circulating erythrocytes in peripheral circulation.

Polycythemia may be relative or absolute.

In the relative polycythemia the increase is in the circulating RBCs are due to the factors that are responsible to cause decrease in the plasma concentration that occurs consequent to vomition, diarrhea, sweating, shock, and collapse, wherein much of water content of the body is lost. Here the increased in the blood cells in the peripheral blod is due to decreased volume of blood.

In the absolute polycythemia the total number of red blood cells is increased and the blood volume remains normal. The absolute polycythemia maybe primary or secondary due to pathological conditions.

Primary polycythemia Vera is due to tumor of erythrpoietic marrow. This has been reported in dogs, cats and in cattle. Experimentally it has been induced in mice by Friend's leukemia virus. The tumor cells even grow in laboratory without erythropoietin stimulation.

Affected animals are presented with reduced exercise tolerance, show signs of polydypsia, signs of neuromuscular dysfunction including head tremors and posterior paralysis. There is mucosal congestion and cyanosis with laboroured respirations. Signs of hemorrhage including epistaxis, haematemesis, and haematuria are seen. Hamematologically thereis marked erythocytosis with RBCs more than 500 million/cm, and haematocirt values of 65 to 80%. Postmortem findings include generalised congestion, cyanosis and arterial thrombosis. Spleenomegaly is seen in most of the cases.

Secondary polycythemia is seen in newborn infants, calves and dogs wherein there is no definite cause has been attributed. Polycythemia oftemporary duration has been observed in animals or individuals who have ascended to higher altitudes. Animals try to adjust for this. Temporary increase in the count of RBCs are seen in animals put to work or in the fight or flight mechanisms due to adrenaline

pouring and consequent to the spleenic contraction. Thus this is seen in sporting dog and racing horses commonly.

Polycythemia is also seen in pathological conditions, wherein there are anoxic conditions consequent to the cardiac and pulmonary diseases. N certain pathological conditions like neoplasms of liver, cerebella haemangiobalstoma, pheochromocytoma, hydronephrosis, cystic adenomas and carcinomas of kidneys, adrenal adenomas and uterine fibroids, there is an increased polycythemia. This polycythemia has been attributed due to increased output of erythropoietin by developing tumors.

Erythropoietin: For erythropoiesis, a humoral substance appears to be of a great importance, in increasing the total number and volume of circulating red cell. The erythropoietin of one species of animal is an active in another species of mammals. It is a glycoprotein containing 24% of carbohydrate and 10% sialic acid. It is found in lower concentrations in the urine also. This is being produced in the kidney. Erythropoietin is a heat stable hormone normally present in small amounts in plasma. The kidney plays a dominant role in the production of this hormone. In response to anoxia the kidney is stimulated to produce erythrogenin (renal erythrpoietic factor); this factor then activates inactive erythropoietin (erythropoietinogen) of hepatic origin. The activated erythropoietin stimulates erythropoiesis causing an increasing circulating erythrocyte mass. In the dog, the kidney is the sole source of erythropoietin; consequently the activity of this hormone is greatly reduced in severe kidney disease. In the cat the carotid body has also been shown to control erythropoiesis.

Erythropoietin production maybe induced in an animal by repeated bleeding, which create anemia or stimulated by use of erythrocyte destroying chemicals. Injection of plasma from erythrocyte-depleted animals stimulates production of erythrocytes, reticulocytes and haemoglobin in normal animals. Tissue anoxia is the specific stimulus for increased erythropoietin production and release. It is presumed that oxygen sensors as opposed to flow sensors occur in the kidney.

Erythropoietin stimulates proliferation ofprimitive haemopoieitc stem cells. There is an increase in the proportion of marrow cells committed to erythropoiesis and with time increase in haemopoieitc marrow volume at the expense of the fat and bone. The mitotic interval is shortened and there is doubling output from that proportion of stem calls. Accelerated haemoglobin from A to C especially in sheep, suggesting an action at the gene level above that of messenger RNA.

The net result of these changes in increased red cell production with an increase in mean cell volume and greater proportion of maturation that spent in the peripheral blood. The presence of shift to polychromatic macrocytes in the blood is erythropoietin dependent they give a rough index of erythropoietin level and effect, indicating both increased levels of erythropoietin and a marrow capability and responding to it.

Types of Anemias in animals and their causes

As stated earlier anemias could be classified as dys-haemopoietic anemias where there is production is less and destruction is normal, and anemias of hameolytic and hemorrhagic crisis where there is more destruction than production.

Dys-haemopoietic anemia is due to less production of number of RBCs from the bone marrow. The destruction of the stem cells is being taking place uniformly every day and every minute. The cause of dys-haemopoietic anaemia can further be divided into the following headings depending how the reduction in the umber of RBCs are taking place.

I) Conditions that affect stromal protein formation

II) Conditions that affect haemoglobin synthesis

III) Conditions that affect marrow itself leading to less number of cell outpour (toxic inhibition)

IV) Conditions that affect the marrow resulting in complete loss of marrow cells (aplasia)

V) Conditions wherein the marrow is replaced by developing cancerous cells etc. (myelophthesic).

I. Conditions that affect stromal protein formation:

i) Dietetic deficiency of B_{12}: Caynocobalamine or B_{12} is required for the synthesis of macromolecules and also for the synthesis of RNA and DNA. B_{12} and folic acid deficiency results in the arrest of or maturation of prorubricyte and Metarubricyte. Depressed DNA synthesis causes delayed nuclear maturation. Ruminants do not suffer with B_{12} deficiency, but they do also not able to elaborate sufficient amount of B_{12} when ruminal flora has been disturbed as in ruminal acidosis, ruminal flora has been disturbed as in ruminal impaction and in a variety of diseases where in ruminal motility is disturbed. The disease is an example of an intact and function stem cell system which is capable of producing hyperpalstic marrow that is not effective in releasing sufficient mature cells, due to inhibition of DNA synthesis and subsequent cell division. Since divisions are skipped, the few resting cells are larger than normal.

ii) Dietetic deficiency of folic acid: folic acid or citrovorum factor is present in most of the plants. On the other hand, there is very little storage of folic acid, and signs of deficiency may appear in animals that are anorectic or received antibiotics. Folic acid depletion occurs in rapidly growing tumors such as high grade lymphomas in dogs and cats. Folic acid is required in the transfer of single carbon atoms and in the synthesis of proteins. Folic acid is required for the maturation of these erythroblasts. In its absence maturation is slowed down and so macrocytic anemia is results.

iii) Deficiency of intrinsic factor: The intrinsic factor which is secreted by the

gastric mucosa helps in the absorption of vitamin B_{12}. The intrinsic factor secreted by the stomach mucosa travels all along into the lower part of the intestine and helps in the absorption of vitamin B_{12} at the lower part of the gut. Whenever gastric disease is there or gastric motility is affected by emotional stresses, the intrinsic factor liberation is questionable. In its absence B_{12} is not absorbed and will be excreted in the faces. Thus ruminants and monogastric animals wherein stomach is affected as in septicemias, bacteriaemic and protozoal diseases and with the plenty of parasites harbouring in the stomach, liberation of intrinsic factor is questionable. This results in setting of anemia.

iv) **Failure to store erythrocyte maturation factor:** Normally B_{12} after absorption will be stored in the liver. In the liver disease sufficient amount of B_{12} is not being stored, resulting anemia setting in.

v) **Hypopituitarism:** anterior pituitary seems to exert a potent influence in erythropoiesis directly or through the thyroid which influences metabolism of carbohydrates, releasing needed energy. Hence in the Hypopituitarism anemias set-in. The blood picture is macrocytic and normochromic one which is becoming to macrocytic hypo chromic if iron stores is lost. Bone marrow is hyperpalstic showing numerous megaloblsts and giant Metamyelocyte.

II) Conditions that affect haemoglobin synthesis: Anemias in animals are mainly due to insufficient synthesis of haeme. This is due to lack of iron or copper or due to chronic inflammatory diseases of bowel.

I. Iron deficiency anemia: Iron is an essential component of haemoglobin, myoglobin, the cytochormes enzymes of mitochondria and hepatic microsomes and metalloflavoproteins and reduced NADH. Iron deficiency results either a deficiency of the element in the diet or maybe due to impaired absorption or excessive loss. The only natural diet of animals is milk which is deficient in iron and therefore deficiency of this is seen is sucking animals. Iron is called as one way element. There is mucosal block operating. Once iron is absorbed and entered into the body unless there is hemorrhage iron won't come out of the body.

Body tries to absorb the amount that is just required for its function. Especially milk of sows is poor in iron and so **piglet anemia** develops if rooting is prevented. Due to burrowing on to the soil piglets can get the iron from the soil. Excessive phosphorous and phytic acid form insoluble complexes of iron in the gut, which are excreted through faeces. In young, growing animals and pregnancy, body requires increased amounts of iron. The piglets are much more susceptible because of its rapid rate of growth. Mortality is higher in the winter than in other seasons, partly because of confinement and partly because of increased susceptibility to cod. This is also seen in puppies of the larger breeds; it is probably responsible also for the anemia which is often observed in calves on diets solely of milk. Iron deficiency seriously impairs defensive mechanisms and predisposes piglets to a variety of infectious diseases. Thus this is called **piglet anemia syndrome**. In this

piglet anemia due to watery blood (viscosity is less due to less number of cells in blood), the heart beats at a faster rate which could be heard form a distance and is called thumps.

Excessive loss of iron is the result of chronic loss of blood and is an important cause of iron deficiency; it is the only cause in the adult animals since normally only very small amounts of iron are excreted and lost.

Normally protoporphyrin plus iron in the presence of copper and Ferro chelate produce haeme structure. 4 haeme molecules unite with 4 globin molecules to form haemoglobin molecule. Molecular weight of haemoglobin is around 66,000 to 69,000. Iron content of haemoglobin is 0.334%; atomic weight of iron being 55.84; the molecular weight of haeme is 16,700. The red cell being the haemoglobin carrier spends only about less than a second in traversing a capillary. When saturated with oxygen, 1 gm of haemoglobin carries about 1.34 ml of oxygen. Lack of iron slows protoporphyrin and globin synthesis and there is delayed rubricyte maturation. The marrow transit time of rubricyte is extended beyond the normal 4 days and the erythropoiesis is thus termed ineffective. The blood pressure is that of normocytic hypo chromic and becoming microcytic and hypo chromic.

ii. Copper deficiency:

Copper deficiency results in diminished haemoglobin formation. Copper forms a component of cytochromic oxidase and diminished activity of this enzyme limit the synthesis of haeme. Approximately, 25% of ingested copper is absorbed, primarily from the stomach and upper small intestine. Absorption is like of iron, in it that is energy dependent two step process involving an intraepithelial metallothionein like protein that may transfer the copper to the plasma carriers. Iron deficiency anemias also go away with copper deficiency.

iii. Dietetic deficiency of ascorbic acid:

Vitamin C or ascorbic acid is a dietary reducing agent and so facilitates the reduction of Fe+++ (ferrous) to Fe++ (ferric) state which is easily absorbed. Vitamin C is also required for the synthesis of folic acid and for its conversion into active form folinic acid.

iv. Dietetic deficiency of pyridoxine: (B_6):

Vitamin B_6 is required for formation of the precursors of deltaminolevuinic acid, which then forms the pyrrole rings and ultimately protoporphyrin. Deficiency of B_6 in swine results in microcytic normochormic anemia.

v. Dietetic deficiency of nicotinic acid:

Nicotinic acid is concerned in the synthesis of pyridine nucleotide which takes part in cell respiration. This deficiency of Nicotinic acid interferes with the respiration of immature red cells this is noticed in dogs and pigs.

iv. Dietetic deficiency of riboflavin:

Riboflavin is concerned in the metabolism and arrangement of amino acids of the protein and haemoglobin molecule and so useful in haemoglobin synthesis. This condition is met within dogs.

vii. Deficiency of thyroxin:

Thyroxin along with vitamin C is required for the conversion of folic acid into folinic acid. Thyroxin is involved in the metabolism of carbohydrate and fats.

iii) Toxic inhibition: The marrow appears to be normal but due to presence of toxins elaborated by different parasites or chemicals, production process in interfered.

I. Chemical poisons : Anticancerous drugs, like nitrogen mustard, folic acid antagonists, certain antibiotics and sulfonamides, metal like bismuth, arsenic and gold; certain other substances like zinc compounds, hair dyes and insecticides will produce this type haemolytic anemias.

Anemias due to uremia: In advance cases of uremia there, is anemia due to suppression of erythropoiesis. 4 principal mechanisms are involved in this anemia. Excessive hameolysis due to retention of creatinine and guanidosuccinic acid, toxic depression of erythropoiesis, loss renal erythropoietin, and blood loss from kidney. The blood picture is normochromic and normocytic anemia.

ii. In parasitic infections like oesphagostomiasis, chronic tuberculosis infection, Brucellosis and in radiation therapy.

IV. Aplastic anemia:

Due to inactivity of bone marrow the anemia is normochromic and normocytic with no regenerative forms. Clinically mucosa is paler, lethargy and reduced activity is seen. This is due to exhaustion of bone marrow as seen in chronic hemorrhages, consequent to blood sucking worms, due to deficiency vitamin K and prothrombin. These are also due to secondary ones. The primary aplastic anemias idiopathic, where no known cause is seen. Viruses cause marrow depression example is of parvovirus and feline leukemia virus. All forms of estrogens drugs potentially myelotoxic, drug like chloramphenical and furazolidine are also myelotoxic.

V. Myelophthesic anemia:

Replacement of bone marrow by other tissues. This condition is found in secondary metastasis other tumors, osteodystrophic diseases where bone marrow, myeloid tissue is replaced by connective tissue another primary tumors of reticulo-endothelial system (Hodgkin's disease). The anemia of this leukemia is due to stem cell displacement. Diseases of bone marrow, immune depression and chachexia. Marrow failure with consequent loss of stromal cells and represents the end of leukemia.

Hemorrhagic anemia

Hemorrhage is the loss of blood that is extra vascular destruction of RBCs. Here the RBCs are producing normally but the destruction is excessive, that is the blood loss is greater than the production. In case where there is balance between blood loss and production, the picture is of normocytic normochromic anemia with many regenerative forms. When the loss of blood is too much and turns to a chronic course, the immature blood cells like rubricytes and reticulocytes are seen in the peripheral blood. When the iron and nutrient sources of the body are depleted, the picture turns to one of microcytic hypochromic anemia. Ultimately, when the bone marrow becomes exhausted and is no more able to cope up (aplastic stage), a normochromic normocytic anemic picture is seen without any reticulocyte shower or immature forms.

Blood loss anemias are usually associated with acute, sub acute or chronic hemorrhages. Acute hemorrhage usually follows trauma or surgical procedures. This is seen in association with ulceration of stomach in pigs, bleeding abomasal ulcers in cattle, cocidiosis in poultry, bovine enzootic haematuria, haemonchosis and ancylostomiasis. Ancylostomiasis occurs in canine whereas cattle, sheep and goats suffer with haemonchosis.

Severe coagulation defect may also produce acute hemorrhages such as that occurring in poisoning associated with sweet clover, warfarin or bracken fern and in animals with coagulopathies.

Coagulation defects like hemophilia, a condition in which coagulation of blood does not occur after an injury. It is an inherited defect. This occurs in dogs and swine.

Prothrombin deficiency is seen consequent to liver disease where liver fails to elaborate fibrinogen, factor V, prothrombin, factor VII, and factor IX. Deficiency of bile is seen liver diseases, leading to decreased absorption of vitamin K. This leads to failure of synthesis of clotting factors, namely prothrombin.

Vitamin K deficiency occurs in fowl's consequent to the disturbance of intestinal flora due to antibiotics feeding. Pigs medicated with sulfa drugs and antibiotics also suffer due to loss of vitamin K producing microorganisms in the intestines. Similarly in diseases of intestines, absorption of vitamin K is interfered with as it is seen in colitis.

Anaphylactic shock in dogs, large amounts of heparin are liberated, heparin acts as an anticoagulant resulting in the bleeding.

Some snake venoms are also act as anticoagulants with resultant bites of these reptiles leads to hemorrhagic anemias in animals.

A common cause of chronic hemorrhagic anemia is parasitism. Internal parasites such as shook worms, stomach worms, coccidia, nodular worms and liver flukes

produces anemia by combination of blood loss and poor nutrition. External parasites such as sticks, blood sucking lice and certain fleas may also produce anemia. Chronic blood loss resulting in anemia may occur in association with gastrointestinal lesions such as hemorrhagic gastritis andeneritis. Bleeding into the genito-urinary tract occasionally produce anemia, which usually occur consequent to the developing neoplasms.

Hemorrhagic diseases occur consequent to the purpura. Purpura is the accumulation of blood, under the skin due to spontaneous rupture of the capillaries. This purpura occurs in a variety of diseases such as hemorrhagic septicemia, and anthrax. In most of the diseases, extensive purpura consequent to the damage to the endothelium leads to bleeding and death of the animal. This bleeding will be exhibited by either petchiae or ecchymotic changes in the blood vessels. Purpura as occur consequent to the damage to the blood vessels in the hypersensitive reactions. In vitamin C deficiency hemorrhages occur due to increased capillary permeability and capillary fragility.

Bleeding in horses is seen consequent to epistaxis. Bleeding through nose occurs due to strenuous exercise. It is due to a nonsex linked recessive character. The walls of the blood vessel are thin and so rupture whenever distended during great exertion as in racing.

Haemolytic anemia

Haemolytic anemia is associated with intravascular destruction of RBCs. Here the production of RBCs is normal, but these are destroyed excessively. The extensive destruction and shortened life span of RBCs may be due to a variety of causes. This is due to blood protozoan parasites, bacteria infections, viral infections, chemical agents, introduction of principles from poisonous plants, metabolic diseases or due to isoimmunisation phenomenon or due to autoimmune reactions.

The most common bacterial diseases where in anemia occurs are leptospirosis, and clostridium hameolyticum infections.

Haemolytic anemia due to letpsoira occurs in cattle, sheep and dogs. The bacteria strains involved in canines are infections with Letpsoira icterohaemorrhagiae. Infection with these bacterial results in hemolytic processes. Clinically the animals are icteric and show hemoglibinuria. Leptosiral infections in bovine are often accompanied by anemia and hemoglibinuria. The species involved is Leptospira Pomona.

Haemolytic anemia so occur is caused by clostridium haemolytic in sheep and cattle. During these infections, there is a fever and haemolytic crisis with accompanying hemoglibinuria. The total RBC count may fall down below to 2mllion/cmm.

Haemolytic anemia Is seen in horses affected with equine infectious anemia virus. Clinically the disease is characterized by intermittent fever, jaundice, oedema

and peticheal hemorrhages in the mucosa. The anemia occurs in a chronic course of the disease. The life span of the RBC will be considerably reduced. The anaemia associated with this disease occurs due to immunological events leading to the premature removal of sensitized cells from the circulation.

A wide variety of chemical agents that are capable of causing haemolytic anemia in animals include copper, lead, phenothiazine, saponin, naphthalene and certain drugs such as acetanilide, nitorfurantoin, neoarsphenamine, phenacetin, and some sulfonamides.

Copper poisoning: sheep are the animals most susceptible to excessive intake of copper, either from the consumption of plants containing high-level of copper or from excessive drug that is used for deworming. Too heavy does of water containing copper sulfate gives as a preventive or curative for stomach worms. The toxic doses of copper sulfate for sheep are 20mg/kg body weight. Copper exhausts the antioxidant system of RBCs. Too much of supplemental mineral mixture containing copper sulfate also is poisonous.

This element accumulates in liver and under conditions of stress may be released to the blood stream resulting in rapid haemolysis of erythrocytes. Hemoglibinuria is constant clinical sign and is accompanied by typical haemolytic crisis. Bone marrow is characterized by hyperpalstic as a result of response to acute blood destruction.

Onion poisoning: Occasionally fatalities occur in cattle and in sheep fed onions, in regions where they are excessively grown. The toxic principle is dipropyl disulphide. In the cattle the intake should notexceed 10 g/ 100 kg of body weight. If the dose exceeds more than 15 g/ 100 kg, death of ruminant is imminent. In the colon dimethyl sulfide is formed which is poisonous. The symptoms are haemolytic anemia with a hemoglibinuria and icterus. The carcass smells that of onion. Poisoning by castor seeds: ricin in castor seeds produces haemolytic and so ingestion of large quantities of castor seeds results in haemolytic anemia.

Lead poisoning: Consumption of lead results in fatal haemolytic anemia. In cattle it may be acute, sub acute or chronic. In horses acute poisoning is common. Lead comes by way of paints, throws away batteries and industrial materials. The licking habit of ruminants makes them especially to suffer with lead poisoning. In animals lead compounds enter the body orally, and when inorganic form through the skin. When lead poisoning is present, haemoglobin synthesis is inhibited leading to an accumulation of Metarubricyte in the bone marrow. Lead poisoning in dogs produces basophilic stippling, i.e., presence remnants of nucleic acid in the cytoplasm. In sheep and human beings, lead is transferred transplacentally. Lead destroys much of central nervous system activity.

Phenothiazine poisoning: (Drug sensitivity): Though it is a good anthelmenthetic, sometimes even in therapeutic doses, has been found to be haemolytic in horses.

Cattle are also susceptible though to a lesser extent than in horses. The symptoms are haemolytic anemia with hemoglibinuria.

Methylene Blue: A severe haemolytic anemia may develop in cats receiving urinary antiseptic containing methylene blue. The packed cell volume dropped from 40 to 13% in certain cases.

Naphthalene used as a moth balls may be accidentally ingested by pet animals and haemolytic anemia results.

Hypersensitivity to certain drugs like sulphanilamide, quinine, paraminosalycylic acid and some antipyretic drugs may result in haemolytic anemia.

Snake venoms: snake venoms contain lecithinase which destroys the membrane of RBCs leading to haemolysis. Not all snakes but certain reptile like cobras contains this enzyme in venom.

Metabolic diseases: Post parturient hemoglibinuria is a disease usually found in high producing dairy cows and occurs at 2 to 3 weeks following parturition. It is characterized by anemia in addition to the hemoglibinuria. The total erythrocyte count may drop down to less than 2 millions/ cmm. The etiology of this disease is unknown. In fact this is present certain part of North India especially in Uttar Pradesh. Phosphorus deficiency has been attributed because of low blood phosphorus value synthesis cases.

Cold hemoglibinuria in calves: Consumption coldwater has the capacity to produce a hemoglibinuria in calves and occasionally in older cattle. It is characterized by an intravascular haemolysis as well as hemoglibinuria.

Immunohaemolytic diseases of the newborn: Haemolytic disease of the new born occurs in the horse, pig, dog, cat and calf. It resembles eryhtroblastosis foetalis in the human. However there is difference between human and animals. In the human, the antibodies against the sensitized antigen passes through the placenta, whereas in the animals as the placenta is having number of barriers (histological layers), the sensitised antibodies against antigens will be excreted in the milk. The newborn animal must receive these antibodies from the colostrums during the first few hours of life. Haemolysis occurs in foals wihtin 12 to 96 hours after the birth. Haemolysis is seen in protozoan infections like anapalsmosis, Babesiosis of cattle, eperythrozoonosis and Ehrilichia canis of canines. Hyperspleenism in certain dogs and even in fact in humans, it is common. The hyperpalstic Reticuloendothelial cells are responsible for causing haemolysis by destroying the RBCs of even normal ones. This is also common in chronic Babesiosis of cattle.

Secondary effects of anemia

The secondary effects and symptoms noticed in anemia are mainly the results of anoxia, which is lead to hyperplasia of haemopoieitc tissues, evidence by

regenerative forms, which are larger and more fragile and less efficient than normal RBCs.

The symptoms are dyspnoea and tachycardia. The animals and human feels fatigue due to incomplete metabolism. There is compensatory hypertrophy of heart in the early stages. If deocompensation sets in chronic venous congestion and resultant hydropericardium and ascites may occur.

There are extensive hemorrhages into body. The mucous membranes appear pale; there is glossitis, anorexia, flatulence, constipation, diarrhoea, vomiting, albuminuria, fever and Spleenomegaly.

Leukocytic disorders

Knowledge of Leukocytic kinetics helps in the assessment of health of the individual. Thus leukocytes consist of a study of granulocytes and granulocytes. The granulocytes are neutrophils, eosinophils and basophils. The agranulocytes are leukocytes and monocytes. Briefly mentioned here is the functional unit of the leukocytes in healthy animal and the counts thereof. Leukocyte counts should be an integral part of clinical evaluation. Correlation of these data which form an integral part of clinical pathology helps in the diagnosis as well prognosis of the disease.

Total and differential leukocyte counts: If properly interpreted, are of value in confirming or eliminating in tentative diagnosis and aid in making a more accurate prognosis. Leukocyte count reflect the susceptibility of the host, virulence of the infecting organism, nature and severity of the disease processes, systemic response of the individual and duration of their disease process. Leukocytes in a hemograms are usually expressed as thousand / cmm. The usual counting method in Neubauer chamber of the peripheral four squares and the dilution mixture consists of glacial acetic acid and 1% aqueous solution of gentian violet.

Furthermore the leukocytes are partitioned by differential counting methods by using any one of the Romanowsky stains like Leishman or Giemsa etc. The differential counting of leukocytes will be done by counting 100 cells then expressing the 5 of the counted types.

Morphology of leukocytes: A. Granulocytes: The granulocytes have an irregularly lobulated nucleus, the segments of which are often connected only by thin filaments. This may give the false impression that the cell is multinucleated. In domestic animals, the granulocytes are larger than erythrocytes and measure 10 to 15μ in diameter. They have distinct amoeboid motility. The cytoplasm contains coarse or fine granules which are distinguished by their affinity for certain dyes in complex stains used on blood smears. According to the staining qualities the granulocytes are classified as follows.

Neutrophils: A slender, curved, segmented nucleus is characteristic. In counting neutrophils, the band or stab cells, which are younger forms, are distinguished

by horse shoe shaped nuclei that show no segmentation or lobulation. The cytoplasm has a fine dust like granules, when stained appear as light purple or violet by the common bloodstains and may be seen to contain oxidative enzymes by peroxidase reaction. The secondary or specific granules are peroxidase negative and form the background of cytoplasmic density of the mature cells. In toxemic state, the primary granules are visible in the cytoplasm of mature neutrophils as fine azurophilic or pink granules when stained with Romanowsky stains. In systemic toxemia there is vacuolation of the cytoplasm and doehle body formation. Doehle bodies are composed of lamellae of rough endoplasmic reticulum persisting from precursors of immature cells and can be seen as bluish which the normal basophilia of immaturity is.

There is considerable variation in enzyme content of granules in various species. With the dog and cat neutrophils there is lack of alkaline phosphatase. In rabbit, guinea pig and chicken, the cells that correspond to neutrophils are called heterophils. They have granules that stain red but are not the same as those of eosinophil granulocytes. The heterophil granules of the rabbit and guinea pig are rounded or rod shaped and is smaller than eosinophil granules which are all round. In chicken the heterophil granules are large, elongated and bright red, whereas the eosinophil granules are round and brick red.

Neutrophils have an average diameter of 12 μ. In man, horses, swine, dog and at, the neutrophils are predominant cells of blood. In ruminants, rabbits and chicken, the lymphocytes are predominant. The normal count of blood cells is given in the table. The total leukocyte counting the animals varies with age. This in bovines the total leukocyte count in adults will be as below as 5000/cmm compared to higher counting in the younger animals. Band neutrophils are commonly seen in the peripheral blood of the healthy bovines. The blood picture in association with parturition of bovine closely resembles as that of stress with leukocytosis and an increased number of neutrophils and a decrease in the lymphocytes and eosinophils of the peripheral blood.

W						W
	R	R	R	R	R	
	R	R	R	R	R	
	R	R	R	R	R	
	R	R	R	R	R	
W						W

Table 5 Ruled area on improved Neubauer haemocytometer. For total leukocyte count, the WBC in the area (W) is counted. The total erythrocyte count is completed by counting all cells in the squared labeled R.

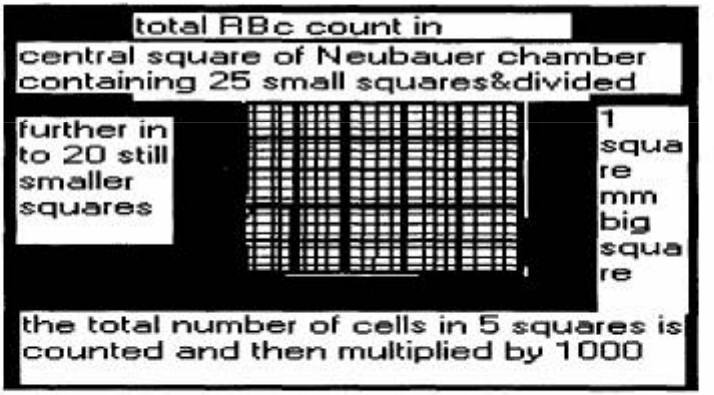


Table 6. Total leukocyte values for various species of domestic animals

Species counts	Range of total leukocyte counts x 10^3 (in thousands)	Average total leukocyte count
Bovine	4-12	7.6
Ovine	4-12	7.6
Caprine	4-13	12.0
Porcine	10-22	16,0
Equine	5.5-14	10.0
Canine	6-15	11.0
Feline	5.5-19	12.5

Table 3. Differential leukocyte values for various species of domestic animals

Species	% Bands Neutro-phils	% Segmenters neutrophils	% lymphocytes	% monocytes	% eosinophils	% Basophils
Canine	0-4	60-75	12-30	3-9	2-10	Rare
Feline	0-2	35-75	20-55	1-4	2-10	Rare
Bovine	0-1	15-45	48-75	2-7	2-15	0-2
Equine	0-2	30-65	15-50	1-8	1-10	0-3
Ovine	0-2	10-50	40-75	1-5	1-8	0-3
Porcine	0-5	28-47	39-60	2-10	1-11	0-2
Caprine	0-2	30-48	50-70	1-4	3-8	0-2
Human	0-1	62	30.0	5.3	2.3	0.4

Factors affect leukocyte count:

The normal total leukocyte count for the cow is influenced by age of animal. Many investigations rest a higher leukocyte count in calves than in adult animals. The leukocyte count in an average healthy cow is around 5000 cells \cmm. The number of circulating lymphocytes is slow in the newborn calf and increases as the animal begins to grow, only to slightly decrease with age. At birth lymphocytes represent only about 33% of total leukocytes and rise to 72% in four months and gradually decrease until the normal adult develop 50 to 60%. There are decrease in neutrophils and an increase in eosinophils as animal's age advances.

Band neutrophils are not common in the peripheral blood of the healthy bovine. Estrous may result in slight increase in the leukocyte count. During parturition there is increased leukocytosis.

The thorough bred horses called as hot blooded have total leukocyte count higher than cold blooded animals. In thorough bred horses there is an approximate 1:1 ratio between neutrophils and lymphocyte's.

Total leukocyte counts are highest in young dogs as high as 15,000 to 16000/ cmm. In older dogs the leukocyte count is 7000/cmm. The % of lymphocytes in the normal adult is over to 20 to 25.

The normal total leukocyte count in the cat is as high as 40,000/cmm.

The normal total leukocyte counts in piglets are 10,000-20,000. The differential count in young piglets is around 75% at birth followed by 45% at the end of the first week. In adult goats, it is around 45 % of neutrophils and around 75% by the end of first week of life. The total count in adult is around 11000/c mm. The neutrophils and lymphocyte ratio in domestic animals are as follows Cattle, 28:58; sheep, 30:60; Dogs, 70:20, Horses, 55:35; Cattle 60:30; pigs, 35:50.

The phagoyctic vacuoles of neutrophils have a pH as low as 4.5 and adherence of activated cells to endothelium may occur and cause vascular injury. Thus two functional compartments are recognized within the blood vessels for neutrophils. The marginal pool consisting of neutrophils which marginates along the vascular endothelium, and the circulating pool, consisting of cells free in the blood. Progression through these compartments, with release into the blood, requires about 120 hours. The blood serves as a vehicle to transport neutrophils to tissue with a transit time of about 10 hours. When neutrophils enter tissues, they do not return to the blood stream. There is continuous movement of neutrophils across the mucous membrane and tissues. Neutrophils complete their maturation under the influence of a number of factors including interlukin-8.

Leukocytosis. Increase in the number of leukocytes in blood is called leukocytosis. As rule, one type of cell only is responsible for the elevation, but there may be simultaneous increase in several types. Usually absolute increase in neutrophils counts will be there. The degree of leukocytosis s depend on several factors like

severity of the infection or virulence of the organisms, resistance of the animal; well marked leukocytosis indicates good resistance of the animal. Mild degree of leukocytosis indicates that the body is not reacting well or that the infection is too slight to elicit much resistance. Leukocytosis absent if the infection is extremely mild or when it is so severe as to overwhelm the animal before it can react. Species vary into their response to stress. Dogs and cats will commonly respond to bacterial infections with a total leukocyte count of 30,000 to 60,000 /cmm. Cattle may show little or no elevation in the total leukocyte count, although there will be a significant increase in the number of neutrophils. The horse demonstrates a more pronounced leukocytosis reaction than that in cattle, but not to the extent displayed by the dog or cat. Greater neutrophilic leukocytosis is produced by localized infectious process than by a generalised process.

As already discussed physiological leukocytosis refers to a total leukocyte count above the normal, without the association of any known disease process. As a rule, all cell types participate in the increase, but there may be a tendency towards a neutrophilia. Young animals like pups, calves have an increased total leukocyte counts. Lower leukocyte counts are seen in piglets, whereas horses and sheep as young or old does not show any significant differences. In the dog, digestion increase in leukocyte and begins with an hour or so after eating, fully reaches maximum in about 3 or 4 hours and then decline. In their total leukocyte count may increase more than 5,000/cmm above than normal count in a period of 2 hours after digestion. Horse showed a weak digestion leukocytosis. Digestion leukocytosis seems to be absent in the herbivore, possibly due to digestion be going slower and also constantly. Leukocytosis seen after strenuous exercise due to a redistribution of cells normally shunted off out of active circulation. The same effect is seen in convulsive seizures. Apprehension, fear and pain may account increase leukocytosis that is usually transient and not accompanied by any new cell formation. The increase occurs promptly disappear within 1 hour. Epinephrine injections produce leukocytosis. In cattle, about $3/4^{th}$ of cows show repartee increase in the total leukocyte count and neutrophils the great increase being observed in the 2 weeks before parturition.

Pathological leukocytosis: The simultaneous appearance of fever and leukocytosis means some exudative inflammatory processes of infectious origin or a tissue destruction from which toxic products are being disseminated. In acute infections with pyogenic bacteria leukocytosis seen. Organisms of staphylococcus, streptococcus, and dipthreoids are responsible for causing leukocytosis in animals. Absence of fever No infection conditions associated with leukocytosis are diabetes mellitus, uremia, malignant neoplasms, acute hemorrhages or haemolytic crisis, and drugs and chemical poisons.

Neutrophilia: Increase in the number of neutrophils in the peripheral blood is called neutrophilia. When bone marrow is stimulated immature neutrophils may be found in the peripheral blood, in greater numbers than normal. This

phenomenon is called shift to the left. To measure this shift to the left, Schilling has proposed his hemograms in which the four following stages of neutrophils are estimated. Myelocytes, juveniles in which the nucleus is indented, the band for or stab in which the nucleus is curved or bent and the segmenter, the fully matured forms.

The shift to the left of neutrophilia either may be a degenerative or re-generative form. If it is a degenerative form, the total leukocyte count will steeply falls down in spite of the immature forms in the blood. On the other hand, the regenerative shift wherein increased activity of the bone marrow immature forms are a little more in number than in mature forms. Hence the total leukocyte count is normal or increased.

In the degenerative reaction the immature forms are far more than in number than the mature ones. In this condition, there is depression in the maturation of leukocytes in the bone marrow and this denotes a very severe infection with unfavorable prognosis. In severe infections, neutrophils contain large toxic granules, i.e., and Doehle's bodies. Thus neutrophils produced under conditions of severe toxemia presumably have decreased function.

Causes of neutrophilia; Physiological: Neutrophilia is found in new born animals, in pregnancy, during exercise and with high protein and in the oestrous of animals.

Pathological conditions: In acute infections, neutrophilia is seen especially in bacterial infections like coccal infections, leptospirosis, and actinomycotic and actinobacillosis infections. Certainof the viral infections like poxand other viruses where secondary bacterial infections will take an upper hand. In certain metabolic diseases like uremia and burns, in poisoning cases with lead, digitalis, mercury heavy neutrophilia is seen. Neutrophilia also common after surgical operations. Neutrophilia is seen in cute infections like generalised septicemia, peritonitis, empyema, metritis, leptospirosis, anthrax and in localized conditions like abscesses, furunculosis, osteomyelitis, pyelitis, otitis, tonsillitis, pharyngitis and intoxications like uremia, acidosis, eclampsia and in lead poisoning, mercury and arsenic poisonings. After acute hemorrhage especially in serous cavities, after acute hemolytic crisis, in surgical traumas and in malignant neoplasms neutrophilia is seen.

The rate of restoration of the marrow maturation and storage pools and the blood pool is determined by the severity of the inflammatory process and rate and degree to which it is controlled. If the infection is rapidly checked neutrophils in numbers return to normal and band neutrophils disappear. However, if the infections not checked, stem cells commitment to granulopoiesis continues.

The immature neutrophils of myelocyte series are elaborated in different leukamemic conditions which will be discussed latter in detail.

Neturopenia: Decrease in the number of neutrophils in the peripheral blood is

called as neturopenia. Neturopenia results from depletion of the circulating and storage pools in animals with overwhelming infections. Dexamethasone suppresses the function of neutrophils rather than the quantity. Neturopenia occurs due to immune mediated functions. Parvo viral infections in dogs and cats and a variety of antibiotic substances also interfere with stem cell synthesis resulting in neturopenia.

Here we introduce a term often used is agranulocytosis, indicates complete disappearance of the granulocytic series in the bone marrow. The causes include toxic chemicals and drugs acting on leukopoeitic tissues those are benzol, arsenical preparations, barbiturates and amidopyrines. Bacterial toxins of Staphylococcus aureus, Streptococcus hameolyticus, streptococcus viridians and X-ray irradiation brings about neturopenia.

Dysfunction of leukocytes; Leukocytes function is significantly altered in endogenous toxins as occurs in uremia, and in immuno-deficiency states of body. Selenium deficiency causes reduced intracellular killing and the 3-omega fatty acid reduces leukotrienes E4 and thus have an inflammatory effects. Dexamethasone suppresses the functions of both neutrophils and lymphocytes. Antibiotics vary in their ability to enter neutrophils that is tetracycline and chloramphenical decreased chemtoaxis, and tetracycline and polymixin-B decreases both phagoyctic activity and oxidative metabolism. Finally the systemic effects of cancer includes impairment of phagoyctic functions.

Leukemia reactions or leukemoid blood picture: This is similar to regenerative left shift. There is sufficiently elevated leukocyte count with left shift to include myelocyte and at times Progranulocyte. The process stimulating leukocytosis is due to the persistence of the infection and not due to any cancerous conditions (leukemia). Such a reaction can be differentiated from a true leukemia by means of bone marrow examination. Pyometra in dogs is an example of leukemoid reaction where the total leukocyte count will be more than 60,000/cmm with a shift to left, and presence of immature forms.

Leucopenia:

Leucopenia is a reduction in the leukocyte count below normal values. Leucopenia either may be balanced that a decease in all cellular elements or maybe confined to a single cellular element. The latter is referred to by the more specific name neutropenia, lymphopenia are eosnopenia. The general causes of neturopenia related to alteration in the bone marrow and are known as three Ds. 1.Degneration (ineffective granulopoiesis), 2. Depression (reduced granulopoiesis), 3) Depletion (reduced survival in blood). If any of these alterations occur in the bone marrow, the number of neutrophils in the peripheral circulation is decreased.

Eosinophils: These are the bilobed nucleated cells and the nucleus looks like a spectacle frame distinguishing the lobes. The nucleus of eosinophil is coarser than

that of neutrophils. The cytoplasm is filled with coarse refractile granules, which have an affinity for the acidic aniline dyes. Their chemical nature is mainly protein and phospholipids. These granules are larger in the horse. In the dog these granules are relatively less abundant than in other species and has bluish gray cytoplasmic background. The cells have a diameter of 10 to 15μ in diameter.

Eosinophils contain a basic protein of their specific granules, a potent peroxidase and halide system and produce substances that inactivate the leukotrienes of anaphylaxis. They have receptors for complement 3b which is probably the means by which they bind to tissue parasites. Another function of eosinophils, which occur in the body surfaces in the modulation of inflammatory reaction, involving mast cells, basophils and IgE antibodies. Products mast cells serve chemo attractant molecules for eosinophils. In allergic inflammation, eosinophils neutralize histamine and are capable of inhibiting mast cell degranulation.

Infiltration of tissue by eosinophils occurs somewhat independently of other leukocytes. Eosinophils are attracted to tissues as part of t-lymphocyte mediated immune response to certain antigens, mostly allergens and antigens of helminthes. Eosinophils are mainly tissue cells especially in tissue with an epithelial surface with the environment such as repertory and gastrointestinal tracts. Therefore it is possible to have marked marrow eosinophilopoiesis and tissue eosinophilia without significantly increased number of circulating eosinophils, since their blood transmission to tissue is short.

Eosinophilia: It means increased number of eosinophils in the peripheral circulation. The causes are allergic diseases such as hay fever, serum sickness, parasitic infections, skin affections like edema, scabies, following recovery; from acute diseases, in chronic eosinophilic myositis of dogs, following spleenectomy, following administration of poisons and drugs such as arsenic, copper, sulfa drugs, chlorpromazine and digitalis. In certain diseases of haemopoieitc system like chronic myelocytic leukemia, Hodgkin's disease and following irradiation.

Eosinopneia: This is a term used to denote the decreased number of eosinophils in the peripheral circulation. This is characteristic of acute infections. Decreased number is seen in stress conditions, after administration of ACH or corticoids as a therapeutic measure and hyperactivity of adrenal gland occurring as a consequence of hyperplasia or neoplasia. In fact any infections or after operations or after drug therapy reappearance of eosinophils in the peripheral blood indicates good prognosis.

Basophils: These are rare cells present in blood and make up about 0.5% of the leukocytes except in chicken, wherein the average at about 2%. They may have a coarse polymorphic nucleus and rather sparse, coarse basophilic granules in the cytoplasm. The granules are water soluble in contrast to those of either granulocyte. If properly stained they give the peroxidase reaction. Basophils are about 10μ in diameter. There is tendency for the granules to obscure the nucleus. The granules

stain blue black and often vary in size within a single cell.

Basophils when they lurk to the peripheral tissues are called as mast cells. The mast cell nucleus is not lobed. The granules are metachromatic stained by a toludine blue given a clear violet reaction. Basophils arise from bone marrow precursors which can fit be recognized at the Promyelocyte stage. Basophils are easily deregulated in slide while staining and may be mistaken for neutrophils. Both basophils and mast cells contain histamine and heparin. The histamine concentration in mast cells is some 20 times greater than in basophils. Mast cells contain hydrolytic enzymes and 5-hydroxy trypamine which are not present basophils. Basophils are capable of phagocytosis and are easily motile. Unlike mast cells, which degranulation by exocytose and can then generate, basophils largely degranulation by diffuse internal lyses and have less synthetic capability.

Basophils and mast cells have IgE binding sites, and following formation of IgE-antigen complexes, activation of the cells results in the secretion of granules contents, such as histamine, slow reacting substance of anaphylaxis, platelet activating factor, eosinophil chemo tactic factor and heparin.

In addition to their specific involvement in hypersensitive reaction, basophils release heparin during postprandial lipemia which activates the enzyme lipoprotein lipase. Steroid hormones appear to cause a reduction in blood basophils, and eosinophils, and basophils are rarely found in blood or normal cats and dogs.

Basophilia: Increase in the absolute number of basophils in the peripheral blood. Seen in hypothyroidism, after protein injection (vaccination), estrogen injection and accompanying eosinophilia. This is seen in immune haemolytic anemias and canine hyperadrenocorticism. Seen in dogs with heart worms. The increase of basophilia is seen with chronic myelogenous leukemia.

Monocytes; These cells often have a diameter of 16μ or more in blood smears. They have abundant, weakly basophilic gray blue cytoplasm, which often show pseudopodia. The large nucleus is usually indented on one side and therefore appears kidney shaped or horse shoe shaped. The nucleus does not stain so intensely as does that of a lymphocyte and the chromatin structure is more delicate. When azurophilic granules are present in monocytes they are much finer than they are in lymphocytes. Newly released monocytes tend to have more cytoplasmic basophilia and lack vacuolation. The vacuolation of monocyte is common in animals with inflammatory disease.

Monocytes leave the blood to replenish the entire spectrum of tissue macrophages known specifically as Reticuloendothelial system such as macrophages of lungs, spleen, marrow, peritoneum, lymph node sinuses, and Kupffer cells of liver, Langerhna's cells of subcutaneous tissue, and possibly the interdigitating reticular cells of germinal centers. Some writers discourage the term of Reticuloendothelial system associated with macrophages and delineate them as specialized cells as reticular cells of interstitial tissue produce reticulum or collagen and are weakly

phagoyctic. They are fibroblast derived and these authors have the opinion that these cells produce fiber which are argyrophlic, whereas macrophages does not so.

Monocytes are produced in the bone marrow, and then migrate to tissues and body cavities, where they differentiate into macrophages. In the bone marrow, Monoblasts, promonocytes and monocytes can differentiate, based on recognition of cell surface glycoprotiens by monoclonal antibodies and the development of granule enzymes. Newly formed monocyte remains in the bone marrow for about 24 hours before entering marrow sinusoids. In humans, monocytes are distributed into circulating pool as 40% and marginal pool as 60%. Most macrophages are derived from monocytes but a small percentage of monocytes/macrophages divide once within 24 hours of arrival in tissues. Tissue macrophage population area constantly being renewed. The rat of Monocyte migration into inflammatory site increases as monocytes in the blood to meet increased requirement and turn over macrophages.

Monocytosis: Increase in the number of monocytes in the peripheral blood is called Monocytosis. Monocytosis occurs in these following conditions. Chronic diseases, particularly those with large amounts particulate matter. Fungal infections accompanied by a granulomatous reactions, retained placenta. Chronic bacterial diseases like listeriosis, brucellosis and tuberculosis and in protozoal diseases like trypanosomiasis, malarial parasites and convalescence after following acute diseases, Monocytosis is seen. Monocytosis is also seen in conditions that also produce leucopenia and neturopenia and also after adrenocarticotrophic hormone administration and corticosteroid treatment in dog, cow and cat. In association with acute stress reactions the dog and cat, Monocytosis is also seen.

Lymphocytes: Lymphoid precursors arise in the blood islands of the yolk sac and colonized the primary lymphoid organs, the marrow and thymus in early embryonic life. In the bursa it is bursa. The thymus, bursa and bone marrow sites remain active in lymphopoiesis, with their progeny circulating to the secondary lymphoid organs constituting of lymph node, spleen, gut and lung associated lymphoid tissue.

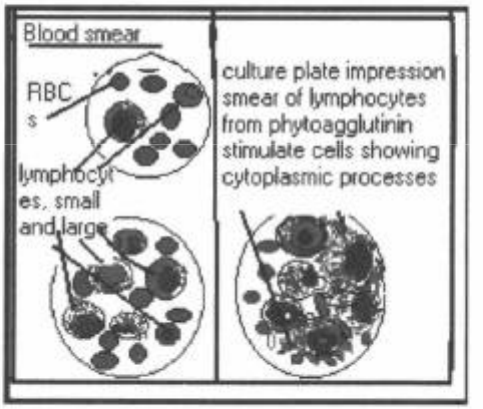
The life of lymphocyte is considerable. It begins as a stem cell, progresses from a lymphoblast through the prolymphocyte stage to the final development of mature cells. The mature cell maybe designated as either a large or small lymphocyte. Although all small lymphocytes appear to be identical morphologically, they are infact different cells with different origin and physiologic functions. In animals the original stem cells for the lymphocyte remains unknown, but it has long been thought the term cells to be the reticulum cells whereas in embryonic lymphocyte come from bone marrow precursor. After birth the thymus is the most active lymhopoietic tissue in the body, having a mitotic rates 5 to 10 times that of other lymphoid tissue. Formation of lymphocytes in thymus is independent immunologic stimuli. In foetal in early postnatal the thymus seeds lymphocytes to the lymph

nodes and spleen. Two distinct populations of lymphocytes have been demonstrated in the thymus: those that are short lived and stationary and those that are long lived and appear to migrate. In the adult animals peripheral lymphoid organs carry much lymphocyte. However, lymphopoiesis continues to occur in the bone marrow independently antigenic stimulation. From here peripheral seeding occurs. The life span of lymphocytes varies from 3 to 4 days to 20 years. Those lymphocytes in the thoracic duct are mostly of the long lived, whereas those in the bone marrow are short lived.

The principle functions of lymphocyte are its immunological memory. Following exposure to an antigen the cellular events can be divided into stages of proliferation and differentiation. The functional activity is either due to humoral response (B-cells mostly) or cell mediated immune response (T-cells). As already stated the B-cell after stimulation to antigen becomes plasma cells and elaborating five types of antibodies namely IBM, IgG, IgD, IgE, and a modified version of IgA. The cell elaborate variety of kinins, which helps I cell mediated immune response.

In addition to their function in the immunologic response of the body, it has been postulated that lymphocytes may perform a role in contribution of essential metabolites, for other proliferating cells. It has also been suggested that the lymphocytes might be precursors for monocytes and macrophages.

The lymphocytes that are seen in the blood smear measures around 10µ in diameter. But we can see small and large lymphocytes. These may either be T or B lymphocytes. This could be differentiated only by lectin stimulation or due to their mitotic activity and rapid division under the stimulation of mitogens. Usually lymphocytes diameter ranges from 5 to 15µ in diameter. They are characterized by a relatively large nucleus. The nucleus is rich in chromatin and therefore easily stained. In some preparations, the chromatin is arranged in clumps around the periperhery like the spokes of wheel. The nucleus is usually spherical, but is often bean shaped, especially in larger lymphocytes. There is usually lighter zone around the nucleus and large, dark, red azurophilic granules often appear especially in ox and horse.



The early response to antigen stimulation is the production of IgG and IgM production in transitory;within 10 days to two weeks following antigen exposure, IgM is replaced by IgG. This is called primary response. A second exposure while elicit an enhanced immune response if an animal has been previously exposed to an immunogen. This secondary response is characterized by presence of sensitized immuncompetent T lymphocytes and antibodies. The predominating immunoglobulin is IgG. Lymphokines act on macrophages, attract macrophages to an area, activate them, and inhibit their migration. Lymphokines affect leukocytes by slowing their migration and by acing as a Leukocytic chemotactic factor. Lymphokines affect leukocytes by slowing their emigration and by acting as Leukocytic chemo tactic factor. Lymphokines affect T-lymphocytes by the production of interleukin-2 which stimulates them to divide. Some Lymphokines suppress lymphocytic activity. Transfer factor is the most unique Lymphokines because it acts on T-lymphocytes to specifically sensitse them to an antigen. Transfer factor is a small molecule, around 10,000 to 15,000 Daltons. When transfer factor is administered to non-sensitized recipients, it will make them sensitive to specific antigens within a few hours, as detected by a positive delayed type hypersensitivity reaction.

Lymhocytosis: Increase in the number of lymphocytes in the peripheral blood usually absolute increase in the number of lymphocytes is rare though relative increase is common. Causes; Certain viral infections Lymhocytosis is common. All conditions that have an associated neturopenia may have a relative Lymhocytosis; Lymhocytosis leukemia's are accompanied by a marked increased in lymphocytes. During recovery of parasitic infections, an increase in the total number of lymphocytes may be observed; adrenocortical insufficiency may be manifested by an absolute increase in the number of lymphocytes; Lymhocytosis occurs following vaccination and in chronic infections when constant antigenic stimulation results in an increased in T-lymphocytes; hyperthyroidism has been reported to have an accompanying Lymphocytosis. Some debilitating conditions have Lymphocytosis.

Lymphopenia: Decrease in the number of lymphocytes in the peripheral circulation. The causes are certain viral disease such as acute distemper, infectious canine hepatitis, parvovirus, gastro-enteritis viruses, corona viruses; stress which produces a moderate to marked absolute decrease in lymphocytes. This is also due to action of gluco-corticocids. The injection of adrenocorticoid hormones of ACTH, ionizing radiation or immunosuppressive drugs produce lymphopenia in animals.

Monocytosis: A Monocytosis occurs in several conditions.

Chronic diseases, particularly those in which large amounts of particulate matter must be removed. Examples are fungal infections and most conditions accompanied by granulomatous reaction. If there is considerable destruction of tissues to be

removed, an increased in monococytes often occur. Certain infectious dieses such as erysipelas and listeriosis in swine and brucellosis in other animals have an increase Monocytosis. A relative Monocytosis is seen in condition that also produces a leucopenia and a neutropenia. Monocytic leukemia and ACTH and corticoids treatments in the dog, cat and cows exhibit a Monocytosis. In association with acute stress reactions, Monocytosis is common in dog and cat and adrenocorticism is also show monocytosis. In cattle, it is common with retained placenta cases in cows and buffaloes. Chronic bacterial disease like tuberculosis and brucellosis exhibit monocytosis in animals.

Eosinophilia: Eosinophilia an increase in the number of circulating eosinophils in the peripheral blood. It is seen in the following conditions. As a reflections of hypersensitivity in conditions such as parasitism and allergic reactions. Parasites that produce increase in eosinophils are those that penetrate the tissues of the animal body such as migrating ascarid larvae, trichinae, and occasionally hook worms. Parasites that produce localized lesion do not usually induce an eosinophilia. Allergic reactions such as asthma, urticaria, allergic bronchitis, allergic dermatitis, and food allergies also produce an eosinophilia.

Anaphylactic reactions that are also a reflection of hypersensitivity are accompanied by an increase in eosinophils. In adrenocortical insufficiency eosinophils may occur but is not usual finding. In recovery stages of some acute infections, a relative increase in eosinophils may be observed. This is usually reappearance of eosinophils following the eosnopenia that accompany stress associated with the more acute stage of disease. Granulocyte eosinophilic leukemias have been reported with relative eosinophilia. Neoplasms, the ovary, serous membranes and bone sarcomas are associated with absolute increase in eosinophils. Eosinophilic myositis of non-specific causes is seen in dogs. Spleenectomy in the dog is followed by eosinophilia at about 30 days after the operation. Eosinophilic gastroenteritis is common in the dog and in associating with some oestrous conditions in dogs eosinophilia has been detected.

Eosinopenia: A circulating decrease in the number of eosinophils in peripheral blood. Any stress conditions and after administration of ACTH or corticoids as therapeutic measures. Hyperactivity of adrenal gland occurring as a consequence of hyperplasia or neoplasia.

Leukemias: Leukemia is a cancerous condition of the haematopoietic tissue (bone marrow) involving one or more types of the tissue.

Leukemias are further categorized as leukamemic leukemia and aleukameic leukemia.In leukamemic leukemia there is frank elevation of neoplastic cells (abnormal immature cells) in the blood; and wherein the blood picture is normal without elevation of neoplastic cells in the blood, is called as aleukameic condition.

Neoplasia of haematopoietic tissue is either lymphoproliferative or Myeloproliferative. Lymphoproliferative neoplasms include lymphosaromas,

plasma cell myelomas and reticulum cell sarcomas. Myeloproliferative neoplasia includes granulocytic leukemia (neutrophilic, eosinophilic, and basophilic), erthremic myelosis, erythroleukemia, myelomonocytic leukemia and megakaryocytic leukemia. Mast cell neoplasia usually has its origin in tissues other than bone marrow.

Leukemias are further categorized an acute or chronic based on cellular maturity, apparent onset and clinical course. Acute leukemias are characterized by the presence of immature cells (Blast cells) in the blood and in haematopoietic tissue and having relatively shorter clinical course. Chronic-leukemias are characterized by predominance of mature leukocytes in the blood and bone marrow, and relatively longer clinical course.

A number of cytomorphological features help in distinguishing lymphocytic, granulocytic and monocytic leukemias. These include, size, nuclear shape, type of nuclear chromatin (fine or coarse), number of nucleoli, amount of cytoplasm (nuclear and cytoplasmic ratio), cytoplasmic basophilia, presence of azurophilic and specific granules and cytological markers (peroxidase, alkaline phosphatase, lipase and nonspcific esterase).

The incidence of leukemias in animals varies with this type of leukemia, the species involved and the geographic location. Although leukemias can occur at any age, myeloid leukemias are common in young animals.

Lot of literature has accumulated about prevalence of bovine leukemias and its causes in western countries (Canada, United States of America, Britain etc). In Indian subcontinent the prevalence of its is less, though isolated cases have been identified.

Canine leukemias are common and vary with the breed. Lymphosaromas are common in sheep and goat. The author had the experience of finding out, the enlarged mesenteric lymph nodes as large as that of 10 cm in size with lymphosaromas condition of goats.

The author has the chance of seeing several cases of lymphoid leucosis (so-called big liver disease) in poultry, which is less prevalent now, due to intensive weeding out of this cancerous gene by selective breeding of the flocks against lymphoid leucosis.

In the beginning, we will discuss the lymphoproliferative neoplasia and then proceed to leukamemic tumors. Among the lymphoproliferative tumors, lymphoma is the foremost important tumors and the major distinction between leukemia and lymphoma is that in leukemia there are neoplastic cells in bone marrow and in circulation and in lymphoma there are enlarged peripheral lymphnodes with a relatively normal hematological picture.

The French-American-British system of classification of the acute leukemia provides for the definition of diseases which are histologically separate but at the

same time provides information that relates strongly to biological behaviour. The classification has been traditionally based on morphology and rate of progression and divides the aucte myeloid leukemias into categories of M1 to M7 and acute lymphoid leukemias into L1 to L3.

Acute leukemias of animals and human because of their high rate of proliferation are most responsive to chemotherapy. In contrast animals with chronic leukemia are often adversely affected by chemotherapy because the mitotic rate of tumor cells is similar to or less than that of the mitotic rate of residual normal marrow.

Acute leukemias

M1: Myeloblastic leukemia without maturation (acute myeloblastic leukemia): This form of acute myeloblastic leukemia is characterized by predominance of blasts in blood and marrow with fewer than 10% having cytoplasmic granulation. At least 5% of malignant blast cells stain positively for Sudan black and Myeloperoxidase. This is a disease of young mature dogs and cats with a tendency for increased frequency in males. Swine are occasionally affected.

M2: Myeloblastic leukemia with maturation

This condition is similar to acute myeloblastic leukemia. Here maturation proceeds to the promyelocyte stage in at least 10% of tumor cells. Half of the tumor cells stain positively with Sudan black and Myeloperoxidase. Most animals presented in good body condition, epistaxis and Melena are there, mucosa is paler and often thrombocytopenia and peticheal hemorrhages are present. Anemia is moderate, anisocytosis mild, Howell-jolly bodies are present, and hypochromia is present. Rubricytosis often present. Rubriblasts are present in the peripheral blood. Total leukocyte count is highly variable 25,000 to 50,000/cmm. The tumor maybe of neutrophil, eosinophil or basophilic type. Cytologically the leukamemic cells in blood have round centrally placed nuclei measuring 2o to 25μ in size with nucleus having cribriform chromatin pattern. One to three nucleoli are present within the nucleus and are visible in the leukamemic myeloblast or Promyelocyte. Abundant basophilic cytoplasm present and cytoplasm contains azurophilic granules. Marrow aspiration reveals the marrow cells are less mature when compared than those that peripheral blood.

M 3 Promyelocyte leukemia: Promyelocyte leukemias a rare disease of young mature animals, which likely occur in all species, but is most commonly recognized dogs and cats and also reported in swine. The course of the disease is usually 1-2 weeks. Death is associated with intracranial hemorrhages. Promyelocyte leukemia differs from myeloblast leukemia by predominance of Promyelocyte in both blood and bone marrow. The cells are larger than that of myeloblastic leukemia and the degree of granulation is variable. The cytoplasmic granule is intensely positive with Sudan black and Myeloperoxidase stains. In humans, the disease is associated with primary chromosomal translocation.

M4. Myelomonocytic leukemia: This is rare disease recognized in dog, cat, horse and humans in which there is concurrent neoplasia of the neutrophil and monocytic cell systems. Both monocytic and neutrophilic series are tumorous. Myelomonocytic leukemia is defined as having at least 20% of both tumor cell lines staining for the neutrophil series (chloroacetate esterase, Sudan black or Myeloperoxidase activity) or for the monocyte series (fluoride sensitive esterase)

Animals are presented in good body condition but with a history of weight loss and there is anorexia. Clinically there is pallor of mucosa irregular arrangement of cervical nodes, thrombocytopenia and leukocyte counts increased between 25,000 to 50,000/cmm. Morphologically the leukocytes resemble those of myeloblastic leukemia with some maturation and acute monocytic leukemia, malignancy as determined by atypical nuclei in the peripheral blood smear. Esterase staining varies with the degree cytoplasmic granulation. Both cell lines are positive for peroxidase activity. Course is 4 to 6 weeks. Thrombocytopenia and bleeding is common. There are peticheal hemorrhages, focal infarction in liver kidney, spleen and oral ulcerations are also present.

M5. Monocytic leukemia; The cells in this leukemia is monocytic precursor which is positive for α-naphthyl butyrate esterase activity. Fewer than 20% of cells stain with Sudan black or Myeloperoxidase stain indicating granulocytic origin. In this two variant forms occur. One variant form characterized by monoblast predominance with little progress into monocytes and the second is characterized many monocyte differentiation. Leukocyte counts to be low or normal. This is seen in young dogs and cats and in mature horses and cattle. Course is generally 2 to 4 weeks. Paler mucosa is seen. Anemia marked. Leukocytes count is usually less than $25x10^9$/ liter there is often mild neutrophilia and shift to the left is common. Cytologically both pro-monocytes and Monoblasts are present.

M6. Erythremic l myelosis

Erythremic myelosis can be defined as a condition in which nucleated erythroid cells of all stages comprise 50% or more of marrow cells. In this at least 10% of cells are dysplastic and 30% of cells are primitive type. Erythremic myelosis is common in cats with feline leukemia virus infection. The malignant erythroid cells are glycogen positive and hence stain with PAS reaction. The lymph nodes are normal, mucosa is pale or icteric. The course of the disease is 1 to 3 months. Anemia is severe. The total nucleated cell count varies from 20 to 200x 10^9/ liter. Neutrophils or at low or deficient levels. Rubricytes count 90% of differential count. The malignant cells mimic benign Rubriblasts with fine azurophilic granules in cytoplasm.

Acute lymphatic leukemia: Acute leukemia of lymphoid type may be either that of B or T cell origin. Bone marrow is involved, but withT-cell leukemia, thymus is also involved. The morphological characteristics of acute lymphocytic leukemia are based on nuclear and cytoplasmic ratio, nuclear size, and shape number and

size of nucleoli, cytoplasmic basophilia and vacuolation.

The disease is seen most often in calves and cats. Younger animals usually suffer with this. Animals are presented with this minimum lymph node enlargement. There is anemia in these animals and Spleenomegaly is also observed.

Histologically the neoplastic cells resemble those of cells of acute lymphocytic leukemia and can be distinguished from acute myeloblastic leukemia by lack of cytoplasmic granulation and reaction to esterase stains.

Chronic lymphocytic leukemia: Chronic lymphocytic leukemia is proliferative disease resulting in the accumulation of clonal population of B-lymphocytes that are morphologically similar and mature but biologically immature.

The basic criteria for diagnosis of the diseases are persistent Lymhocytosis of mature cells, presence of cell surface immunoglobulin and involvement of marrow with 305 of more mature cells. Immune dysfunction is slowly progressive, hypogammaglobulinemia eventually develops, and immune haemolysis results in the onset of anemia. Karotype abnormality is seen in affected and dividing lymphoblast.

Chronic lymphocytic leukemia of large granular lymphocytic type: T-cell involvement has been reported in dogs, horses and cow. This is usually observed in aged animals. Lymph nodes are not enlarged, but there is always presence of Spleenomegaly.

There is severe Lymhocytosis that may range from 50 million to 60 million cells / cmm. There is moderate anemia. The blood picture is of normochromic and anisocytosis is also seen. Histologically the bone marrow has greater than 505 of cells.

Lymphoma: As already stated in lymphoma there is marked development of lymph nodes and elevation of blood cells is not normal.

The lymph nodes which have also increased rapidly in size will have a capsule that is as stretched and thinned. Some of the commonly occurring lymphomas are described below.

Low grade lymphomas of diffuse type: The tumor cells are small (lymphocytes) are involved and nucleoli are not present in these cells. Mitoses are rare. Chromatin is aggregated into closely packed and large dense chromocentres are present. These occur in the gastrointestinal tract. These are multicentric in origin.

Intermediate lymphoma: These are found in enteric tract and are multicentric. Mitoses are rare. Intestine including associated lymph nodes are involved. The division of the cell makes the tumors as diffusely infiltrating tumors with cleaved nucleus. These tumors are in association with enzootic bovine leukotic tumors.

High grade lymphomas: These contain big lymphocytes and are called as

immunoblasts. These cells have prominent single central nucleolus and a high mitotic rate. Most of the mediastinal tumors of dog and cat belong to this type. These are seen in dog, cat and cow. In dog, with these types of tumors hypercalcemia is seen. These are multicentric.

Bovine lymphomas; Lymphomas in adult cattle are enzootic in nature and hence called as enzootic bovine leucosis. The etiological agent is a retroviral infection (bovine leukemia virus) and is transmitted horizontally by direct contact. Infection once established is life long.

Affected cows have high antibody levels to the viral antigens. The virus is cell associated and viremia is seldom seen. The virus stays as provirus in the bone marrow. The increase in transmission occurs in summer months. Genetic involvement is suspected in the affect of the disease. As already discussed previously this is not a problem for the cattle Indian content and in prevalent in western countries alone. This seen mostly in matured animals. The common lymph nodes are retrobulbar, pharyngeal or inguinal. In enteric form mesenteric lymhnodes are involved and these are enlarged. Any organ starting from liver, kidney and spleen are involved.

Sporadic form of bovine lymphomas occurs and these are not due to viral infection. **Enzootic bovine leukemia** occurs in certain tract where bovine leukemia virus is seen. These have been classified into 3 types. Calf type, thymic type and skin form. In calf type there is leukemia where kidney, liver and spleen are also involved. Thymus is not affected. In the thymic form a special type, aleukameic condition is seen. In the skin form two to three years of old cattle are affected. White plaque like lesions is seen on head, sides and perineum.

The tumor cells are of moderate size (T-lymphocytes) with a narrow rim of cytoplasm and nucleus having a thin nuclear membrane.

Ovine and Caprine lymphomas: In these cases no leukemia is seen. Bone marrow is also not involved. A retro-viral infection has been attributed for these conditions. These animals can contract the infection from bovine viruses. Here portal involvement of liver occurs resulting in hepatocytomeglay. Histologically the lymphocytes have a large nucleus and show frequent mitotic divisions.

Equine lymphomas: Several forms are seen namely leukamemic form, solid form, alimentary form, abdominal form and spleenic form. This is multicentric in origin.

Canine lymphoma: These are multicentric in origin. Enteric type, cutaneous type and thymic types are observed. Dogs affected with these tumors show reduced exercise, tolerance, dysphagia and hemorrhages and bleeding into the body cavities with severe impairment of circulation is seen.

Felinelymhomas: A retrovirus has been attributed for the occurrence of these lymphomas in these species. Horizontal spread of the tumor virus is there. The

virus showed wide geographical distribution and 2% of cats is affected. These tumors are multicentric in origin; gastrointestinal, mediastinal, renal, skin and ocular lymph nodes are involved.

Porcine lymphomas: 25% of large white pigs suffer with this type of tumor. Genetic tendency to susceptibility of tumors is seen. Lymhnodes are enlarged. Animals show Spleenomegaly and hepatomegly. Histologically, the tumor cells have nucleus which does not show any cleavage.

Lymphomas in laboratory animals: Lymphomas have been observed frequently in nonhuman primates particularly when primates are infected with immunosuppressive lenti viral infections.

Hodgkin's like lymphoma; This is rarely seen in animals. The author observed this in goat, where mesenteric lymphnodes were involved. The diagnosis of Hodgkin's disease rests on the demonstrating of Reed-Sternberg cells in appropriate background of lymphoproliferation. The mirror image nucleus could be seen in dividing cells. But in formalin fixed tissues section cytoplasmic contractions is common. Starry type of reticular cells surrounding the Reed-Sternberg cells in lymph nodes is a common feature. Multiple myelomas: Multiple myelomas are characterized by proliferation of neoplastic plasma cells in the bone marrow, with resultant osteolytic lesions. Multiple myelomas involving IgG or IgA producing antibodies have been described in the dog, cat and horse. The characteristic protein, Bence-Zones protein which on heating at 56°C will dissolve and reappears on cooling, are found in the urine. Acute or chronic renal failure occurs. Lameness, bone pain and fractures are common.

Acute leukemias: In these tumors blood picture reveals presence of neoplastic cells.

Acute myeloblastic leukemia without maturation; predominance of blast cells is seen in blood and bone marrow. Cytoplasmic granulation is seen. 5% of malignant blast cells stain positively for Sudan black and myeloperoxidase. This tumor is frequently occur in dogs and cat.

Myeloblasticleukemia with maturaiton: Here mature neoplastic cells are seen in 105 of tumor population. Tumor cells show positive to Sudan black and mylepoeroidase.The total leukocyte count is around 25,000-50,000/cmm. Liver and spleen is normal. Lymphnodes are not enlarged. Cytological the leukamemic cells in the blood are round and have centrally placed nuclei. The cells measures 20 μ in size, and the nucleus having 11 to 15μ in size. One to three nucleoli are found in the cell. The cytoplasm is moderate in volume and stain blue and has a smooth outline. There is sufficient azurophilic granulation in the cytoplasm, thus identifying that they are of myeloid origin.

Promyelocyte leucosis: This is a rare disease of domestic animals. The course of the disease is usually 1 to 2 weeks. Death mat be associated with intracranial

hemorrhages. Predominance of Promyelocyte is there in the blood. The cells are larger than myeloblastic leukemia and the degree of cytoplasmic granulation is variable. Cytoplasmic granules are positive to Sudan black and with Myeloperoxidase stain.

Myelomonocytic leukemia: this is seen in dog, cat and horse. Myelomonocytic leukemia is defined as having at least 20% of both tumor cells staining for the neutrophil series or monocytic series. The leukocyte count is generally between 25,000 to 50,000/cmm. Cells resembling morphologically to myeloblastic leukemia. Cells stain positive for peroxidase activity.

Monocytic leukemia: Two forms occur. The first one is monoblastic predominance with little progression to monocytes; the second one is the cell that differentiates into clear cut monocyte. Leukocyte count is less than 25,000/cmm in earlier stages, and may be increased to 50,000 and 1, 00,000 at terminal stages. Bone marrow examination reveals 75% of marrow cells as undifferentiated blasts, Monoblasts, promonocytes with nuclear hyperchromicity prominent nucleoli and moderate mitotic rate. Cytoplasm is positive to α- naphthyl butyrate esterase activity.

Erythremic myelosis: This is tumor of nucleated erythroid precursors. This is seen in cats and cows. The course of the disease is 1 to 3 months. Haemoglobin levels will drop down to 2 to 5 g%. Total nucleated cells count is 20,000 to 2, 00,000/cmm. Neutrophils are low. Lymphocytes may be 10,000/cmm. Rubricytes comprise 90% of differential count and the rubricytes are polychromic, normochromic and metarubricytes. On gross examination all tissues are pale and there maybe slight icterus. Histologically bone marrow is highly cellular and dense cellular packing. Spleen is uniformly enlarged, fresh and dry. On cut surface, 90% of the cells are blast cells and presence of haemoglobin in the cytoplasm is seen.

Erythroleukemia: This is due to the simultaneous occurrence of both erythroid and neutrophilic precursors. It is rare disease of dogs and cats, which is characterized by sudden onset of weakness, depression and anorexia. Terminally myeloblastic component is more prominent. Total nucleated cell count is 50 million/cmm. Haemoglobin levels are brought down to a less than 2 g%.

M7. Megakaryoblastic leukemia: This is seen in dogs. It could be confused with myeloblastic leukemia and acute lymphocytic leukemia. Platelet derived growth factor from the tumor cells is responsible for the proliferating of benign stroma. Clinically fever, subcutaneous hemorrhages and gastrointestinal haemorrhages are seen. The animal is in good condition. It is rapid in onset. Course is 2 to 4 weeks. Total leukocyte count is around 5x 109/litre. Peripheral blast cells are present in blood. Tumor nuclei are24 to 25 u in size. These are round but irregular constricting and binucleated in appearance. Chromatin is dense and cribriform and nucleoli are not prominent. Clear vacuoles may penetrate the tumor nuclei and cytoplasm as if number of platelets is there. Scant cytoplasm with blunt processes. Basophilia of cytoplasm is prominent and azurophilic granules are

present in the cytoplasm. The cytoplasm stains with strongly positive to PAS. Myelophthesic and very rapid failure of marrow is there. Clinical signs are typical of acute leukemia, often with fever, subcutaneous haematomas and gastrointestinal hemorrhages.

There is pancytopenia with anemic features and a total leukocyte count 5,000/ cmm with neutropenia and peripheral blast cells.

Polycythemia Vera; this is seen in dogs and cats and occasionally seen in cattle. In mice this has been reported to Friend leukemia virus. Here erythroid stem cells grow and bring about the cancerous condition. Affected animals are presented with reduced exercise, polydypsia, and often neuromuscular dysfunction; including head tremors and posterior paralysis. There is epistaxis, haematemesis, haemogram reveals RBC count as high as 1000 million/cmm. Haemoglobin levels are around 20 to 25 g% and a PCV of 65 to 80%.

Chronic granulocytic leukemia: This is seen in aged dogs and cats. There is a history of weight loss, extending over several months, with recurrent in appearence and diarrhoea, and having slow healing of superficial lesions. Lymph nodes are nromal and the course is of 1 to 4 years of age.

Anemia is mild to moderate. Leukocyte count is greater than 50,000/cmm amd may exceed. There is toxic vacuolation in leukocytes, granulated Myelocytes and promyelocytes are seen in blood. Autopsy examination show enlarged spleen and liver.

Platelets:

Thrombocytes (platelets) are small cytoplasmic fragments from megakaryocyte and are found in the circulating blood. These arise from the committed haemopoieitc stem cell of bone marrow. The stem cells are same for the erythroid and megakaryocyte systems. In the foetus megakaryocyte are found successively in the liver, spleen and marrow and adult they are found in the marrow, lung and spleen.

Total thrombocyte count in various animal species may vary from 1,75,000 to 5,00,000/ µl that is 1,75,000 to 50,000/cmm. The volume of marrow occupied by megakaryocyte bears a constant relationship to peripheral platelet consumption. The duplication of platelet cells occur by end mitosis. It has been estimated that about 50 platelets are produced per nuclear lobe or 1600 platelets from a 32 N cell. That means megakaryocyte is a multinucleated cell. In most species, platelets can be produced in 4 days. They have a circulation time of 9 days. The rat of thrombopoiesis is probably controlled by regulatory T-lympoytes at the stem cell level and the -2 globulin level, thrombopoiesis proteins help at the level of differentiation and maturation.

The thrombocytes of mammals are a nucleated, whereas in birds these are nucleated. The cytoplasm is pale blue and nucleus is usually round with closely

packed chromatin clumping, resembling a lymphocyte nucleus. Eosinophilic specific granules are usually at one pole of the cell. The normal thrombocyte count in birds is 20,000 to 30,000µl. of blood. In a normal blood smear one will see one or two thrombocytes per oil immersion objective filed (100 xs). In animals these blood platelets rediscoid cells generally 1/3 to ½ of the diameter of RBCs. They clump at one place in Leishman or Giemsa stain.

Platelets have mitochondria, and cytoplasm has granules. They have the glycolytic enzymes. Platelets contain fibrinogen, and contractile protein thrombasthenin. They secrete serotonin, histamine, and ADP. They help in the synthesis of factor VIII (thromboplastinogen or antihameophilic factor).

Avian platelets have little involvement with initiation of clot formation. The rat of thrombocyte clumpingis slower than the platelet clumping. Avian thrombocyte contains large quantities of serotonin but little thromboplastin. They have phagoyctic function, contain acid phospholipase and are able to phagocytose bacteria and viruses.

Platelets help in haemostasis. Injured endothelium release factors resulting in the adhesion of platelets and aggregation of platelets and release of their secretions.

Platelet disorders

1. **Thrombocytopenia:** Decreased number of thrombocytes in the blood. Thrombocytopenia may result form increased destruction of platelets, decreased production of platelets in the bone marrow and sequestration of circulating platelets in the spleen. Excessive destruction of platelets due to immunologic reactions involves auto antibodies, allo-antibodies, iso-antibodies and drug associated antibodies.
2. **Megakaryocytic hypoplasia:** It is a common cuase of thrombocytopenia. This is seen in systemic infections. Canine ehrlichiosis, feline leukemia virus infections, myelophthesic and myelotxicosis.
3. **Megakaryoblastic leukemia:** It is rare disease mainly seen in dogs. Platelet derived growth factor released in these tumorous conditions results in myelopthesis and very rapid marrow failure. Clinical signs are fever, subcutaneous haematomas and gastro-intestina lhaemorrhages. The course is usually of 2 to 3 weeks. There is neutropenia. Total leukocytes are dropped down to 5000/cmm. Nucleoli are not prominent in the neoplastic cells. Nucleus occupies 2/3 of the cell. The cytoplasm is scanty and the outer rim of cell wall show one or two blunt pseudopodia and bluish stained areas. Tumor cells are positive to α -naphthyl acetate esterase reaction.
4. **Megakaryocytic myelosis:** This is a chronic form of Megakaryoblastic leukemia. This is seen in dogs and cats older than 5 years. Clinical course is 1 to 3 years. Clinically characterized by bleeding and thrombosis of tip of tail and ears and Hamematologically by massive thrombocytosis. Platelet

count is decreased. Histologically bone marrow sows marked megakaryocytic hyperplasia and increase basophilia and hyper chromatic nuclei. Liver sinusoids show megakaryocytic infiltration.

Diseases of spleen

Spleen has been classified as either storage or defense organ. Spleen acts as a storage organ in horses. In other animals spleen which is poor in trabaculae but rich in lymphoid tissue, can be considered as defense organ. Thus spleen of human and rabbit are examples of defense spleen, whereas those of cats, dogs and cattle are storage spleens. The functions of spleen are production lymphocytes, through the Reticuloendothelial system. Phagocytosis of foreign particles, phagocytosis of effete erythrocytes, Conversion of haemoglobin to bilirubin and storage of iron. Spleen is involved in extramedullary haemopoiesis, involved in the production of antibodies.

The spleen can be defined as a haematopoietic organ which filters blood through sinusoidal system. The vascular system of spleen consists of arteries, veins, and efferent but not afferent lymphatics. As a consequence , all antigens reaches the spleen through the blood, which determines that primary sensitization and antibody production takes place in the spleen only if the first contact with antigen occurs by haematogenous sensitization. On subsequent challenge, the germinal centers of the spleen play an important role in the humoral secondary response both by local production of antibody and by the provision of committed B-memory cells to the peripheral lymphoid organ. The clearance of bacteria from the blood by the spleen predominates only if opsonisation is deficient. In other circumstances, the clearing appears to occur mainly in hepatic Kupffer cells. Thus, spleenectomy increases susceptibility to number of blood borne infections including septicemia and Protozoal infections.

The circulation of spleen is central to its function and consists of arborising arterioles which form the pencillary artery. They arise largely at right angles to the large vessels and form nutritive and antigen sources for the germinal centres. The periarteriolar sheath of small lymphocytes invests the eccentric germinal centres to provide a mantle zone of small lymphocytes similar to those surrounding germinal centres in lymph node. The pencillar arterioles end abruptly on leaving the germinal centre, and are ensheathed by few reticular cells, which form an ellipsoid like structure. Normally almost all the blood delivered to the spleen passes directly to the venous system, whereas little as 3% perfuse the sinus areas where sorting and processing by the macrophages is carried out to remove effete injured red blood cells. The flow of blood through the spleen is large and all of the blood passes through the sinusoidal system once per day. With increased arterial flow or decreased direct drainage to veins, the spleen functions an open vascular system in which the pencillary arterioles discharge largely into the sinuses, and thus much greater fraction of the arterial flow passes through the sinusoidal filter.

The structure of the sinus wall is central to the filtering function. They are composed of elongated endothelial cells which are irregularly supported by encircling reticular fibers like the supporting pillars of the barrel. Adjacent endothelial cells are not joined by junctions and the therefore form a lattice work through which blood cells readily permeate to pass from the sinuses or filtering area back into the venous or systemic circulation. The sinuses consist of macrophages, lymphocytes and plasma cells in loose reticular network.

Spleen like lymph node consists of germinal centres, flooded with lymphocytes which are bone marrow derived. The lymphocytes surrounding the larger arterioles are the; lymphocytes derived from thymus. The germinal centres are composed of three layers of cells consisting of germinal centre itself, a corona of medium sized lymphocytes immediately peripheral to the germinal centres which are bone marrow derived, and peripheral to the corona a small mantle of lymphocytes which are B and t-lymphocytes and continuous with periarteriolar lymphatic sheath which are populated by T- lymphocytes.

Haemal nodes occur in ruminants have similar structures of lymph nodes but the germinal centres and the paracortical areas are much reduced compared to the lymph nodes. Not like lymph nodes, where the sub capsular sinus is poorly cellular, haemal lymphnodes contains red cells.

Anomalies: Accessory spleen is acquired and is found scattered in the gastro-spleenic omentum. These are implanted pieces, produced by traumatic rupture of the spleen.

Doughnut spleen is a circular spleen with hole in the middle, rarely seen in the horse sometimes lobulated spleen is found.

Aplasia and hypoplasia of spleen is commonly seen in animal.

Hyperplasia of spleen is common in old dogs and is characterized by round, soft and grey projecting nodules.

Amyloidosis of spleen occurs as a part generalised Amyloidosis. The amyloid distribution may be focal as sago spleen or diffuse as that of bacon spleen. In sago spleen central arteries of Malpighian corpuscles are affected. In bacon spleen which is diffuse the arterioles and fibers of the reticulo-endotheialsystem are affected. The organ is enlarged with rounded edges and cut surface is smooth and translucent.

Rupture of spleen: Due to trauma that occurs in automobile accidents that occur commonly in dogs and cats. Pathologic rupture may occurin any species with any minor trauma if the spleen is enlarged and the capsule is thinned. This occur consequent to the spleenomegaly that occurs due to congestive heart failure, haemolytic infections, infections of septicemia or toxemic nature and neoplastic types. Lymphoma in poultry, and all animals' leads to spleenic enlargement and

rupture with fatal hemorrhages. Following rupture of the spleenic capsule and spilling spleenic sinus cells in to the abdominal cavity, there may be widespread seeding of the spleenic explants on to the serosal surfaces. This is called splenosis. These accessory spleens are functional and there may be hundreds on the omentum with a few on the peritoneum. They appear grossly like haemal lymph nodes and histologically like normal spleen.

Torsion of spleen: This occurs in pigs, dogs and humans and rarely in horses, and in dog does torsion of spleen with stomach also occur. When the whole spleen is twisted, on its mesentery, there is severe congestion and hemorrhagic infarction due to occlusion of the vein and ultimately blockage of the artery. Spleenic torsion occurs in large breed of dogs, there is enlargement of upper abdomen with painful grunting of teeth on palpation, and passage of dark brown urine. Hamematologically there is characteristic discoloration of plasma due to leakage of blood pigments through the capsule as it becomes necrotic.

Species of the animal	Diseases involved
Cattle and sheep	Anthrax, slamonellosis, Lymphoma, babesiosisi, trypanosomiasis, anapalsmosis, congestive Spleenomegaly, acute septic process with bacteremia and toxemia
Horses	Equine infectious anemia, lymphoma, metastatic melanoma, isoimmuno-haemolytic anemia, salmonellosis, anthrax
Pigs	Torsion, congestive Spleenomegaly, slamonellosis, erysipelas, lymphoma, isoimmunehameolytic anemia, protozoan diseases of blood,
Dogs and cats	Barbiturates, lymphoma, acquired hameolytic anemia, histoplasmosis, Amyloidosis, leishmaniasis, haemangiomas, Haemangiosarcomas, torsions, mast cell tumors

Infarction of the spleen is common; if the spleenic artery is occluded by an embolus the whole organ may undergo infarction. It is common in hog cholera to see the infarcts in spleen especially marginal due to occlusion of the follicular branches of the spleenic artery by proliferated endothelial cells results in hemorrhagic infarct.

Infarcts of the spleen are common in poultry with inclusion body hepatitis, and in Ranikhet disease.

Spleenitis: inflammation of the spleen. It maybe acute or chronic. Acute spleenitis is a common feature in generalised infections disease such as salmonellosis, anapalsmosis, infectious anemia of horses, and eperythrozoonosis of dogs and swine erysipelas. Grossly the spleen is enlarged dark and soft. The pulp is fluid; if infection is pyogenic organism abscesses are found. Histologically necrosis of the pulp and neutrophilic infiltration may be seen in the sinusoids which are congested. Certain amount of proliferating lymphocytes is present and there are reaction germinal centres. In the red pup proliferation of the reticular cells and macrophages may be found. In Rinderpest infections necrosis of lymphocytes

brings about washed out appearance of germinal centres and atrophic spleen.

Chronic spleenitis occurs in such chronic diseases as tuberculosis, glanders, acitnomycosis, pyaemia, pseudotuberculosis of sheep and histoplasmosis. Grossly the spleen is enlarged, firm and tough.

In aflatoxicosis, atrophy of the spleen and as well hemorrhages on the surface of the spleen are common.

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Chapter 3

Diseases of Respiratory System

Summary

Physiology of lungs-Histological features of lungs-Defense mechanisms of lungs-Disease of lungs – Emphysema, Alveolar, Interstitial-Acute alveolar emphysema chronic alveolar-emphysema – Pulmonary oedema – Pneumonia, Types and classification of-peumonia,Verminous-pneumonia interstitial and verminous Pneumonia, Viral-pneumonia, Bacterial – pneumonias, Tuberculous – neumonias, Mycotic – pneumonia, hypostatic congestion,neoplastic diseases of lung, diseases of pleura

Respiratory system

The main function of the respiratory system is the exchange of oxygen and carbon dioxide between the blood and environmental air. As such to discharge this function, respiratory system depends upon the work of the heart. The system is constantly exposed to the external environment, which contains noxious substances. The surface of the respiratory tract is vast and is more than 200 square meters in human lungs. Around 2400 kms of capillary bed is there in the lungs of a human.

The process of respiration which consists of inspiration and expiration can be divided into four major mechanistic events, 1) pulmonary ventilation which means the inflow and out flow of air between the atmosphere and the lung alveoli, 2) diffusion of oxygen and carbon dioxide between the alveoli and the blood, 3) transport of oxygen and carbon dioxide in the blood and body fluids to and from the cells, and 4) regulation of ventilation and other facets of respiration.

The lungs can be expanded and contracted in two ways, 1) by downward and upward movement of the diaphragm to lengthen or shorten the chest cavity, 2) by elevation and depression of the ribs to increase and decrease the antero-posterior diameter of the chest cavity. Normal quite breathing is accomplished almost entirely by Inspiratory movement of the diaphragm.

Normal quite breathing is accomplished almost entirely by Inspiratory movement of the diaphragm. During inspiration, the diaphragm pulls the lower surface of the lungs downward. Then, during expiration, the diaphragm simply relaxes and the elastic recoil of the lungs, chest wall, and abdominal structure compress the lungs. During heavy breathing, however, the elastic forces are not powerful enough

to cause then necessary rapid expiration, so this is achieved by contraction of the abdominal muscles, which forces the abdominal contents upward against the bottom of the diaphragm.

The second method of expanding the lungs is to raise the rib cage.

The lungs stay in thoracic cavity and are under negative pressure. That is any injury to the thoracic cavity makes the air to enter into the cavity and collapse of the lung results. The thoracic cavity is lined by parietal pleura and the lungs by visceral pleura. The pleural cavity formed between the visceral and parietal pleural linings. It is a potential cavity having little fluid in the life and thus makes the lungs to act without any friction. This facility is lacking in the elephants among animals.

The airways from the pharynx conduct through larynx into the tracheal tube. Further trachea branches into primary and secondary bronchi. These bronchi further divide as bronchioles and terminate into alveoli. The trachea is a non-collapsible structure and is supported by the tracheal rings which contain cartilage. These cartilage structures continue unto primary bronchi. The mucosa from trachea to the primary bronchi is lined by columnar ciliated epithelium interspersed with non-epithelial cells (Clara cells) which are the components of tracheo bronchial epithelium. The non-ciliated cells functions as stem cells for repair in the bronchi and have the capacity to divide and differentiate into ciliated cells or other non-ciliated cells.

Tracheo-bronchial epithelial cells actively metabolize arachidonic acid to eicosanoic acids such as prostaglandin E2 and 12 HETE (leukotrienes, hydroxy- eicosa-tetraenoic acid) which may regulate local smooth muscle cell tone and vascular flow. Bronchial epithelial cells also can up regulate expression of intercellular adhesion molecules (ICAM-1) following injury and interaction with cytokines. ICAM-1 promotes adhesion and migration of circulating neutrophils and monocytes into airways during an inflammatory reaction.

Trachea, bronchi and bronchioles contain lymphoid tissue (bronchus assssociated lymphoid tissue) in the lamina propria and submuosa, analogues to gut associated lymphoid tissue in function. In addition, there can be a more diffuse distribution of lymphocytes and plasma cells. Other cells such as macrophages, dendritic cells, neutrophils and mast cells at low density within the lamina propria participate in normal base line in immune and inflammatory processes. Both B and T cells are distributed in bronchus associated lymphoid tissue. This is much more strikingly seen in poultry respiratory tract with infections of Mycoplasma organisms. Sub mucosal accumulation of lymphoid aggregates is prominent and characteristic of Mycoplasma infection. Similarly in Maedi of sheep aggregates of lymphoid submucosally in bronchi are common and characteristic of this disease. In respiratory secretions, IgA can prevent binding of bacteria to epithelial cell entry and adsorption of virus to respiratory epithelial cells, and block infection.

Airway potency in trachea and bronchi is maintained by presence of minimally deformable cartilages. Airflow is rapid in these airways, and even minimal broncho constriction or air wall oedema and inflammatory cell infiltration can result in profound increases in overall respiratory resistance and ausculatable airway sounds. There are around 200 cilia on each epithelial cell and the beating of cilia is 10 to 20 times per second. Consequent to the beat of cilia the movements of fluids are towards the pharynx, and the net effect of ciliary's frequency of around 1000 beats per minute propel the mucous around 10mm per minute.

Most of the mucous secretions of the respiratory tract, and the pharynx and the particulate matter they carry, reach the pharynx and are swallowed. Swallowing of material originating in the lungs also serve as a mode of spread of diseases such as tuberculosis and as a part of the migratory pathway of helminthes eggs and larvae. The flow of nose and nasopharynx are important in that by their specialize surface structures (pili) to receptors on cilia and surfaces of epithelial cells thus they prevent adherence and colonization by more pathogenic flora. Warming and humidifying principally occur during passage of air through the nose.

Lung also does several metabolic, immunologic and other functions such as synthesis and release of prostaglandins I- 2, E and F, leukotrienes such as D4, conversion of cortisone to cortisole, conversion of angiotensin I to II, partial or total clearance of serotonin from blood, similarly clearance of prostaglandins E and F, aldosterone, cortisol, cortisone, and bradykinins. As a result with lung infections increased temperature of the animal is common as they produce most prostaglandins and leukotrienes.

Alveoli are completely lined by mosaic of two types of epithelial cells, namely type I and II. Type I cells (pneumocytes) has a flattened nucleus and their cytoplasmic extension covering large areas of alveolar wall. This cell is extremely vulnerable to injury.

Type II cells (granular or secretory pneumocytes) are more numerous. They have a cuboidal shape. They quickly renew and useful in repair. A third cells type, brush cells, found rarely in the alveoli of various species of animals. Type II cells synthesize pulmonary surfactant, which contains complex mixture of phospholipids and small amount of proteins. Lysozyme, lactoferrin and complement are all present in alveolar lining liquid. The main function of pulmonary surfactant is to decrease the surface tension in alveolar space during expiration. In the absence of surfactant, lung expansion is extremely difficult, often requiring intrapleural pressure as low as -20 to -30 mm. of Hg to overcome the collapse tendency of the alveoli. In few young born calves or foals there is lack of surfactant which makes lung expansion difficult. These die soon after birth because of inadequate ventilation. This condition is called hyaline membrane disease or respiratory distress syndrome.

Surfactants acts by forming a monomolecular layer at the interface between the fluid lining the alveoli and the air in the alveoli. This prevents the development of a water air interface, which has 2 to 14 times as much surface tension as the surfactant air interface. The special character of surfactant helps to stabilize the size of the alveoli causing the larger alveoli to contract more and the smaller ones to contract less. The surface tension of the fluid in the alveoli not only tends to cause collapse of the alveoli, but also tends to pull fluid into the alveoli from the alveolar wall. Therefore one of the consequences of the absence of surfactant is severe pulmonary oedema.

The expansibility of lungs and thorax is called compliance. Factors that cause abnormal compliance like destruction of lung tissue by fibrosis or oedema, blocking of bronchioles causes decreased lung compliance. Thus deformities of chest cause, fibrotic pleurisy and fibrotic muscles can all reduce the expansibility of lungs and thereby reduce the total pulmonary compliance.

Bronchioles in proximal generations are often lined by epithelium which is indistinguishable from those in distal bronchi. More distally, small caliber bronchioles are lined by a simple columnar to cuboidal epithelial lining almost entirely composed of ciliated cells and nonciliated bronchiolar cells (Clara cells). The nonciliated cells function as stem cells for repair in the bronchioles and have the capacity to divide and differentiate into ciliated cells or other nonciliated cells. The noncilaited cells lining bronchioles in some animal species have abundant agranular endoplasmic reticulum in their apical cytoplasmic projections and are the pulmonary cells with the greatest concentration of cytochrome P-450-monoxygenase enzyme systems. These enzyme systems are sensitive to toxic injury by xenobiotic compounds.

Alveolar parenchyma is divided into structural and functional units called acini. An acinus is the gas exchange unit of the lung supplied by a single terminal bronchiole. In birds respiratory bronchioles exist and Para bronchiolar connection takes place and acinus unit is a modified structure. Air sac connections are there to the Para bronchi, thus the lungs are much more exposed to the outside air and differs in the negative pressure of the mammalian system.

Adult lung always contain the air. The respiratory muscles cause pulmonary ventilation by alternatively compressing and distending the lungs, which in turn cause the pressure in the alveoli to raise and fall. During inspiration the intra-alveolar pressure becomes slightly negative with respect to atmospheric pressure, normally less than -1mof Hg. And this causes the air to flow inward through the respiratory passages. During normal expirationon the other hand, the intralveolar pressure rises slightly less than +1mm of Hg. And causes air to flow outward through the respiratory passage ways. During maximum expiratory effort with the glottis closed the intra-alveolar pressure can be increased over to 100 mm. of Hg. In the strong healthy human male and during maximum Inspiratory effort it can be reduced to as low as -8o mm of Hg.

The lungs have a continual elastic tendency to collapse and therefore to recoil way from the chest wall. This elastic tendency is caused by two different factors. First throughout the lungs, there are many elastic fibers that are stretched by inflation and therefore attempt to shorten. Second and even more important, the surface tension of the fluid lining the alveoli also causes a continual elastic tendency for the alveoli to collapse. This effect is caused by intermolecular attraction between the surface molecules of the fluid that tends to continually to reduce the surface areas of the individual alveoli; all these minute forces added together tend to collapse the whole lung and therefore to cause its recoil away from the chest wall. The elastic fibers in the lung account for about 1/3rd of the recoil tendency, and the surface tension phenomenon accounts for about 2/3rds. The total recoil tendency of the lungs can be measured by the amount of negative pressure in the intralveolar spaces required to prevent collapse of the lungs, and this pressure is called the intra-pleural pressure or occasional, the recoil pressure. It is normally about – 4mmof Hg.

Tidal volume is the volume of the air inspired or expired with each normal breath (500ml for an average young man). Inspiratory volume is the extra volume to the air that can be inspired over and above the normal tidal volume (in humans it is around 3000 ml in young man). Expiratory reserve volume is an extra amount of air that can be expired after normal tidal expiration (In young human this is around 100 ml). Residual volume is the volume of air remaining in the lung after forceful expiration (in young humans this is around 1200 ml).

Each lung is divided into various lobes. Lungs of different species can be identified by carefully observing the degree of lobation from external fissures, and the degree of lobulation by connective tissue between lobules. The degree of lobulation determines the degree of air movement between the lobules. The interlobular movement of air, and the communication between the alveoli through the pores of Kohn, and the communication between bronchioles and alveoli, constitutes what is known as collateral ventilation. It is poor in cattle, pigs and good in dogs and cats.

Mucociliary and bronchial associated lymphoid tissues in defense mechanisms: Mucociliary clearance is the physical removal of deposited particles, or dissolved gases, from the respiratory tract. It is the main defense mechanism of nasal cavity, trachea and bronchi. Mucous is a complex mixture of water, glycoprotiens, immunoglobulins, lipids and salts. It is produced by goblet cells that line the glands of trachea and it is present on the inner surface of bronchi. The amount of mucous secreted is around 10 to 1000ml per day, in the adult humans. When soluble gases come into contact with the muco-ciliary blanket, it mixes with mucous. This reduces the concentration of gas reaching deep into the alveoli. The bronchial mucosa is associated with lymphoid tissue. Lymphocytes of the bronchi and associated lymphoid tissue contribute to both cellular and humoral response.

The alveoli have a three layered wall consists of vascular endothelium, alveolar interstitium. These three layers of cells constitute what is known as air blood barrier. The epithelial side of alveolus is lined by two distinct types of epitheilial cells, as already stated namely type I and II pneumocytes. Apart from these alveoli contains alveolar macrophages which are highly phagoyctic cells derived largely from blood monocytes and also originate from interstitial macrophages. Unlike connective tissue macrophages, the life span of alveolar macrophages is short and at least onyx for a few days. Most bacteria are rapidly destroyed by alveolar macrophages. Pulmonary clearance by alveolar macrophages operates in a well coordinated manner with other cells and secretions of lungs. These cell to cell interactions are complex and involve many cells, which include alveolar macrophages, lymphocytes, dendritic cells and type II pneumocytes. Thus the alveolar macrophages are the cells involved in lung inflammation, immune response and as well repair. When damaged they release such enzymes as collagenase and elastase which cause destruction and pathological changes in lungs such as emphysema and fibrosis.

Macrophage populations in the lungs include alveolar macrophages, interstitial macrophages, pulmonary intravascular macrophages and dendritic cells. In normal lung alveolar macrophages are derived from blood monocytes that migrate into the lung after undergoing maturation step in the interstitial space. During inflammatory states, alveolar macrophages are derived directly from infiltrating blood monocytes. Macrophages can also be derived from division of local macrophages, although this contributes little to the expansion of pulmonary macrophages populations that occur in most inflammatory lung disease.

Alveolar macrophages have a wide array of functions in addition to their capacity to phagocytosis and kill infectious agents and to degrade other phagocytose particles. They function as regulatory cells controlling inflammation, immune and repair processes through release of a wide array of cytokines and other regulatory molecules. Pulmonary intravascular macrophages are unique mononuclear phagocytes found in the lungs, they are large, mature macrophages present in the pulmonary alveolar capillaries, which form membrane adhesive complexes with the underlying endothelium. These cells are highly phagoyctic and play a role in the clearance of circulating bacteria and particulates in the pulmonary circulation. Bacteria or solid particles deposited in the alveoli and are phagocytosed by alveolar macrophages. A particle is either digested or carried to the ciliated bronchiole and from here the macrophage is propelled to the oropharynx and then swallowed. Alternatively the macrophages enter into interstitial spaces or lymphatics and from there to the lymph nodes and finally reach the blood.

Alveolar fibroblasts include a morphological heterogeneous group of connective tissue cells that may have varying protein synthetic activity, contractile function and cell and matrix interactions. They are responsible for synthesis of interstitial matrix and collagen types me, III, IV, V and VI as well as elastin. Collagens type

I and III predominate. Pulmonary fibroblasts also synthesize laminin, fibronectin, glycosamino-glycans and proteolglycans which together with the other synthesized components, contribute to the mechanical properties of lungs.

Pulmonary defense: The upper respiratory tract functions to warm and humidify inspired air, and to remove larger particles and water soluble gases by means of the mucous lining. Warming and humidifying occur principallyduring passage of air through the nose, and are facilitated by the extensive surface area and the rich, readily engorged vascular plexus septum. Many particle lies in inspired air are first deposited on the mucosal lining of nasal passages and conducting airways and hence cleared by movement of the muco ciliary blanket. The large particles are removed efficiently in the upper air ways. Deposition on the surface is mainly in inertial impaction, gravitational sedimentation, diffusion or a combination of these. Diffusion of particle is due to molecular collision and affects only the very smallest of the particle of less than 0.3μ in size. Deposition of particles greater than 10 μ aerodynamic diameter is virtually complete above the larynx. In addition, large % of inhaled particulates smaller than 10μ also interacts, initially with the mucosa of the nasal cavity and nasopharynx. As a result many viable bacteria and bacterial disease have initial stages of deposition or multiplication in the epithelium and lymphoid tissues of the upper respiratory system before they either spread systemically or are nebulised during inspiration to be redistributed into the lower respiratory tract.

Normal lung is free from bacteria. A number of defense mechanism clear or destroy any bacteria or viruses inhaled with air or deposited in the air way. One of this is the nasal clearance. This will be done by sneezing or blowing the next one is the tracheo- bronchial clearance. This is accomplished by muco-ciliary action. The beating motion of cilia moves a file of mucous continuously from the lung towards to the oro-pharynx, and particles are deposited on this film and are eventually either swallowed or expectorated. The third done is the alveolar clearance. Bacteria or solid particles deposited in the alveoli are phagocytosed by alveolar macrophages. Particle is either digested or carried to the ciliated bronchiole; from here the macrophage is propelled to the oro-pharynx and then swallowed. Alternatively the macrophages enter into interstitial spaces or lymphatics and then to the lymph nodes and to the blood and then cleared by various mechanisms including antibodies.

In this following condition the clearing mechanism of the body are interfered resulting in flaring up of the disease in the individual or animal. These are–

1. Conditions that induce loss or suppression of cough reflex, chest pain and neuromuscular disorders and colic.
2. Injury to Mucociliary apparatus by either impairment of ciliary function or destruction of ciliated epithelium as in viral diseases or mycoplasmal infections.

The entire output of the right ventricle flows through the low pressure pulmonary circulation. The defense anatomizing network of capillaries in alveolar septa provides the equivalent of sheet flow when they are all patent. The arrangement provides both for easy trapping of emboli in the pulmonary vascular bed and for minimizing the deleterious effect of blockage. Effects of blockage are minimized further by the dual pulmonary and bronchial arterial blood supplies to the lung. The quantity of blood flowing through the lungs is essentially equal to the flowing through the systemic circulation. The blood volume of the lungs is approximately about 9% of the total blood volume. That is in 70 kg human it is around 500ml. in this 70 ml around $1/7^{th}$ is in the capillaries and the remainder is divided about equally between the arteries and veins. Lungs store 50% to 200% of blood present in the circulation. Shifts of blood between the pulmonary and systemic circulation results due to cardiac pathology such as valvular stenosis or mitral regurgitation. The blood flow through the lungs is essentially equal to cardiac output. Therefore the factors that control cardiac output also control pulmonary blood flow.

Diseases of respiratory system

Pathology of nasal cavity and sinuses

Congenital anomalies involving nasal cavity and sinuses such as absence of nose, asymmetrical or displaced nose, deviation of nasal septum, absence of turbinate bones, cystic nasal concha and cyst of maxillary sinus. The accumulations of seromucous secretions are referred to as mucocoele and the accumulation of purulent exudates is referred to as empyema of the sinus. Purulent inflammation of the sinuses is more significant than rhinitis because of proximity to the brain. It is also less likely to spontaneously drain and resolve and therefore likely to cause epithelial atrophy and metaplasia, and distortion of the body walls of the sinuses by pressure or osteomyelitis.

Cleft palate or palatoschisis: It is a fairly common defect seen in newborn animals. There is abnormal connection between the nasal cavity and mouth and hence milk passes into the lungs. Animals do not survive long and die with pneumonia and starvation.

Congestion: congestion occurs whenever animals are exposed to cold air. The blood vessel in the nasal passage dilates so that the air breathed may be sufficiently warmed.

Epistaxis: It is the hemorrhage from the nasal cavity. The causes in the animals are trauma convulsive expirations, parasites that stay in the nasal cavity, especially in the case of sheep the larvae of estrous ovis popularly called nasal bots. Sheep tend to live with these bots. Other causes of epistaxis are erosions of the nasal vessels by growing tumors, compression of jugular vein in horses by tight collars and uremia in dogs. It is also seen in certain poisons like nitrates, mercurials and sweet clover and brake fern. Bloody discharges from nose are common in glanders

and anthrax of animals. Incidentally bleeding is common through nose in women. In a few with onset of menstruation as nose vessels also respond to hormonal action, or due to adenomysois externa, resulting in uterine remnants in nasal tract.

Acute rhinitis or coryza: this is the acute inflammation of the nose. The causes are very many, starting from cold weather to infection with viruses, bacteria, parasites, fungi and due to allergic reactions. It is very common observation in humans with viral infections (common cold) secretions of serous fluid in the beginning of the infection which will become mucopurulent consequent to the bacterial proliferation and invasion.

Thus rhinitis my also be classified as serous, catarrhal, purulent, fibrinous and granulomatous types. Except for granulomatous rhinitis the inflammatory process in the nasal cavity usually resolves completely. Thus the common irritants like dust, foreign bodies like chaff, pollen, parasites like *Linguatula serrate*, larvae of *oestrous ovis* in sheep, fungi like *Aspergillus fumigatus*, bacteria like glanders, *streptococci, staphylococci, Bordetella bronchi septic, Mycobacterium tuberculosis.* Actinomyces, Actinobacillus and Pateurella organisms are responsible for rhinitis. In poultry, infections with *Haemophilus gallinarum* are responsible for acute rhinitis. Viruses like Rinderpest, equine influenza, infectious laryngotracheitis, blue tongue, canine distemper, and fowl pox etc., are involved in cattle and buffaloes in nasal grnaulomas with eggs of *Schistosoma nasale* are common in India.

Histologically the mucous membrane is swollen and hyperemic. Respirations may be difficult and sterterous. Inflammatory exudates with inflammatory cells and hydropic degeneration of epithelial cells are commonly seen.

In bovines infections with infectious bovine rhinotracheitis (red nose) virus and bovine malignant catarrhal fever virus produce rhinitis and are common in western countries but the occurrence in India is questionability.

Atrophic rhinitis of swine: This is a catarrhal inflammation of the nasal turbinates, which is characterized by atrophy. The snout of piglets and pig will become almost all flat due to collapse the scroll bones (ethmo turbinates). Clinical signs include sneezing, coughing and mucopurulent nasal discharges. In severe cases atrophy of the turbinate bones cause facial deformity and mucopurulent nasal discharges. The etiology is complex. Bacteria, *Bordetella bronchiseptica* and some toxigenic strains of Pateurella multocida and feeds deficient in calcium and phosphorous all have been incriminated in the production of this disease. There is inhibition of osteoblastic activity of nasal bones and with resultant production of secondary hyperparathyroidism.

Strangles in horses: Adenitis equorum)

It is an acute contagious disease of horses characterizes day inflammation of the upper respiratory tract and abscessation in the regional lymph nodes. It is caused

by streptococcus equi an obligate parasite on upper respiratory mucous membrane of equidae. The pathogenesis of the infection involves epithelia adherence especially to soft palate and pharynx and internalization of the organism into epithelial cells. The nasal lesions are those of purulent rhinitis. Streptococcus equi, organism is regarded as the causative factor of a disease of young horses known as strangles. Streptococus equi belongs to group C of Lancefield's classification. Capsule possess antiphagocytic properties and virulence varies with the capsule, because of capsule of streptococcus equi possess a strong negative charge and repel phagoyctic cells. As the culture ages, hyaluronidase is synthesized and remove the capsule. Fimbriae are responsible for colonisation and attachment to epithelial cells.

Routes of infection: *Streptococcus equi* is a very resistant microbe and is able to withstand environmental influences. Infected animals contaminate, through their nasal discharges the pasture feeding and watering utensils adpersons handling the animals. Infection is mostly by ingestion. Inhalation of droplets may be another route in few other cases. Vulva may be infested by an infected nosing stallion or infection may be transmitted to it through penis from some other infected vulva. Scabs of cutaneous eruptions may infect other animlas. Udder may be infected by suckling cots. Wounds may also is the portals of infections and lastly uterine infections may sometimes occur.

Incubation period; 4 to 8 days.

Pathogenesis: the streptococci enter the mucous glands of the nasopharyngeal mucosa from there reach the local lymph nodes via the lymph spaces. In the lymph node they grow and produce toxins, which exert positive chemo taxis and hence large number of Europhiles infiltrate. Lymphoid tissue undergoes necrosis and liquefaction, thereby forming an abscess. If the abscess is evacuated recovery may result. Sometimes the organisms gains entry into the lymph and blood vessels by penetration through their walls and also infect distant lymph glands and visceral organs, setting up suppurative inflammmation. Death may be due to septicemia and pyaemia.

Symptoms: The disease develops suddenly with high temperature and anorexia attendant with nasal discharges, which is serous at first becoming purulent subsequently. Pharyngitis and laryngitis develop with cough and difficulty in swallowing. After the temperature subsides 2 to 3 days, abscesses develop in the lymph nodes of the throat. These become hot, swollen and painful. The sub maxillary lymph nodes may open discharging thick creamy pus. If no other complications occur, recovery ensues.

If the infection is severe, other lymph nodes in the body may be infected and metastasis abscesses maybe found in lungs liver spleen and brain. Infection may spread to the guttural pouches and into the thoracic cavity. Affection of the mesenteric lymph nodes is followed by colic. Involvement of lungs results in pneumonia.

Lesions: Abscesses are found in the pharyngeal and sub-maxillary lymph nodes, primarily mediastinal bronchial and mesenteric may also reveal the abscesses. Pericarditii, pleurisy and suppurative pneumonia may be noticed. If premier develops, abscesses may be noticed in the liver, spleen, brain, kidney, testis, thymus and muscles of neck, auxiliary and inguinal regions.

Sequleae: Roaring and purpura hemorrhagic may be developing if the animals survive.

Diagnosis: Recently isolated strains kill the white mice when injected subcutaneously within a day or two with septicemia when injected. Larges doses may kill rabbits and guinea pigs also. This organism has a strong haemolytic β-toxin and zone of clearance on blood plates could be observed.

Glanders:

Glanders is a contagious disease of solipeds (equines and donkeys) and can infect man and other animals. The formation fibrocaseous nodules in the upper respiratory tract, lungs, characterize it and skin. Farcy is the term often applied to the cutaneous lesion.

The disease is caused by *Pseudomonas mallei*, a gram negative, nonmotile anaerobic rod shaped organism, which has no tendency to form spores. The organism was previously being called as *Actinobacillus mallei or Malleomyces mallei and Pfeifferella mallei, Loefferella mallei.* The organism is relatively resistant to adverse influences and survives around 2 to 3 months outside the body. This organism is pathogenic to guinea pigs wherein subcutaneous inoculation results in generalized infection and the infecting takes an acute course, wherein spleen, lung, liver are involved. If the organism is injected intraperitoneally into a male guinea pig suppurative orchitis results in 4 to 5 days (Straus's test).

Species affected: The horse is the most commonly affected and the disease in this species is chronic, whereas in the donkey and mule it is often acute. Man and dogs are affected. Cattle and pigs are susceptible. Of the laboratory animals as stated earlier guinea pigs are susceptible and mouse is also highly susceptible species.

Transmission: Transmission follows ingestion of contaminated water or food, although it is considered inhalation also plays an important role. Indirect transmission by fomites such as harness or utensil contributes to the flaring up of the disease. In man, infection is thought to be by contaminated cuts and by abrasions. Carnivores will contract the disease eating infected carcasses. Oral route of infection caused chronic respiratory infection and whereas nasal route causes acute infection.

Pathogenesis: Infection is by either ingestion or inhalation. The organism may enter the lymphatic, penetrating the pharyngeal or intestinal mucosa; ultimately they reach the general circulating from which they enter the pulmonary capillaries.

A septicemia phase is seen. The organism induces emboli in pulmonary capillaries and resulting hemorrhages are produced. The organisms enter the capillaries of lungs and induce inflammatory reaction resulting in bronchopneumonia. These lesions show suppurating tendency.

Wherever the bacilli stay, suppurating granulomas originate. At the places where the bacilli are lodged in the alveoli, polymorph nuclear leukocytes accumulate, soon followed by alveolar histiocytes. The neutrophils degenerate. The macrophages become epitheloid cells, and may fuse to become giant cells. Old lesions are walled off by a fibrous granulation tissue. Thus the histology of glanders nodule differs with age, in the young nodules there is degeneration of polymorphs surrounded by a zone of histiocytes, red blood cells and fibrinous exudates and lymphocytes. In older nodules, the central degenerated area is surrounded by epitheloid cells and giant cells. In very old nodules, there are even scattered foci of calcification in the central necrotic area.

In the proliferate type of lesions, wherein there is predominant epitheloid cells and giant cells and lymphocytes. In these areas suppuration does not occur. Variation in the toxigenicity of different strains of the organisms is seen. This accounts for regional variations in the incidence of suppuration or proliferation. The chronic syndrome of ganders is frequently divided into nasal, pulmonary and cutaneous varieties. The same animal may suffer with the three varieties at the same time. Involvement of all three sites is common in the acute form of ganders in donkeys and in exacerbations of chronic disease in horses.

Symptoms: The incubation period is variable. It may be as short as 2 weeks and may extend for several months. The infection may remain a chronic course also.

As cited earlier, clinical forms of glanders are described and as per lesions these could be described as per lesions as pulmonary, nasal, and cutaneous forms (farcy). Mixed forms are also common. In the acute disease, there is fever, coughing and discharges from the nostrils. Rhinitis is usually commenced as a unilateral nasal catarrha, but the inflammation may be bilateral and also involve the pharynx and larynx. The typical nasal lesions are multiple small nodules lying in the sub mucosa and surrounded by a narrow hyperemic halo. The sub maxillary gland is enlarged and painful. There is acute distress and the anima dies within 2 weeks. Per acute form is common in donkeys and mules and is rare in horses. In chronic form, the horse shows uneasiness, coughing is pronounced, there is intermittent fever followed by nasal discharges and cutaneous lymphangitis. There are suppurating nodules on the nasal mucosa. These nodules discharge oily pus, and leaves punched out area with irregular borders.

Farcy is cutaneous form. It is essentially a lymphangitis and lymphadenitis of limbs, more commonly of hind limbs. Small nodules, called farcy buds, are formed all along the course of lymph vessels, which become thickened and corded, i.e., farcy cords. The vessels are dilated and tightly packed with leukocytes. The

nodules may open and discharge oily pus. The whole leg may become swollen (elephantiasis), with enlarged regional lymph nodes.

Lesions: In the lungs suppurative as well proliferative nodules are found. They are found in the parenchyma and underneath the pleura. On the nasal mucous membranes, trachea and larynx, these rupture leading to ulcers. Lesions in the trachea mucosa are usually ulcerative but are occasionally pyogranulomatous nodules. Organisms from pulmonary form reach these areas and form suppurating nodules. Due to suppuration in the centre, these nodules show punched out appearance. Each nodule consists of a focus; of intense cellular infiltration with an inner core of neutrophils and a periphery of macrophages. The core liquefies and the overlying mucosa may slough. The nodules maybe isolated or semi confluent with suppurative cores separated by grnaulation tissue. A discrete slough of the necrotic tissue over individual nodules cans occur, leaving a craterised form of ulcer which has a sharp margin and a smooth base. Penetrating the cartilage, the ulcers may perforate the septum. These ulcers may give rise to an oily, sticky often blood stained discharge and may heal by granulation tissue. Epithelium covering the scar finally ruptures leaving stellate scars. Relevant lymph glands namely submaxillry, bronchial and thoracic glands are swollen and oedematous. Enlarged spleen is seen and it contains nodules.

In acute stage there is hemorrhagic and fibrinous exudation. The more exudative foci typically have necrotic centers composed of karyorrhectic neutrophils. They are basically pyogrnaulomatous lesions, but the relative proportions vary depending on the exudative or proliferative type.

The lesions of glanders in alimentary tract are rare. Haematogenous metastases are common in the spleen and less common in other viscera or in locomotor organs.

Diagnosis: Intradermopalpebral mallein test, wherein 0.1 ml of concentrated mullein is injected into the skin around 5 mm below the lower eye lid, a positive reaction results in local swelling and mucopurulent discharge which reaches its height within 24 hours and lasts for 2 to 7 days. Subcutaneous and ophthalmic tests are also available.

Serological tests: The glanders antibody is demonstrable by complement fixation test, isolation of the organisms and conducting Straus's test. Histo-pathological examination gives a clue to the disease.

Differential diagnosis: clinically cutaneous glanders can be confused with epizootic lymphangitis and ulcerative lymphangitis. Acute glanders can be confused with strangles. The use of mallein test or demonstration of the causal organism will differentiate them. A table has been furnished in the text how to differentiate between glanders, ulcerative lymphangitis and epizootic lymphangitis.

Allergic rhinitis:

It is seen as sporadic cases in dogs, cats and horses. It is diagnosed on the basis of occulonasal discharge, sneezing, nose rubbing, head shaking, and perhaps epistaxis, and the presence of eosinophils in nasal exudates or ravage fluid. This is seasonal. Affected animals have nasal discharge, lachrymation, sneezing, and evidence of nasal itching. The nasal mucosa is pale and thick from oedema fluid and mucosal erosions may be visible in the anterior nares. The exudates is at first serous but later becoms mucouruletin or contains floccules of detritus and mucous. Eosinophils are prominent component of exudates. Histologically the surviving nasal epithelium is hyperpalstic or eroded and is infiltrated by eosinophils. In more severe cases, in which there are extensive superficial diphtheritic changes, many of the small mucosal vessels show fibrinoid necrosis.

Nasal granulomas

Nasal granulomas are seen in Indian cattle mostly due to *Schistosoma nasale* infection. The eggs create the granulomatous condition and sterterous breathing. There is actinobody formation with epitheloid cells, lymphocytes and plasma cells around the spinous process of the egg of Schistosoma.

Less commonly nasal granulomas in cattle are attributable to fungal infection. They occur in the anterior portion of the nasal cavity. Histologically in the centre of granulomas one can see the hyphae and chlamydiospores of the fungi. *Aspergillus fumigatus* is the commonest cause in the dog that produces granulomatous rhinitis. In cats *Cryptococcus neoformans* is the most frequent cause. Acitnomycosis and Actinobacillus are involved in the granulomatous rhinitis in sheep. The incidence of nasal and facial actinobacillosis in sheep is highest in drought feeding conditions, probably as a result of injury to the lips.

Rhinosporidiosis in animals is a chronic polypus rhinitis caused by *Rhinosporidium seberi*. The disease occurs in horses and cattle, and to lesser extent in dogs, goats and water fowl. It also occurs in humans. The fungal sporangium is seen as a rounded or oval structure and measure 100-400μ in diameter which is seen as whitish spot to the naked eye in the lesion or growth. The sporangia have thick, double contoured, chitinous walls and contain numerous spherical sporangiosphores of 7μ in diameter. The mature sporangium releases the sporangiosphores into tissue or into the nasal discharge and these in turn form new sporangia to complete the life cycle. Initiation of the disease is thought to be influenced by local trauma to the nasal mucosa and an association has been observed between the *Rhinosporidiosis* and the nasal lesions produced by *Schistosoma nasalis*, as well as with punctures of nasal septum for nose leads.

Grossly the lesion is a polyp, usually, single and unilateral. The polyps range from sessile to pedunculated and caulifower like. They vary in size unto a diameter of 2 to 3 cm. They are soft pink and bleed easily because of their myxomatous in

nature. Histologially, the bulk of the polyp consists of stroma of fibrous or fibromyxoid tissue covered by usually by intact epithelium. The organisms are present in stroma tissues, as spherical bodies of various sizes. There is scant reaction to them except when sporangia rupture. Then there is granulomatous and occasionally a neutrophilic response.

Neoplastic diseases of nasal cavity and sinuses:

Ethmoidal tumors are very common and are commonly prevalent in cross bred cattle where European blood has been introduced, to indigenous Zebu cattle.

These tumors are important in dogs, next in cats and horses. There is no clear relationship between frequency of nasal tumors in various breeds of dogs and lengths of their noses. The breeds with significantly increased risk such as Collie and German shepherds do have long noses and this has led to the generalization that dolichocephalic breeds as a whole are at a greater risk. Epithelia tumors of the nasal cavity and sinuses are classified as follows; papillomas, adenomas, carcinomas such as squamous cell carcinoma, spindle cell carcinoma, transitional carcinoma, adenocarcinoma, mucoepidermoid carcinoma, undifferentiated (anapalstic) carcinomas and tumors of olfactory neutroblastomas are common.

Squamous cell carcinomas predominate in the cat and horse. In the cat, a large proportion originates from the nasal vestibule, whereas in the horse the maxillary sinus is common. Transitional carcinomas are common in the dogs. With lower number of squamous cell carcinomas, adenocarcinoma, and undifferentiated carcinomas. Transitional cell carcinomas are being called as nonkeratinising squamous cell tumors. Transitional cell carcinomas typically consist of thick stratified layers of mostly cuboidal cells with rounded nuclei, indistinct cell borders, and a distinct basement membrane beneath the layer of neoplastic cells. Small micro cysts are present beneath the layer of neoplastic cells. Adenocarcinomas have a predominant of papillary folds and glandular acini formed by single layer of cuboidal to tall columnar cells with a basement membrane. Undifferentiated carcinomas are mostly solid tumors in which there are large packets or nodules of round to polygonal cells with no discernible pattern. The olfactory neutroblastomas is a rare tumor of the caudal nasal cavity and is confining to mostly ethmoturbinate region. These tumors are typically highly cellular and consist of a uniform population of round to elongated cells with moderately dens nuclei and small amounts of cytoplasm. An important diagnostic feature is the presence of palisade around vessels and rosette formation.

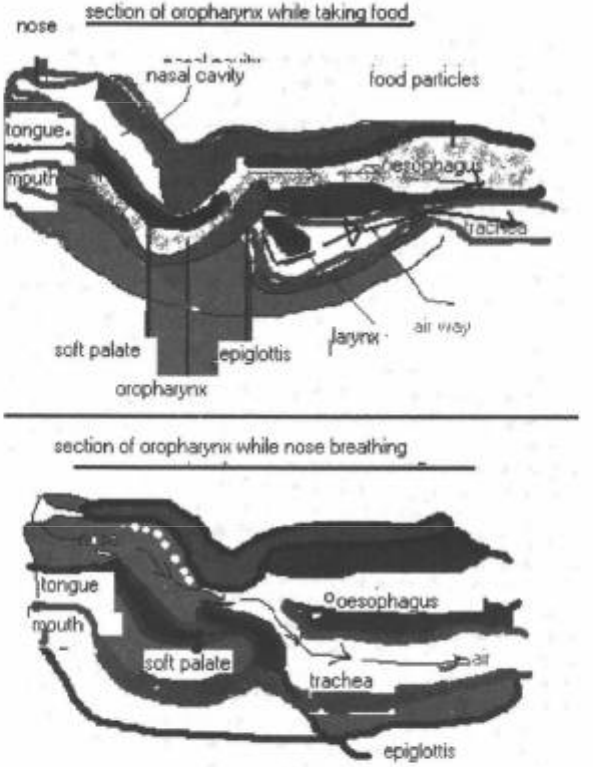
Endemic tumors of ethmoturbinate have been reported throughout the world including India. The endemicity depends on the observations that multiple cases occur in few flocks and herds and may continue to occur over several years, and that more than one species can be affected on individual farms. The incidence pattern encourages the view that the neoplasms are caused by a virus. Type C-viral particles has been isolated in some tumors.

The guttural pouches of Equidae are ventral diverticula of the Eustachian tube. They tend to become involved in inflammatory processes in analogous fashion to the paranasal sinuses. Guttural pouch mycosis is common due to Aspergillus infections in horses. A less common condition is guttural pouch tympany is seen mostly in young animals, and the accumulation of air is presumed to be due to valvular action of nasopharyngeal orifice of the Eustachian tube. Tumors of the guttural pouches are rare, but when encountered are most likely to be squamous cell carcinoma.

Diseases of larynx and trachea:

Roaring or laryngeal hemiplegia

In normal health, the arytenoids cartilage is drawn outwards during inspiration to allow ingress of air. The important muscles that operate this are the crycoartenoides. If for any reason there is injury and degenerating of the nerve supplying the muscle then the cartilages cannot open and so will stand in the way of air passing freely into the wind pipe.



In horses a condition is noticed in which there is hyaline degeneration and fibrosis of the left crycoartenoides muscles together with demyelination and Wallerian degeneration of the left recurrent laryngeal nerve that supplies the muscle. The cause for the paralysis of the nerve is obscure. One theory is that it is subjected to repeat trauma by the pulsation in the aorta as the nerve circles round aortic arch where the nerve is situated during its course.

Other causes are lead poisoning and pressure on the nerve by aneurysms, enlarged lymph nodes, abscesses, tumors, esophageal diverticula, and other traumatic conditions.

The extent to which damage is caused by traumatic interruption of axoplasmic flow, neuritis by extension from guttural pouch disease, vitamin deficiency or neurotoxin are implicated in the production of this disease. Organophosphourous ingestion and poisoning has also been incriminated.

When the nerve is paralyzed, and the muscle are degenerated and replaced by fibrous tissue, the arytenoids cartilage does not open during inspiration and so air cannot enter the trachea freely and this condition is accentuated when the animal is exercised, and a noise is heard by brushing of air with the arytenoids cartilage. This is therefore known as roaring.

In cases detected clinically, histological examination of the nerve fibers reveal loss of myelinated fibers in the middle and distal portions of the left recurrent laryngeal nerve.

Parasitic disease of larynx and trachea: *Syngamus trachea*, the gape worm occurs in the poultry. The male and female nematode worms are unison and it creates difficulty in respirations. *Syngamus larynges* occur in the larynx of cattle. Capillaries aerophila parasitises the trachea and bronchi of dogs, foxes, and occasionally cats. These are the slender worms of 2 to 3 cm long. The eggs which are operculated lay in the airways, moves with mucous to the pharynx and are swallowed and passed on to the faeces. The larvae develop to the infective stage within the egg and remain there until the egg is swallowed by suitable host. Hatching occurs in the intestines. The larvae reach the lungs in less than a week and are mature in the trachea in less than 6 weeks. Heavy infestations causes are severe irritating as well some obstruction to the lumen of the airway.

Filaroides osleri is an ovo-viviparous, filiform worm 5- 15 mm long and is found in the dog and related species. The typical lesions are protruding sub mucosal nodules in the region of the tracheal bifurcation. The thin walled eggs contain its stage larvae, are coughed up and swallowed and hatch before being passed as infective larvae in the faeces. Pups are infected by the larvae in the saliva or faeces of their dams. Larvae migrate from the gut to the lung through the blood. The worms lay in tissue spaces between the cartilaginous rings of the trachea and large bronchi and in the adventitia and lymphatics. Dead worms provoke foreign body reaction

with infiltration of neutrophils and few giant cells. Immature worms without significant tissue reaction are found in the pulmonary lymphatics and occasionally in the alveoli.

***Broncho stenosis** is a narrowing of the bronchial* lumen due to obstruction of peripheral pressure. The causes are due to aspiration of foreign bodies. Accumulation of exudates, parasites within the lumen, inflammation of the wall of the bronchus producing alterations in it and the exudates infiltrating the wall produces the diameter of the bronchi. Pressure from outside the bronchial wall like abscesses, tumors, enlarged lymphnodes and exudates of the pleural cavity and spasms of muscles of bronchi as seen allergy all cause broncho stenosis.

A partial closure of the bronchi to bronchioles results in ballooning of the lung involved, since air that enters during inspiration is not expelled during expiration and so is trapped. Repeated inspirations will therefore result in ballooning of the alveoli. Complete obstruction of a bronchus resulting in collapse of the lung.

Bronchiectasis: This is dilatation of the bronchus. The causes are Sequleae to the chronic inflammation of the bronchi, in which the elastic tissue and the musculature and even the cartilages may be destroyed. Due to loss of elastic tissue, contractile power of the bronchus is lost and so the bronchus dilates at the place of dilatation, exudates accumulates thereby still further dilating the bronchus. In chronic pneumonia, the contraction of the fibrous tissue exerts a pull thereby widening the walls. The dilatation is facilitated by a weakening of the wall in brohcus, which may also be found. In bronchostenosis, air accumulates during inspiration and so causes dilatation of the bronchi below the level of obstruction when the bronchi are completely closed resulting in atlectasis, there is an elastic pull on the bronchial wall due to negative pressure in pleural cavity.

Grossly two forms are recognized namely the saccular and cylindrical variety. The saccular one is less common, is an out pouching of the bronchial wall, usually results due to localized necrotizing foci in bronchitis, found in cattle and sheep in lung worm infection. The cylindrical variety, which is more common, especially in cattle, is a uniform dilatation of the bronchi. Histologically the wall of the affected bronchi shows variable infiltrating by chronic inflammatory tissue. The musculature, cartilage and the lining epithelium may disappear in varying degrees. The affected lung is collapsed and fibrosed. Plural adhesions with the inflammed lung are common. These results in persistence cough and complications include abscess with spread to neighboring bronchiolitis resulting in bronchiolitis and bronchopneumonia. Usually in animals the pathogenesis of bronchopneumonia arises in this way.

Neoplastic disease of larynx and trachea: Variety of epithelial and mesenchymal tumors has been observed. Epithelial tumors are papillomas are squamous cell carcinomas. Adenocarcinomas are exceedingly rare. Leomyomas and

rhabdomyosarcomas arise in or close to the wall. Chondromas or osteochondromas occasionally originated from the laryngeal or tracheal cartilage.

Oncocytomas are rare benign tumors arising as solitary projecting nodules in or close to the lateral ventricle of the canine larynx, particularly in young dogs. They consists of lobular masses of pleomorphic cells with abundant deeply, eosinophilic, granular or foamy cytoplasm. Oncocytes (Oxyphil cells) occur in a variety of endocrine glands and epithelial tissues of humans and occasionally give rise to tumors. Evidence indicates that they are atypical neuroendocrine cells.

Bronchitis

In acute bronchitis the exudates may be catarrhal, mucopurulent, fibrinous, fibrinopurulent or purulent. Catarrha bronchitis is the simplest form of inflammation. Acute mild irritation of the bronchial mucosa causes discharge of secretion from goblet and serous cells and from such seromucinous glands. Hyperemia and oedema of the lamina propria accompany the secretory discharge. Ciliated epithelial cells are more sensitive to insult with irritant are often the fist to undergo necrosis and slough. Neutrophilic infiltration is heavy. If the inflammation is transient regeneration and restoration of epithelium is quick due to proliferation of nonciliated secretory cells and basal cells. Purulent or suppurative bronchitis occurs and the exudates in the bronchi become yellowish and viscid. The pus material consists of necrotic cells and dying neutrophils. Ulcerative bronchitis occurs in severe viral bacterial infection during which large areas of epithelium are destroyed. In bacterial infections there is heavy purulent bronchitis. Fibrinonecoritc bronchitis is characterctised by exudates forming thick yellow membranes which is firmly attached to many points. Severe necrotizing bronchitis occurs in brochiectasis (dilatation bronchi) as a result of aspiration foreign materials.

Chronic bronchitis: The causes are mild continuous irritants like smoke and dust. Chronic venous congestion as seen in heart diseases; chronic infections of upper respiratory tracts and chronic sinusitis; Bronchiectasis' nematode infections of respiratory tract and lung abscesses.

Grossly the bronchial mucosa is thickened and has a velvety feel. Sometimes it may be congested but more often it is pale and edematous. The exudates are mucoid or mucopurulent and in cases of worm infection, it is mixed with worms and their eggs. The bronchi may also be dilated.

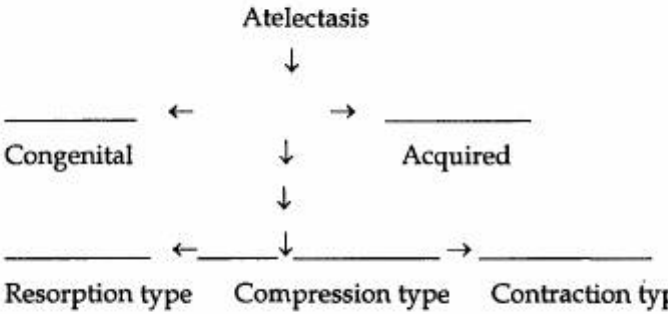
Histologically there is infiltration of lymphoid cells. The ciliated epithelium is lost and replaced by a cuboidal variety. The mucous glands may show atrophy. There is hyperplasia of peribronchial glands which now resemble goblet cells. There is increased fibrosis of the walls, producing polypoid projections and the projection into the lumen called as brochiolitis obliterans. Follicular aggregates in

the form of lymphoid nodules are seen. This is common with myoplasma infections in birds.

The results of chronic bronchitis is spread of infection results in bronchopneumonia with lung involvement, it may leads to atlectasis of the lungs or it may result in Bronchiectasis of the bronchial tree or it may lead to emphysematous condition of the lung with results in chronic venous congestion due to failure of the right side of the heart.

Disease of lungs

Atelectasis: This is the failure of the alveoli to open and contain air or to say it is an incomplete expansion of the lungs or to the collapse of previously inflated lung substance producing areas of relatively airless pulmonary parenchyma. The alveoli become collapsed. The part sinks in the water. This condition may be congenital or acquired atelectasis could be classified as follows.



Resorption atelectasis is the consequence of complete obstruction of airway, which in turn leads to Resorption of oxygen trapped in the dependent alveoli, without impairment of blood flow through the affected alveolar walls since the lung volume is diminished, the mediastinal may shift towards the atelectasis lung. Resorption atelectasis is mainly cause principally by excessive secretions (mucus plugs) or exudates with smaller bronchi and is therefore found in chronic bronchitis, Bronchiectasis aspiration pneumonia.

Compression atelectasis results where the pleural cavity is partially or completely filled by fluid exudates, tumor blood or air from outside. This is encountered in patients with cardiac failure, development of pleural fluids due to mycobacterial infections and origin of exudates due to neoplasms.

Contraction atlectasis occurs when localized or generalised fibrotic changes in the lung or pleural adhesions bring this.

Congenital atelectasis: The causes are due to the obstruction of the bronchi by mucous or by inhaled muconial shreds. Damage to the respiratory centre that may occur injure to the brain while at birth may also lead to this.

Grossly the lungs are dark and reddish hue in color due to dialtation to the alveolar capillaries. The lungs are firm to the touch and sink water, since there was no aeration. The alveoli are collapsed and the epithelium lining the alveoli is cuboidal. Sometimes the alveoli may contain fluid.

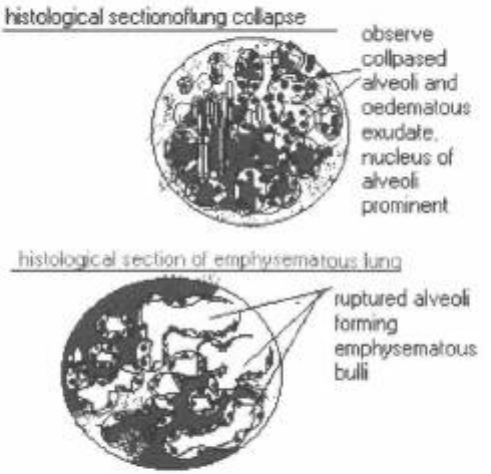
Acquired atelectasis is due to obstruction of the lumen of bronchus is where the air in the alveoli is reabsorbed. The causes of obstruction are obstructing to the lumen like foreign bodies, pus, mucous, masses of parasites and such enlarged objects like tumors, abscesses, enlarged lymph nodes, and cysts pressing on the bronchial lumen. Any compression like extra pulmonary compression due to hydrothorax, pneumothorax, hydropericardium and abdominal distension as in tympany of rumen and ascites results in atlectasis of lungs.

Collapse is a word strictly used for the neonatal collapse and atelectasis for the collapse of lungs in other times in life.

Grossly there is collapse of lung. The affected lung tissue is dark and depressed from the level of surrounding healthy lung and the affected part sinks in water and is leather in consistency. Pleura are thickened and wrinkled.

Histologically the alveoli are devoid of air. They may appear as small or enlarged clefts or the wall may lie in apposition with each other with no lumen viable. Due to the pressure of alveolar air, the capillaries become dilated and engorged with blood.

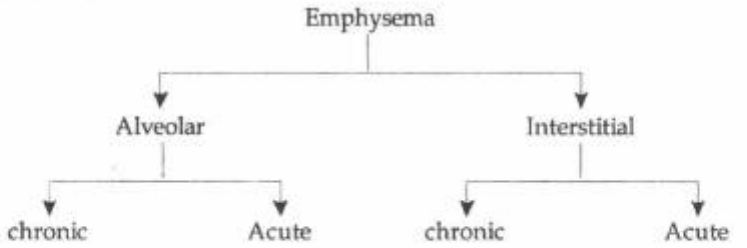
Seqelae: Because of the collapse of lung, parenchyma can be expanded, atelectasis is a reversible disorder. Atlectatic parenchyma is prone to develop super imposed infection.



Emphysema

Emphysema is excessive air in the alveoli leading to distension of it. It is divided into alveolar emphysema of acute in nature and chronic alveolar emphysema. The air in emphysematous cases ruptures the alveolar membrane and enters into the interstitium and then this condition is called interstitial emphysema. Thus emphysema could be classified as follows.

Classification



Emphysema could also be classified depending on the surface of the appearance of the affected lobe. Thus, it can be centri acinar, panacinar, paraseptal or irregular. Other type of emphysema described in human literature is compensatory emphysema, senile emphysema and bulbous emphysema.

Compensatory emphysema is due to dilatation alveoli consequent to the loss of substance.

Senile emphysema is due to voluminous over distended lung that occur in the old aged persons. This is due to the age related alteration of the internal geometry of lungs where in larger alveolar ducts and smaller alveoli that occur without loss of elastic tissue or destruction of lung substance.

Acute alveolar emphysema

In Acute alveolar emphysema the alveoli are greatly distended and sometimes may rupture forming vesicles or bullae. Some scientists called this as vesicular emphysema. There is excessive amounts air within the air spaces or alveoli. Interstitial emphysema is the presence of air within interlobular, sub-pleural and other interstitial zones of the lung.

Emphysematous condition is extremely important condition in human beings. In animals often this is discernible at postmortem.

The causes of alveolar emphysema are as a compensatory mechanism of breathing when lung has collapse in pneumonias or consequent to the atlectasis when affected portion of lung cannot dilate other healthy parts dilate to a greater extent to fill the space created by the expansion of the chest cavity. Overexertion of alveoli as occurs in severe coughing and struggling for ventilation. Feeding on lush pasture; allergic or toxic agent's exposure.

Regardless of distribution, severely emphysematous lung is grossly voluminous, pale and puffy. When the lesion is diffuse, the lung fill the thoracic cavity even after the chest has been opened and even the imprints of the ribs are seen on the pleural surface of the lung. The enlarged air spaces are often visible as small vesicles, and in severe cases coalescence of air space can produce large air filled bullae measuring one to several centimeters in diameter. Histologically, enlargement and coalescence of air spaces in inflation in section reveal as white space with ruptured shred as that to ruptured borders of balloons after forceful inflation. It can be fund in the postmortem the apices and along the sharp ventral border of the lungs. In rare case emphysematous bullae cause fatal pneumothorax and leads to acute interstitial emphysema. Several causes like genetic factors atrophy of alveolar septa due to ischemic or unknown causes and mechanical factors leading to widening and rupture of air spaces have been attributed. In human emphysema cases it is dùe to deficiency of 1-antitrypsin deficiency or 1-protease inhibitor leads to emphysematous condition. This could be attributed to the excessive proteolysis and elastolytic activity of alveolar lining membranes. The neturophil elastase from lysosomal granules also contributes to this mainly. Thus genetically controlled protease-antiprotease imbalance is presumed to lead to emphysematous conditions in certain humans when compared to others.

Acute interstitial emphysema

Acute interstitial emphysema is often accompanied by the acute alveolar emphysema. In this condition, air collects in the interlobular space beneath the pleura and other interstitial tissues of the lung. This is seen more often in cattle and sheep.

Interstitial emphysema is distinguished from alveolar emphysema by the presence of air in the connective tissues and lymphatics of lung, chiefly the interlobular septa but also beneath the pleura and around vessels and airways. Interstitial emphysema occurs mainly to lung with well developed interlobular septa. Lungs of cow, sheep and pig have this feature. The cow is much more susceptible to this lesion. Any condition causing forced expiratory movement's even as agonal cause the condition in the cow. It is common in Kosher killed animals for food purpose. It occurs in most dramatic forms as a prominent feature of acute intersitital peumonia in cattle. Constant bellowing as seen consequent to oestrum in cows and condition when the cow I separated from calf it is seen. Forced breathing as in old hunting dogs and pulmonary ancylosis are also contributory. In these cases alveolar emphysema when it occurs is so severe that the alveoli rupture and air escapes into the interstitial tissue of the lung, especially in the interlobular septa. In severe conditions, air may escape via the thoracic in left into the sub cutis of the neck and may accumulate there along the spine from pole to the base of the tail.

Chronic alveolar emphysema (Heaves or Broken wind)

Chronic alveolar emphysema is commonly called as broken wind or heaves in horses this is also called as chronic brochiolitis-emphysema complex. In pathophysiolgical terms, it is being called as chronic obstructive pulmonary disease.

The relative importance of allergy, infection, and toxicity has also been attributed. The frequent presence of eosinophils, circumstantial evidence of clinical exacerbation on exposure to mouldy hay, bedding or stable dust, and limited information from aerosol challenges using suspect fungal antigens like Aspergillus fumigatus spores in the hay are important causes. From the point of view of the characteristic goblet cell metaplasia and mucous hyper secretion, there is evidence that histamine, prostaglandins, and leukotrienes released during type I allergic responses have a stimulatory effect on mucous secretion.

Working horses immediately after a heavy meal when the digestive organs are distended and so prevent the expansion of diaphragm during inhalation. So animal make violet respiratory efforts for breathing. Dusty and mouldy feeds make cough response to generate which is responsible for deep respirations. Obstruction of the bronchi as in brochiolitis and allergic substance have all incriminated in causing heaves in horses. So during violent cough and Inspiratory movement's alveolar walls are subjected to undue pressure. This process, repeated for months and years produces atrophy of the walls and their subsequent rupture. Pressure also interferes with capillary circulation so the nutrients and oxygen supply to the alveolar wall is diminished with resultant fatty degeneration to the alveolar epithelium degeneration and disappearance of elastic fibers and the inter-alveolar and interlobular septa resulting in rupture of the alveolar walls. Hence the adjacent alveoli become confluent bullae. When air passes through the pores of Kohn that this the communication between the two alveoli, adjacent alveoli become ballooned to cope up collateral ventilation.

Owing to their diminished elasticity and permanent distension, alveoli expand with difficulty at each inspiration and also contract less easily on expiration and consequently continue to increase in size and finally rupture.

Besides the mechanical stress that produces emphysema as detailed above, it may primarily be also due to inflammation of respiratory bronchioles, alveolar ducts and alveoli. These structures become necrotic and weakened thereby become ballooned due to the pressure of air that may be trapped.

Grossly the affected lung is voluminous and is pale due to decreased blood circulation. Lung pits on pressure easily and the indentation of the ribs is seen clearly.

Histologically the alveoli are over distended. Their walls are atrophied and then rupture of some of the alveoli with confluence of neighboring alveoli and give to giant alveoli or bullae. As result the sequel is hypertrophy and dilatation of right

ventricle with resulting chronic venous congestion.

Thus chronic alveolar emphysema suffering horse shows decreased work performance, chronic coughing, and abnormality of lung sounds, pulmonary and cardiac dysfunction.

Emphysema in human beings: This is a common problem in humans. Cigarette smoking brings about much worse disease conditions in emphysematic patients. Smoking produces chronic bronchitis and emphysema. The pathogenesis lies that smokers have greater number of neutrophils and macrophages in their lung alveoli. Neutrophilic releasing chemotactic factors (IL-8) are released by smoking. Nicotine is thus chemotactic for neutrophils. Cigarette smoking activates alternate complement pathway. Smoking releases elastase from neutrophils and smoking also enhances elastolytic protease activity in macrophages. Macrophage elastase cannot be inhibited by -α- antityrpysinase activity of serum, and can proteolytically digest this enzyme. Oxidants in cigarette smoke and 0_2 free radicals secreted by neutrophils inhibit α1-antitrypsinase and thus decrease net antielastase activity in smokers.

Diseases of lungs

Circulatory disturbances of lungs

Pulmonary ischemia occurs following emphysematous or fibrotic changes in the lung parenchyma. Because of the dual blood supply from the pulmonary and bronchial arteries, and the extensive collateral circulation, congestion rather than ischemia is the usual sequel to arterial obstruction.

Active hyperemia is part of the acute inflammatory response and is feature of acute pulmonary injury of many types. Most animals that die in early stages of pneumonia at postmortem always reveal either that of active hyperemia or that of congestion.

Pulmonary congestion is most commonly caused by left sided or bilateral cardiac failure. This is the terminal event that occurs in most ofthe bacteria or septicaemic diseases. A piece of lung when it squeezed abundant amount of blood will be oozed out.

Pulmonary oedema

The lung tissue is much more prone to accumulation of fluid as there is much loose tissue and empty spaces.

Pulmonary oedema is a frequent complication of many diseases and is therefore one of the most commonly encountered pulmonary abnormalities. Most causes of oedema are by increasing capillary hydrostatic pressure, by increasing permeability of the air-blood barrier or by combination of both factors. Decreased plasma osmotic pressure, such as occurs in hypoalbuminemia and lymphatic obstructions caused for instance by widespread tumor infiltration of lymphatics are also

responsible for causation of pulmonary oedema. Many agents cause pulmonary oedema by damaging alveolar type I epithelium and capillary endothelium. The increase in permeability leads to oedema of more rapid onset and of higher protein concentration than in cardiogenic forms.

Causes for Pulmonary oedema:

Homodynamic oedema: Increased hydrostatic pressure, left side heart failure, mitral stenosis, volume overload, pulmonary vein obstruction, decreased oncotic pressure, hypoalbunemia, nephritic syndrome, liver lesions, and protein losing syndrome and lymphatic obstruction.

Oedema due to micro vascular injury: Infectious agents like viruses, bacteria like *Pateurella* and *Mycoplasma* organisms; inhaled gases like O_2, SO_2, cyanides and smoke. Liquid aspiration of gastric contents near drowning. Drugs and chemicals, chemotherapeutic agents, chemical like kerosene and organo-phosphorus compounds. Inhaled corrosive gases including 80 to 100 % oxygen, systemic toxins, anaphylaxis in certain species such as cow and horse, endotoxin and shock like states all can cause acute pulmonary oedema.

Diffuse alveolar damage in endotoxemia: endotoxemia is associated with gram negative organisms and endotoxin acts on multiple targets. It induces monocytes and fixed macrophages to release mediators, including tumor necrosis factor –α (TNF- α), and chemotactic peptides like leukotrienes B4 and IL8. Endotoxin induces, activation of complement, and release of C5a, which together with bacterial lipo-polysaccharides and TNF activates polymorph nuclear leukocytes and up regulate binding avidity of adhesion molecules. Endotoxin also activates endothelial cells, to up regulate adhesion molecules that facilitate binding of neutrophils. Activation of polymorph nuclear leukocytes helps in release of oxidants, proteases and prostaglandins. The net result is the sequestration of polymorph nuclear leukocytes in pulmonary capillaries, damage to the endothelial and epithelial cells, and the development of interstitial oedema and alveolar hyaline membranes.

Oedema of undifferentiated origin: This is seen in high altitudes and as well due to neurogenic factors. Trauma and sepsis and radiation also induces pulmonary oedema.

Edematous lungs are wet, heavy, and do not collapse completely when the thorax is opened. Frequently there is excess fluid in the thoracic cavity. Sub plural and interstitial tissues are edematous, and in lung with well developed interlobular septa, there is an increased pattern because of the septa become distended with oedema fluid.

Foam is discharged from the nostrils in severe cases, and foam variously mixed with fluid is often present in the trachea and intrapulmonary airways. Fluid oozes out from cut surfaces of edematous lungs.

The colour of oedema fluid and foam depends on the amount of hemorrhage. If absent, the interstitial oedema is clear, colorless, to slightly yellow and the foam is white. Various amounts of hemorrhage cause corresponding degrees of blood staining of fluid and foam. The pulmonary parenchyma and cut section of lung is usually bluish red in colour according to the amount of congestion or hyperemia. When severe it is difficult unless seen histologically weather it is an early stage of pneumonia or acute oedema.

Histologically oedema fluid is acidophilic and in Haematoxyin and Eosin stained sections, it is red in colour with faintly granular material filing alveoli except for occasional discrete holes which represent trapped air bubbles. Oedema due to inflammatory response is more acidophilic than the transudates of cardiac origin.

When the lungs are congested, the capillaries are distended and intra-alveolar hemorrhage is common. Alveolar macrophages containing haemosiderin granules are present and these are popularly known as heart failure cells. Hypertrophy of the muscular walls of small pulmonary vessels and thickening of pulmonary capillary walls by fibrous tissue is seen in dogs and cats suffering with pulmonary hypertension.

Pneumonia

Inflammation of the lungs is called pneumonia. Pneumonia is a common disease condition seen in animals and man. Pneumonia in individuals occurs whenever defense mechanisms are interfered or impaired whenever the resistance of the host in general is lowered. While pneumonia itself is a reaction taking place in the alveoli and their walls, the interlobular septa and other connective tissue structures are also distended with exudates especially with serous fluid.

There has been a tendency to use the term pneumonia for more acute and exudative inflammation and Pneumonitis for more chronic and proliferative lesions. Pneumonitis and chronic interstitial pneumonia are largely and synonymously being used by pathologists.

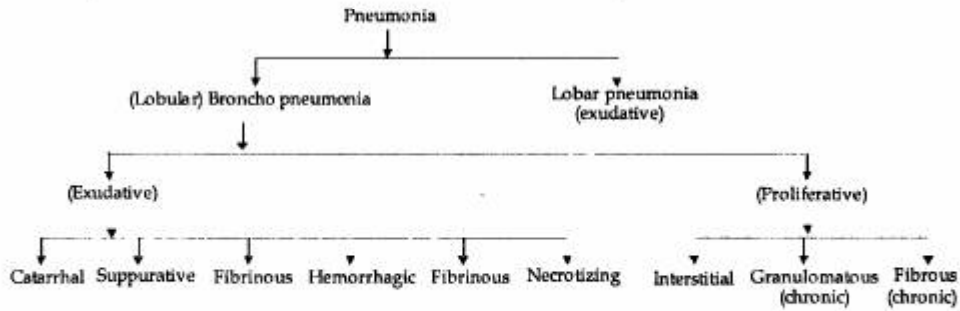
Anatomic patterns of pneumonia

The pulmonary inflammatory response varies according to the nature of the causative agents (bacterial, viral, parasitic, fungal and other nonspecific causes), their distribution particularly by the route by which they reach the lung, and their persistence (acute, sub-acute, chronic) and the inflammatory response which it exhibits (exudative catarrhal, fibrinous, hemorrhagic, diphtheritic, gangrenous) or the cells that infiltrate (granulomatous, lymphocytic, chronic) or morphological features. Morphologically, there are two approaches. As already told one criteria is the type of inflammation, and two subcategories as exudative covering catarrhal, fibrinous, suppurative, hameorrhagic, necrotizing and or as proliferative pneumonia.

The second and more useful morphologic approach is to classify pneumonias

according to initial site of involvement and pattern of spread of the lesion. On this basis, most pneumonias fall into three main categories namely broncho pneumonia, lobar pneumonia and interstitial pneumonia.

Acute pneumonias usually are of infectious in nature, produced plenty of exudates and spread by bronchus. On the contrary, chronic pneumonias are of highly varied cause, proliferative in nature and often interstitial pattern.



Most of the pneumonias in animals are of broncho-pneumonia type; only in humans with bacterial infection with diplococcic and lobar type of pneumonia is seen as such whole lobe is affected.

Agents that cause pneumonia in animal

Bacterial agents

Species of animal	Causative agent
Horses	*Corynebacterium equi, streptococcus equi, Malleomyces mallei (glanders)*
Cattle	*Pateurella multocida, Actinomyces spp, Mycoplasma mycoides, Corynebacterium pyogenes, Actinobacillus ligniersei, staphylococci, Streptococci, Mycobacterium tuberculosis*
Sheep	*Corynebacterium pyogenes, Pateurella haemolytic, Corynebacterium ovis, staphylococcus, streptococcus, Escherichia coli,*
Dog	*Bordetella bronchiseptica, staphylococcus, Klebsella spp.*
Swine	*Corynebacterium pyogenes, Haemophilus suis,pasteurella multocida, salmonella cholera suis*
cats	*Pateurella multocida, Escherichia coli*
poultry	*Pateurella aviseptica, Escherichia coli, Salmonella pullorum, Salmonella gallinarum, Mycoplasma gallisepticum, Haemophilus paragallinarum*

Viral agents

Species	Name of the virus
Equines	Equine infectious pleuropnuemonia Equine influenza
Cattle	Parainfluenza viruses, respiratory syncitial viruses
Sheep	Parainfluenza viruses, maedi, jaagsikete Sheep pox
Poultry	Ranikhet disease
Dogs	Canine distemper

Parasitic agents that cause pneumonia in cattle (Verminous pneumonia)

Species affected	Name of the parasite	habitat
cattle	*Dictyocaulus viviparous* *Paragonumus westermanii , hydatid cysts , Fasciola-hepatica, Fasciola-gigantica, Schistosoma nasalis, Syngamus laryngeus , toxoplasma gondii*	Bronchi Bronchi-and alveoli
sheep	*Dictyocaulus filaria* *Prtostrongylus rufescens* *Mullerius capillaries* *Paragonimus-westermanii, hydatid cysts, schistosoma nasalis,paragonomus westermanii, oestrous ovis larvae.*	Bronchi Bronchi Alveoli and blood vessels Lung,-alveoli and bronchi
swine	*Metastrongylus apri* *Ascarid larvae,hydatid cysts*	Bronchi Migratory larvae
horse	*Dictyocaulus ornifieldi , , hydatid cysts, Habronema spp.*	Bronchi
dog	*Angio strongylus vasorum* *Paragonumus westermanii* *Aleurostrongylus abstrus* *Angiostrongylus vasorum*	Pulmonary arterioles Cysts in lungs and bronchi
cat	*Aleurostrongylus abstraus*	Bronchi
poultry	*Syngamustrachea, Typhlocoelum cymbium*	Trachea
swine	*Paragonumus westermanii Paragonimus kellicotti, , hydatid cysts*	

Variety of irritant like inhalation of dust, pollen, foreign bodies, smoke, hot and cold air, insecticides, war gases and medicinal agents are responsible for causing varieties of pneumonias in domestic animals.

Routes of infection:

Though the respiratory passages- mainly bronchogenous, this is by the far the most common route. Through the blood vascular system-haematogenous- many bacteria and viruses and parasitic larvae this system. Through penetrating wounds external trauma and penetrating the lung and producue pneumonia

Aspiration pneumonia is very common in animals due to wrong drenching and foreign objects stay in the lungs and caused pneumonia of acute nature.

Predisposing conditions: Conditions the predisposing factors make the animals more susceptible to diseases of respiratory system. Most of the larval infections may flare up whenever stress in the animals there. The stresses are transport, lack of water, excessive exposure to hot and cold conditions and starvation.

These affect the general stamina of the animals by depleting the antibodies and the resistance of the animals and as well bring about the destruction of ciliary movement and defense systems of the body of the animal. Oedema of lungs that results in acute irritants like phosgene or chlorine gas and oedema that occurs to cardiac lesions and other factor create ideal conditions for occurrence of pneumonia as the edematous fluid is a good medium for the organisms to multiply and develop. In fact hypostatic conditions where the animal lies for a prolonged periods and in bed ridden conditions, hypostatic pneumonia develops.

Stages of pneumonia

In developing pneumonic lesions in the animals these following one or all the stages will be passed. Fully developed pneumonic lesion, which sinks in water by depleting air spaces, will have the following lesions. A stage of congestion or oedema followed by a stage of red hepatisation, a stage of grey hepatisation and finally ends with a stage of resolution wherein recovery from the pneumonic lesion or death of tissue and complications ensue.

Stage of congestion and oedema: This is the earliest stage where there is active hyperemia of lungs, due to presence of irritant. Copious oedema also occurs in the alveoli.

Grossly the lungs are congested and swollen, the cut section and kept in water still floats. On squeezing the tissue blood tinged fluid with froth will come out.

Histologically, the capillaries on the alveolar walls are dilated and filled with blood. Alveoli contain little serous exudates and often a few RBCs. Depending on the irritant, this may develop within a few minutes to a few hours.

Stage of red hepatisation: This is the second stage in the development of pneumonic lesion. By this time most of the lung tissue is being destroyed, and as lung librates plenty of prostaglandins and detoxification mechanism of leukotrienes are interfered, animals show signs of fever and labored breathing characterized by increased temperature, vomiting, thirst, increased pulse etc.

Grossly the affected portion of the lung is quite clear and one can easily demarcate this from the healthy lung tissue. In animals, usually it is patchy in the beginning. The affected part is red, and consolidated, with the alveoli losing air spaces, by naked eye as well in histological sections; it looks like a solid organ, liver; it has the same degree of firmness as liver tissue; hence it has been quoted as hepatisation. Still it is red because of certain amount of hemorrhage by diapedesis. Portions of the affected parts sink in water, since all air is replaced. Over the area the pleura is inflammed and dull red in colour. A membrane may form. Lymphatics are obstructed by fibrinous plugs and the pleural fluid is increased. The peripheral and perivascular lymphatics are dilated with protein rich fluid.

Histologially, the alveoli reveal fibrinous exudates containing RBCs, neutrophils mainly polymoprhonuclear leukocytes, few lymphocytes and macrophages and desquamated epithelial cells. Dilatation of lymphatics and wideningof septal cells are observed.

Stage of gray hepatisation: This is the third stage in the sequence of development of pneumonic lesion.

Grossly, the lung is still consolidated and sinks in water. The colour appear gray due to depletion of blood supply to the alveoli. The capillaries are destroyed and their lumen is blocked by fibrinous shred. Still tinge of redness is observed at certain places of lesion and this is due to persistence of capillary hyperemia or the hemorrhages that occur after the persistence of the lesion.

Histologically, the alveoli appear to be less filled than in the previous stage. Fibrin can clearly be seen and strands maybe found to pass from one alveolus to another through the pores of Kohn. RBCs have almost disappeared and disintegrated liberating plenty of haemosiderin deposits and as well presence of macrophages filled with haemosiderin deposits. As already told the greyness of the affected tissue in this stage is attributed to ischemia of alveolar capillaries due the pressure of exudates on them, increased infiltration of leukocytes, thrombosis of the blood vessels and capillaries of the alveoli and lyses of red blood cells.

With the liberation of enzymes from neutrophils and macrophages, the cellular exudates will be liquefied and the nuclei of polymorphs become blurred and less distinct. But the macrophages still persist.

Stage of resolution: The invading pathogens having been overcome and destroyed and the hyperemia having subsided, the cells and fibrin which filled the alveoli are gradually but rather rapidly liquefied. At this stage liquefaction and removal

of the exudates takes place. The liquefied material may be absorbed via lymphatics or veins or may be expectorated.

Grossly, the exudates are disappearing.

Histologically, There remains granular polymorphs which are disintegrated are either absent or the few that remain are deranged. A number of macrophages derived from alveolar epithelium lining as well as from blood.

While pneumonia itself is a reaction taking place in the alveoli and their walls, the interlobular septa and other connective tissue structures are also distended with exudates, especially with the serous fluid. This is recognized by desquamation and disappearance of epithelial lining cells, by an infiltration of lymphocytes and other leukocytes in the wall of the bronchus or bronchiole and an accumulation of exudates, usually polymoprhonuclear leukocytes in the lumen. However, if the bronchial lumen contains pus or other exudates while the epithelium and wall still appear normal, it may be concluded that the exudates came from some other area, the bronchus merely serving as drainage way.

In the vicinity of the pneumonic changes, there are almost sure to be areas of atelectasisi and areas of emphysema. The former are due to plugging by masses of exudates of the bronchioles which served them. The emphysema involves which expand unduly because of decreased space occupied by neighboring alveoli which are either atelectatic or consolidated.

Unfortunately the prompt and complete resolution described above does not always occur and complications develop. One of these are the spreading of the pneumonic process to new areas of lung tissue. These must then proceed through the same series of stages of pneumonia, recovery of the patient being delayed. This is the characteristic of lobular pneumonia. These will interfere with pulmonary function.

With delayed recovery in a given area, certain chronic changes may develop. The alveolar lining cells, normally flat and not seen clearly may undergo hyperplasia and resemble cuboidal epithelium. Their nuclei are very dark and the cells are inconspicuous, sometime being known as cells tripper. The condition has also been called foetalisation of the lining cells, since they resemble those of the foetal lung.

In a fibrinous or partially fibrinous exudates remains long that is two or three weeks in the alveoli the same thing happens that occurs when fibrin persists in a thrombus or in fibrinous exudates else where. The fibrin is organized by fibroblasts which build into from surrounding tissue. Such an area is then converted permanently into fibrous tissue, a process known carnification of lung. That is flesh like appearance of lung.

Description of different types of pneumonia encountered in animals

(Special types of pneumonia)

1. Bronchopneumonia

This is the common type of pneumonia encountered in domestic animals this is correlated with a predominantly aerogenous portal of entry of the causative agents, involvement usually of anterio-ventral gents of the lungs. Usually this is patchy and being called as patchy or lobular pneumonia. There are three main reasons for the susceptibility of this region. First they are the major sites of deposition of small articles of less than 0.5 to 3.0μ in diameter capable of reaching deep lung. Second, the epithelium of bronchioles is probably susceptible to damage because it is not protected by the mucous blanket of larger airways or by an effective alveolar macrophage system and third one that is the cellular that is filled with macrophages and non-cellular material cleared from large volume of alveolar parenchyma has to pass through the narrow lumen or its parent bronchioles are easily plugged funnel bottle neck, especially where lack of collateral ventilation hampers expulsion of exudates.

The important infectious bronchopneumonia of animals usually develop only when the balance e is tipped in favor of disease by an increase in number of pathogenic microorganisms reaching vulnerable bronchiolo-alveolar regions of the lung or when pulmonary defenses are underdeveloped or impaired. Increased exposure to pathogenic microorganisms is particularly likely to occur when animals from a varied of sources are congregated. And also lack of immunity in the animal as well has the exposure to a virulent organism. Mucociliary blanket destruction, reduction the alveolar macrophage defense system, dehydration, extreme chilling, viral infection, inhalation of toxic gases , introduction of certain anesthetic agents for surgical purposes, all make the anima to susceptible to bronchopneumonia infection.

Most outbreaks occur in young animals, intensively managed animals, especially soon after stresses associated with transport.

Gross lesions: irregular consolidation of lobes in anterio-ventral regions. The anterior and middle lobes are most often affected in those species like cattle, sheep, goat, buffaloes, horses and pigs where well defined lobation is present. Consolidated lung varies from dark red to gray in colour. Palpable firmness of tissue is the criteria and it sinks in water. The more uniform and rapidly spreading the pneumonia, the more homogenous and extension the consolidation. Even where complete lobes become involved, however, the bronchopneumonia pattern can often be detected on careful gross examination, by the presence of multiple, small, evenly spaced gray white bulging foci separated by narrow deep red zones. The bulging foci denote areas of exudation centered on bronchioles and the deeper red zones represent more congested, edematous and Atlectatic alveolar

parenchyma in peripheral region.

The gross pattern is more usual in bronchopneumonia of dogs and cats, which have rudimentary interlobular septa and in the enzootic bronchopneumonia of ruminants and swine.

In catarrhal or suppurative bronchopneumonia, consolidated lobules are moist on cut sections; mucopurulent or purulent material can be expressed from small airways and can be seen in fluid or foamy state in the larger airways. Frank abscesses can be present in severe suppurative inflammation. The cut surface of fibrinous inflammation, in contrast, has a dull dryish appearance. In aspiration pneumonia gangrenous changes exhibited by presence of extraneous particle presence, like pollen grains, fodder particles and other drenched fluids in the rumen could be found in the lungs.

Histologically, the nidus of inflammation in bronchopneumonia is in the brochio-alveolar junctions. In early bronchopneumonia, bronchioles and immediately adjacent alveoli are filled with neutrophils and sometimes a mixtures of various amounts of cells debris, mucous, fibrin and macrophages. The bronchiolar epithelium varies frcm necrotic to hyperplastic, depending on the nature and pathogenicity of the causative agent.

A catarrhal or mild purulent bronchopneumonia can begin to resolve within 7 to 10 days and the lung returns to normal within 3 to 4 weeks. Once the agent has been overcome by the cellular and humoral defense, macrophages become the predominant cell and pahgocytose debris and aid in lyses of RBCs. Severe bronchopneumonia causes death mostly is a combination of hypoxemia and toxemia. Complete resolution cannot occur, but requires integrity of alveolar basement membrane, readily cleared exudates, and rapid killing of the infections agent. Necrosis of alveolar septa intractable exudates or persistence of the agent therefore precludes complete resolution. Even if the animal survives. The resulting complications range form healing with scarring, though atlectasis, chronic bronchopneumonia and Bronchiectasis to abscessation or necrosis with sequestration.

2 Interstitial pneumonia

Interstitial pneumonias are inflammatory conditions in which there are predominantly exudative and proliferative responses involving alveolar walls. A variety of agents produce acute, diffuse damage to alveolar walls causing an early intraleolar exudative phase that is quickly followed by fibrotic and proliferative response. These are the following causes could be attributable to interstitial pneumonias in animals.

Causes of interstitial pneumonia in animals

species	Agent involved	Type of pneumonia
dogs	Canine distemper, inhaled chemicals, oxygen, smoke	Acute
Calves	Septicaemic salmonellosis, lung worm inhaled chemicals, oxygen, smoke	acute
Pigs	Septicaemic salmonellosis, migrating ascarid	Acute
All domestic animals	Inhaled chemicals, oxygen, smoke, all systemic viral, bacterial and parasitic involvement, ingested toxins, adverse drug reactions, endogenous metabolic toxins, uremia, and disseminated intravascular clotting.	Acute
sheep	Ovine progressive pneumonia	Chronic
Domestic animals	Tubercular organisms	Chronic
Domestic animal	Silicosis, pneumoconiosis with variety of dust particles	Chronic
Domestic animals	Pyrrolizidine alkaloids, hypersensitive reaction to microfilaria, irradiation, verminous pneumonias	chronic

Interstitial pneumonia results from diffuse or patchy damage to alveolar septa. Grossly the lesions are distributed widely throughout the lungs, often with greater involvement of anterio-dorsal regions of lungs. Histological changes in the beginning consist of flooding of alveoli with serous exudates and mononuclear cells. Fibrin, other serum proteins and cell debris frequently condense to form hyaline membranes lining air spaces or aggregates plugging their lumina. Proliferation of alveolar epithelial cells (type II). Foetalisalition of alveoli is prominent in number of cases. Fibrosis of lesions set in and intensity of fibrosis varies with the amount of destruction by the dose of the toxin circulated in the lung.

3. Emboli type of pneumonia (metastatic or suppurative)

This may be acute or chronic. This is due to embolic deposition of pyogenic organisms from lesions somewhere in the body. This may be due to consequence of septic; metritis, mastitis, lesions due to strongylus infection, navel ill in calves with coli infections, and Cory bacterial infections involving here in vegetative endocarditis developed.

Gross lesions: Embolic type of pneumonia is characterized by numerous pneumonic foci which are rather evenly scattered through all lobes of both lungs,

the greater number of foci being near the pleural surface until they become confluent and their site of origin can become obscured. The sub pleural location is attributable to the fact that this area contains the largest proportion of small arteries and arterioles in which an embolus may be lodged. In contrast, the haematogenous pneumonia which accompanies septicaemic disease is diffuse. The lodged emboli produce individual abscesses in case of bacterial load rather than area of hepatisation. The diaphragmatic lobe is mostly affected as it is having largest blood supply. The abscesses having thick capsule, and the thickness of which indicates the duration of the process:

Histologically embolic pneumonia in early stages if seen differs from bronchopneumonia in that the foci spread out from blood vessels and not from bronchi.

4. Verminous pneumonia

The type of worms in cattle is mainly Dictyocaulus viviparous and Paragonumus westermanii, whereas in sheep it is mainly Dictyocaulus filaria, Mullerius capillaris and Prtostrongylus rufescens. In India, Dictyocaulus worms are confined to northern zone, where cooler climates exist and the larval forms can survive for a prolonged time. The lung worm's presence in South India is not recorded.

In verminous pneumonia, the diaphragmatic lobes have their full share of pneumonic areas because these depend upon the localization of the worms. The larvae of ascarid worms pass through the lungs, especially in swine but may leave only negligible lesions. The inflamed area is verminous pneumonia are usually small, scattered and in different chronological stages, a fact of diagnostic value. The adult nematodes are usually found in the bronchi and bronchioles where they incite a mucopurulent bronchitis. Their embryonated ova or larvae are present in the bronchial exudates, with which they leave the lungs for the extraneous part of their existence.

Thus the pathology produced by these lung worms may therefore be described in two stages. In the first stage, the larvae enter the alveoli, develop and mature and in the second, they settle down in the bronchioles and bronchi. There may not be any clear cut demonstrating of the two stages, which may therefore overlap. In the place where the larvae enter the alveolar walls are round microscopic necrotic foci surrounded by infiltrating neutrophils, eosinophils and macrophages. The thickening of alveolar walls occurs. Interstitial pneumonic changes are prominent. A few giant cells are also seen. In massive infection, there maybe severe stages.

When the parasites have become mature, they migrate, into the respiratory bronchioles and bronchi where they set up inflammation the walls. A thick mucous exudates containing neutrophils, eosinophils and macrophages form at the site, often occluding the bronchi. The epithelium of the bronchi and bronchioles becomes hyperpalstic and thickened. Weakening of the bronchial wall decease of pressure

and inflammatory process results in Bronchiectasis. Obstruction of the bronchiole and bronchi results in emphysema, since during inspiration of air enters but to which is not exhaled. So repeated trapping of their results emphysema. In places where there is complete occlusion of the bronchioles, atlectasis develops as the air in the alveoli is resorbed. The lesions are found mostly in the diaphragmatic lobes and of focal wedge shaped areas of emphysema and atelectasis. Secondary bronchial infection complicates the picture.

Grossly the lesions are of bronchopneumonia. The exudates in the bronchi consist of worms with their embryonated eggs along with inflammatory cells. In alveoli may contain besides inflammatory cells, worms and ova.

Sometimes liver flukes may be found in the lungs of sheep and cattle and buffaloes but this is an aberrant condition.

5. Necrotic, gangrenous and aspiration pneumonia

Aspiration pneumonia refers to pneumonia caused by aspiration of foreign material, often in liquid form reaching the lungs through the airways. The response of the aspirated material depends on three factors, namely, the nature of the material, the bacteria which are carried with, and the distribution of the material in the lungs.

The causes are faulty drenching in cattle, buffaloes and horses. Inhalation of irritant drugs, oils, anesthetics or feed. Aspiration of milk or gruel in pail fed calves; penetrating of sharp foreign bodies though rumen and reticulum by sharp objects and direct infection by *sperophorus necrophorus* organisms. Lipids and sometimes plant material can be seen in the lesion. Aspiration of ruminal contents can produce similar picture in recumbent cattle and buffaloes, but these cases the aspirated material is usually obvious and there is often hemorrhagic tracheobronchitis.

The aspiration of material from simple stomached animals is often rapidly disastrous, and death occurs from laryngeal spasm or acute pulmonary oedema before there is time to develop much inflammation.

Cattle and lamb frequently aspirate inflammatory exudates from necrotic laryngitis. Lambs with nutritional myopathy affecting the muscles of deglutition aspirate milk and plant material includes whole grain. Pigs in dry and dusty environments and fed on dry, finely particulate food can aspirate starch granules and particles of plants from the food. Any cause of dysphagia, pharyngeal paralysis, in particular is likely to lead to aspiration pneumonia.

Histologically there is extensive consolidation of the anterior and ventral portions of the lung with foul-smelling exudates. The affected parts are greenish or black in colour and sometimes large cavities are seen. The area around these lesions shows congestion and intense inflammatory reaction.

Sequlae: The irritant entered into the lungs produce severe inflammation and extensive thrombosis of the blood vessels results in necrosis. The leukocytes and bacteria produce liquefaction of the necrotic material, resulting in cavitations. Saprophytic organisms invade with resultant gangrenous formation.

6. Viral pneumonias

Most of the important viral pathogens of the lung have an aerogenous route of entry and induce characteristic pulmonary inflammation in lungs. Number of predisposing cause including stress has been attributed for the flaring of viral infections. If the virus also replicated in macrophages and or is immunosuppressive or can evade host defense mechanisms, more diffuse interstitial pneumonia may result as well as dissemination to other tissues.

Paramyxovirus infections: Parainfluenza virus infections: Parainfluenza type 3 virus induces acute respiratory disease in a wide variety of species including cattle, sheep, goats and horses. This causes enzootic pneumonia in calves the disease is either clinically in apparent or causes coughing, moderate fever, tracheal rales, and a slight mucoid or mucopurulent nasal discharge.

The virus sets a broncho interstitial pattern of pneumonia.

Gross lesions consist of mild mucopurulent inflammation of nasal passages and upper airways. Anterio ventral portion of lung, apical lobes may show consolidated reddish areas.

The virus multiplies in ciliated, nonciliated and mucous epithelia cells of respiratory system.

Histologically in the more severe viral infections, there is initially an acute bronchitis and a more clear brochiolitis with extension to adjacent alveoli. Neutrophilic infiltration is abundant and oedema and hemorrhages are present in the alveoli. From 2 to 4 days after infection, bronchiolar epithelium is hyperpalstic or vacuolated and necrotic. Acidophilic intracytoplasmic inclusion bodies are present in type II alveolar epithelial cells. Occasionally binucleated or multinucleated syncitial giant cells are seenin the alveolar lumen. Multinucleated cells are rarely found in bronchioles. The F- glycoprotein in the envelope of parainfluenza virus has a fusion protein function which mediates viral entry into cells through the fusion of the viral envelope and the host cell plasma membrane. During viral assembly, viral glycoproteins are inserted into the membrane of the infected cell, and these results in cell fusion and the formation of occasional multinucleated cells.

The exudates in bronchioles and alveoli contain macrophages and lymphocytes mixed with neutrophils and serofibrinous material. Many alveoli are atelectatic because of bronchiolar obstruction. Lymphocytes and plasma cells also accumulate around vessels, bronchioles and within alveolar septa. Virus replicated in

macrophages and can induce decreased pahgocytosis and killing of bacteria resulting in flaring up with Pateurella infections.

The role of Parainfluenza type 3 virus infection in sheep is similar to its role in cattle in that it acts mostly to pave the way for severe Pateurella pneumonia. The experimental lesions in lambs are essentially the same in those produced in calves.

Viral pneumonias -Parainfluenza type 2 virus infection

Parainfluenza type 2 virus infection in dogs produces infectious tracheobronchitis. The acute viral induced airway lesions are characterized but mild epithelial necrosis with undercurrent mixed cellular inflammatory infiltrates and sub mucosal oedema.

Respiratory syncitial virus: It produces broncho-interstitial pneumonia with peak involvement of 5 to 8 days after infection. Syncitial giant cells of bronchiolar and alveolar epithelium are an outstanding feature during this period, and may contain intracytoplasmic inclusions.

Prominent clinical signs are coughing, respiratory distress with open mouthed breathing and forced grunting expiration.

Sheep are also susceptible to respiratory syncitial virus and spontaneous infections sheep have been detected. The pulmonary lesions are similar to those induced by the bovine virus.

Viral pneumonias-Canine distemper virus

Canine distemper remains one of the most common and serious disease of dogs.

Host spectrum: All members of the Canidae including dog, fox. Wolf, jackal and raccoon, ferret are susceptible.

Properties of virus: Care first demonstrated that the causative agent is a filterable virus. The virus is a pramyxo virus and subgroup of Morbili virus, a RNA virus. This is a pan tropic virus.

Pathogenesis: The virus is shed in all the excretions from infected animals during the systemic phase of the infection and natural transmission is usually by inhalation. After aerosol exposure the virus appears in macrophages of the bronchia lymph nodes and tonsils during the first 24 hours. The virus proliferates in the bronchial lymph nodes and 2 to 5 days after exposure is distributed throughout the lymphatics, including bone marrow, thymus and spleen. The animal becomes febrile and viremia and even leukocytes contain the virus.

If protective levels of antibodies are not reached at early stages of infection, the infection persist in lymphoid tissues and spreads to the epithelium of the alike alimentary, respiratory and urogenital tracts and the skin and endocrine glands and may reach the brain. In the central nervous system the virus appears first perivascular meningeal macrophages, but infection of the choroids plexus

epithelium occur early and the cerebrospinal fluid contain large amount of virus. The virus effect is more pronounced in young animals in which the immune system is less well developed. Toxoplasmosis which is activated develops in dogs whose immune system has been damaged by the distemper virus.

The incubation period of canine distemper is characterized by its onset of acute fever unto 5 days.

Symptoms: The febrile reaction is typically biphasic with a second peak occurring at 11 days. The fever is continuous for the course of the systemic infections, which may last some weeks. The clinical sings vary in the severity. Severe leucopenia is seen and chiefly it is lymphopenia. The lymphopenia persists in acute diseases until the death of the dog.

Respiratory form: Syndrome consisting catarrhal occulonasal discharges, pharyngitis and bronchitis is common. Inflammation of nasopharynx is characterized by serous discharges in initial stages and in the course of 3 or more weeks, it becomes catarrhal and sometimes purulent. Signs of pulmonary involvement accompany moderate to severe damage and interstitial inflammation develops.

Enteric form: Enteritis is expressed in the form of diarrhea, and the faeces become semi fluid, slimy foul smelling and occasionally streaked with blood. The animals loose weight and dehydration results.

Cutaneous form: Vesicles and pustules develop on the skin. The cutaneous lesion are confined to the epidermis beginning in the deeper layers, and particularly to be found on the thin skin of the abdomen and inner aspects of the thigh. They are bacterial complications with intervene of staphylococcal and streptococci. Cutaneous parakeratosis and hyperkeratosis occurs. Alopecia with oedema is common on the palepebral region and oral commisures.

Nervous form: Blindness or some loss of vision is common. Keratitis developing as an extension of conjunctivitis is rare. There are degenerative and inflammatory changes in the retina.

The onset of neurological signs is usually sudden and follows. Systemic signs show by 1 to 5 weeks. Certain pattern of signs could be identified; such as generalised convulsions; these are due to affection of cerebral cortical regions of neurons; ataxia. The rest of cerebellar or vestibular dysfunctions, posterior paralysis are due to spinal cord damage. Convulsions, depression, paralysis and rhythmic motor movements (Myoclonus) are the most common. Myoclonus persists as a residual sign of the disease in animals that recover from the infection.

Lesions: Visceral lesions of canine distemper are common in the respiratory system, but they may be subtle. Inflammation of nasopharynx is characterized by serous discharges in initial stages and in the course of 3 or more weeks, it becomes

catarrhal and sometimes purulent. The mucosal vessels of the larynx and trachea are congested, the bronchi contain a small amount of foamy serous fluid which comes from the edematous lungs and they may contain mucopurulent exudates in complicating bacterial pneumonia.

Histological lesions: Inclusion bodies: The histological changes in canine distemper, when present are fairly specific; characteristic intracytoplasmic and intra nuclear inclusions could be demonstrable in various types of tissues. These coincide with row follows shortly after the appearance of systemic signs of illness from 10 to 14 days after the infection. By about 5th or 6th week their numbers rapidly diminish in most tissues and disappear.

Inclusion bodies persist long in the lung. Inclusion bodies can be found in the central nervous system before changes of encephalomyelitis are present. The inclusion bodies are acidophilic and occur either in the nucleus, or cytoplasm depending on tissues.

Intracytoplasmic inclusion bodies are found in the transitional epithelium of the urinary tract especially in the acute systemic disease. In bladder epithelium it is characteristic feature. Intra-nuclear inclusions are less common in this organ. In some cases inclusions are found in the epithelium of collecting tubules. Mild epdidiymitis and orchitis are common in canine distemper and inclusion bodies are found in the epididymial epithelium.

Inclusion bodies can be found occasionally in the bile duct epithelium of liver and pancreatic ducts of lining epithelium.

Inclusion is common in gastric epithelium but not in intestines. In the stomach they are found in the superficial epithelium as well as in chief and parietal cells.

Lymph nodes: By ninth day lymphocytic depletion in the cortical areas and the cortical areas are reduce to thin rims. Lymphocytolysis is extensive. Sinusoids and cords are infiltrated by neutrophils. Multinucleated giant cells are found in the lymph node. Repopulation of nodes by both T and B cell occurs in recovering dogs. In young pups thymic atrophy is seen.

Lungs: In lungs interstitial pneumonia is seen. But it is complicated with Bordetella and other bacterial infections complicated bronchopneumonia develops. Syncitial giant cells formed by type II epithelial cells are found. Many contain intracytoplasmic acidophilic intracytoplasmic viral inclusions. Even bronchial mucosa contains inclusion bodies. The changes and presence of inclusions in alveolar cells persist even after postmortem changes are set in soft tissues.

Viral pneumonias -Feline calci virus infections

Feline calci virus infections are commonly affects upper respiratory tract. Their pathogenesis is limited to oral and respiratory mucosa and to a lesser extent to the conjunctiva. Clinic signs are principally fever, oral ulceration, rhinitis,

conjunctivitis, and pneumonia. Histologically the lesion is an interstitial pneumonia. Hyaline membranes are present in the alveoli.

Adenovirus infections

Adenovirus infections these cause necrotizing and proliferative brochiolitis pneumonias. Canine adenovirus type I causes infectious canine hepatitis infection. Systemic viral infection pneumonia is seen.

Canine adenovirus 2 is more strictly associated with respiratory disease. The salient feature is necortising brochiolitis and presence of large amorphophilic intranuclear inclusions in the swollen nuclei of degenerating alveolar epithelial cells (cowdry type A). Affected bronchioles are filled with debris of sloughed epithelium and neutrophils. After the infection alveolar foetalisaliton and hyperplasia of epithelial cells of alveoli could be seen.

Equine adeno virus infections cause pneumonia in horses, the anterio-ventral portions show consolidated patches. Histologially the main lesion is severe brochiolitis and bronchiolar epithelium is hyperpalstic in later stages and presence of amphophilic intranuclear inclusion bodies.

Swine influenza : Influenza virus A belongs to family Orthomyxoviridae are pathogane for horses, swines, mint seals, whales, fowl and humans. Influenza A viruses defending on the viral proteins of haemagglutinin (15) and neuraminidase (9) have been categorised. H_1N_1 and H_3N_2 are from swine. At present H_1N_1 became pandemic and causing human disease and respiratory tract affection causing severe pneunomia. Swine die with bronchos-pneumonia. Fatality rate is only at 1% level. Pneumonic lesions are seen in apical cardiac lobes of lungs. Histologically epithelial surfaces are divided and obstruct bronchioles causing interstinal pneumonia.

Diagnosis :

1. By chick embryo inoculation
2. Cell culture studies
3. Immuno-assay
4. Homadsaption studies

Clinical features in swine with influenza virus : After an incubation period of 24 to 72 hours. The disease is abrupt often appearing in many animals in a herd at the same time. There is fever of rise of temperature of 42°C. Apathy inappetance, hudding and reluctance to move. Signs of respiratory distress, coughing, sneezing, rhinitis, nasal discharge, bronchial rabs. After 3 to 6 days they recover.

Retroviral infections

(Ovine progressive pneumonia. Maedi)

Chronic progressive pneumonia of sheep is a slow virus infection of the ovine lung characterized by gradually progressive interstitial pneumonia. The Maedi in

sheep means the shortness of breath for which the diseased sheep struggles for respirations.

The pulmonary disease caused by Maedi-visna virus is distributed throughout the globe. The virus is spread by close contact among sheep and in milk from ewe to lambs. In utero infection can also occur. Infection of sheep is common in regions where the disease is endemic. Because of the slow rate of progression of pulmonary lesions, clinical signs are uncommon until sheep reaches two years of age. Evidence of disease is most frequent among sheep of 5 – 10 years of age. The early signs are loss of weight and increased respiratory rate on exertion. Once sings begin, death usually occurs within 6-8 months because of continuing deterioration in condition and increasing respiratory difficulty.

The specific lesions of ovine progressive pneumonia occur in the lungs and their associated lymph nodes. Grossly, the lungs of severely affected sheep do not collapse fully when the thorax is opened, and sometimes the impression of the ribs is retained. In cases uncomplicated by bronchopneumonia or abscessation, the lungs are mottled grey, and the pleura are smooth and glistening. Lungs are much heavier than usual, often two or more times the normal weight. Close examination of the lung reveals that, although the lesions are widespread, there is relatively sparing of the anterioventral region in the absence of secondary bronchopneumonia.

The lungs have a soft rubbery consistency or are moderately firm. The cut surface is moist but without oozing of free fluid. There is enlargement of bronchial and mediastinal lymph nodes and the cortical region of lymph nodes are grey in colour in cut sections.

Histologically the most characteristic feature of ovine progressive pneumonia is the extensive lympho-follicular proliferation which occurs predominantly in the perivascular, peribronchial and peribronchiolar sheaths in association with the pulmonary lymphatics. Many of the follicles contain germinal centres. These prominent lympho-follicular features have led to the designation, lymphoid interstitial pneumonia.

The next striking feature is hyperplasia of smooth muscles. These are evident in the wall of the terminal bronchioles, alveolar ducts and also extend into the alveolar walls of the neighboring alveoli. Alveolar septa are thickened by infiltration of lymphocytes and macrophages. The amount of interstitial fibrosis is slighter.

Pulmonary adenomatosis of sheep

(Jaagsiekte)

Pulmonary adenomatosis of sheep is an infectious form of bronchio-alveolar tumor with the behavioral characteristic of a low grade carcinoma. The disease is characterized by hyperplasia and hypertrophy of the alveolar epithelium. The

cause has been attributed to type B/ D retrovirus. It is also otherwise known as **jaagsiekte** or **driving sickness**. It is distributed throughout the world where sheep population is there. The disease is less common where populations of sheep are dispersed. It is catergoriesd as a slow virus disease of lenti group.

Symptoms: Early signs of disease are coughing and exercise intolerance. On driving frequent coughing is characteristic feature. When the anima is lifted by hind quarter's abundant fluid comes out from the nostrils. The exudates are discharged from the nose, especially when the head is lowered, and is an important diagnostic clinical feature.

Gross lesions consist of consolidated diaphragmatic or apical lobes of lungs with surrounding inflammed zones. These lesions in early stages appear as firm grey lesions distributed in these lobes. The lungs are heavy and fail to collapse and later they become confluent and diffuse.

Histological lesions consist of multiple proliferative foci of cuboidal or columnar cells and form papillary projections into their lumina (alveoli). The papillary proliferation of cuboidal or columnar epithelium in the absence of significant interstitial inflammation is in marked contrast to the lymph follicular interstitial inflammation of chronic progressive pneumonia (Maedi). Wherein alveolar epithelial hyperplasia is an inconstant and relatively minor feature.

The papillary proliferationinvolves both alveoli and bronchioles in many nodules. Ultrastructurally the cuboidal cells usually have lamellar bodies characteristic of alveolar type II cells, whereas columnar cells have secretory granules and glycogen compatible with origin from secretory bronchiolar epithelia cells (Clara). Occasional metastatic foci are observed in the bronchial or mediastinal lymph nodes.

Sequleae include bronchopneumonia and fibrous pleural adhesions.

Pulmonary adenomatosis has been observed in humans who are removing silages from silage pits. The nitrogen peroxide coming from silos has been attributed for the adenomatosis change.

7. Bacterial pneumonias

Pasteurellosis:

Pasteurellosis: The Pateurella are gram negative coco bacillary bacteria and are strict parasites of animals, their usual habitat being the mucus membranes of the nasal pharyngeal region and oral region. The type specie is *Pateurella multocida*. Less virulent strains like *pasteurella haemolytica* also cause pneumonic Pasteurellosis in sheep, goats, cattle and buffaloes.

Mammalian isolates of *Pateurella multocida* are typed by biological characteristic (biotypes) and as serotypes. The important strains are assigned on the basis of capsular antigens as one to 5 serotypes namely, A, B, D, E, and F. Further

characterization has been made on the basis of 11 somatic antigens. Types B and E are the cause of epidemic Pasteurellosis and cause the classic hemorrhagic septicemia of cattle, sheep, goat's deer and buffaloes. Type B is widespread in tropical Asia and Africa and in southern Europe. Strains of *Pateurella haemolytic* are also classified by biotypes and serotypes. The organism is weakly haemolytic and two biotypes namely A (arabinose fomenters) and T (trehalose fermenters) are identified. There are 16 serovar depending on capsular antigens. Type strains are associated with pneumonia in sheep and septicemia in lambs. Type T causes septicemia in lambs.

The bacteria may harbor or carry in pharyngeal regions and outbreaks occur when local and systemic defense mechanism are impaired or massive proliferation occurs prior to invading the nasopharyngeal mucosa or being inhaled in large numbers into the lungs.

Predisposing factors such as stress created by transport, crowding, climatic changes and bad management or the damaging effects of respiratory viral infections.

Hemorrhagic septicemia

Hemorrhagic septicemia is a septicaemic disease characterized by high fever, rapid prostration with profuse salivation in cattle and buffaloes. The postmortem picture is characterized by peticheal hemorrhages on the serous membranes and in the various visceral organs especially in lungs and muscles. It causes fibrino-haemorhagic broncho-pneumonia.

The lymph nodes are swollen and hemorrhagic and serosnaguinous fluid is observed in pericardial, pleural and peritoneal cavities. Hemorrhagic gastroenteritis is a characteristic feature.

In **edematous form of hemorrhagic septicemia** which is common in buffaloes and being popularly called as barb one. Oedema of the throat with infiltration of gelatinous subcutaneous fluid is seen. Bipolar organisms could be recovered from this fluid. It is characterized by extensive swelling of the subcutaneous tissues, especially of the throat but also affect the whole head, tongue brisket or limbs. The swellings are produced by copious clotted straw colored fluid.

Pneumonic Pasteurellosis:

Another form known as pneumonic Pasteurellosis occurs in cattle, buffaloes, sheep and goats. Severe acute fibrinous or firbrinonectroc pneumonia caused by Pateurella haemolytic type A 1 strain is responsible for this. The pneumonia is a typical bronchopneumonia.

Grossly the apical, cardiac and diaprhagmatic lobes and their ventral portions of lungs show consolidation and are reddish in color. Gelatinous thickening of interlobular septa, fibrinous peluritis is also prominent.

Histologically the picture is a fibrinopurulent bronchopneumonia, with alveoli are flooded with neutrophils, lymphocytes. Fibrin shreds cross from one alveoli to other alveoli through pores of Kohn. Macrophages with haemosiderin deposits are also seen. Foetalisaliton of alveoli is prominent. Concomitant infection with parainfluenza viruses brings about interstitial pneumonic changes. Acute infection in necrotizing broncho pneumonia where plenty of organisms are present in the lung in bronchi. Edematous and alveolar edematous fluids. In recovered lesions oat like cells, with elongated streaming nuclei are present.

Porcine contagious pleuropnuemonia

The causative agent is *Actinobacillus pleuropnuemonia (Haemophilus)*. The characteristic lesion is a severe Fibrinonecoritc and hemorrhagic pneumonia with accompanying fibrinous peluritis.

Deaths in the per acute and acute forms occur suddenly or after a short period of depression. Fever, and possibly hemorrhages from nose and mouth are seen. The main lesions are bloody nasal discharge, blood stained foam in the trachea, and bronchi and large regions of hemorrhagic of Fibrinonecoritc pneumonia accompanied by fibrinous pleurisy. In complicated cases, that is chronic ones abscesses of lung which is tightly bound to the thoracic wall by fibrous adhesions are observed.

Contagious Bovine Pleuropneumonia

Contagious bovine pleuropnuemonia is a cute, sub-acute or chronic disease of cattle and buffaloes characterized by pneumonia, serofibrinous pleurisy and oedema of interlobular septa of lungs.

Species affected: Cattle and buffaloes, bison, yak, reindeer and antelope. Experimental infection can be induced in sheep, goats, mice and embryonating eggs.

Etiology: the disease is caused by Mycoplasma mycoides sub species mycoides. This organism is pleomorphic and lacks a cell wall and is bounded by plasma membrane only. Its shape varies from small coccal bodies and measures from 0.3 to 0.8μ in diameter. A well defined capsular layer, apparently consisting of polysaccharide galactin can be demonstrated by electron microscopy. The organisms can be stained by Giemsa. They can be isolated from the blood and lungs.

Epizootiology: Under natural conditions, infection is contracted by inhalation of the organisms expelled by in infected animal, and there is no evidence of intermediate hosts. The carrier animal is known as lunger, which appears clinically healthy but has a localised focus of infection in its lungs. Dead tissue surrounded by fibrous tissue is known as sequestrum. So long as the fibrous capsule persists, the carrier animal does into disseminated infection, but in time, perhaps after several months the capsule may break down allowing the still viable organisms to escape through the bronchi and so infect susceptible in contact animals. Incubation period is usually between 3 and 6 weeks.

Pathogenesis: The organisms enter the bronchioles via the respiratory tract. Inflammation of the bronchiolar walls is set up. Passing through these walls, the organisms enter the interlobular septa where again inflammation is set up followed by copious oedema. There is thrombosis of the lymph vessels. The inflammatory process subsequently spread to the lung alveoli setting up croupous pneumonia, which is manifested by red hepatisation followed by grey hepatisation.

Spread of inflammation to the branches of the pulmonary arteries results in thrombi and necrosis of the affected part. Such necrosed areas become clearly demarcated and circumscribed by fibrous tissue. This isolated and enclosed lesion is called sequestration. In these sequestrate, Mycoplasma remain viable for years. The animals act as carriers. The carriers are also known as lungers. During violent coughing the fibrous capsule may rupture, liberating the organisms into the surrounding lymph spaces from where the enclosed tissue may be infected and thus the disease process may be set up in other parts of the lung. Since the lesions are of different ages in different parts, the affected areas reveal different stages of the process red hepatisation in some parts and grey in others. In some animals a purely septicaemic form may occur without any lung lesions and the organisms may be excreted in the urine, milk, nasal discharges and amniotic fluid.

Symptoms: The acute form of bovine pleuropnuemonia is characterized by rise in temperature, accelerated respirations, anorexia, rough coat, and frequent coughing, which is dry at first and then becomes moist. The breathing becomes laboured and expirations may be accompanied by grunting. In fatal cases, death occurs in 2 to 3 weeks after the onset of symptoms. Oedematous infiltration in the lower part of the chest is seen. In sub acute and chronic cases signs are less marked, although usually cough can be induced by making the animal run after the period of rest. In a herd about a quarter of the affected animals become carriers.

Lesions: lesions are only found in the thorax. Lungs showed marbled appearance on sections due to marked infiltrationof interlobular septa by clear straw coloured exudates, the lymph in which time becomes gelatinised and organised. The thickened septa surround various lobules, which are in different stages of hepatisation that is either grey or red. Rarely caseation and calcification may be noticed. Other extra pulmonary lesions are serous or fibrinous pericarditis, peritonitis, serofibrinous arthritis, and periarthritis.

Diagnosis: A provisional diagnosis may be made from the post-mortem examination. The mosaic appearance of the affected lobes of the lung, presence of serosnaguinous fluid in the thorax, pleurisy with adhesions of the lungs, which are very difficult to separate out from the thoracic cavity are characteristic features.

Contagious Caprine pleuro pneumonia

Contagious Caprine pleuro pneumonia (CCPP) is a per acute, acute or chronic contagious disease of goats characterized by a fibrinous pneumonia, pleurisy and profuse pleural exudates.

Etiology: The causative agent is the *Mycoplasma mycoides sub species Capri*. The classical disease is caused by *F 38* strain of Mycoplasma sop which has so far been isolated from Kenya, Sudan and Libya. The present author has seen similar cases

with path gnomonic lesions of serofibrinous pleurisy and pericarditis in goats in several cases. These strains have not been identified. It appears that *Mycoplasma mycoides sub species Capri* is probably the cause of only sporadic cases of Caprine pleuropnuemonia. Another Mycoplasma subspecies mycoides, large colony biotype, has been isolated from goats in many countries. This mycoplasma also causes Caprine pleuropnuemonia, but is more commonly associated with other disease manifestations, including polyarthritis, mastitis, keratoconjunctivitis and septicemia, particularly in young kids.

Species affected: F-38 strain is only infectious to goats; other Mycoplasma sop not only affects goats but also less commonly in sheep. These strains when injected subcutaneously into goats results in massive cellulites at the inoculation site, pyrexia and even death.

Transmission: Natural infection occurs by contact. The incubation period in natural infection is generally considered to be 3-5 weeks.

Pathogenesis: The organism enters the bronchioles via the respiratory tract. Inflammation of the bronchiolar wall is set up. Passing through these walls, the organisms enter the interlobular septa where again inflammation is set up followed up copious oedema which causes dilatation and subsequent thrombosis of the blood vessels. Inflammatory process may subsequently spread to the lung alveoli setting up croupous pneumonia, which is manifested by red hepatisation, followed by grey hepatisation. In virulent strains, septicemia occurs and the organisms may be excreted in urine, milk, nasal discharges and amniotic fluid.

Symptoms: In per acute and acute forms, characteristic signs of pneumonia are easily recognized. In per acute cases there is a rapid course at around 3 to 5 days and death may occur, even within 24 hours of the onset of clinical signs, Mortality rate of 60 to 100% are common. In the chronic form, the characteristic signs are nasal catarrhal and chronic cough, enteritis, general death and emaciation. Some chronic cases may suddenly relapse and develop acute signs, indicating that little or no immunity was acquired from the first attack.

Lesions: In acute cases consists of unilateral or bilateral pneumonia with varying degrees of consolidation and pleurisy; sections of lung present a mosaic appearance. Affected areas of lung are commonly covered with a lemon-yellow deposit containing much pleural exudates. A clear straw coloured exudates, which may measure around a litre is almost invariably present. There is sometimes unilateral or bilateral fibrinous pleuro pneumonia. Pleurisy is found with copious exudates which on exposure to air clots and becomes gelatinous. Marbling of lungs though seen is not so prominent. But the author has observed in several cases the serofibrinous layer lying on pericardium and pleura is that of a whitish coated membrane. Bronchial and mediastinal lymph nodes are congested and oedematous. In chronic cases, the lungs are found to be in various stages of resolution with encapsulation of acute lesions. Firm fibrinous adhesions attaching the lung to the chest wall are commonly seen.

Diagnosis: The characteristic signs of nasal catarrh, respiratory distress, coughing and general weakness are seen. Significant path gnomonic lesions at post-mortem

confirm these symptoms as CCPP. Recognition of Mycoplasma from pleural exudates and isolation by laboratory methods could be done. For laboratory examination, fresh material such as pleural exudates, mediastinal lymph nodes and diseased lung tissue should be submitted, preserved in 50% glycerin if necessary. Lung tissue preserved in formalin could also be sent to laboratory. Biological test consists of subcutaneous inoculation of lymph into healthy goats results in an oedematous swellings locally and death of the goat within a week.

Tuberculous pneumonias

Tuberculosis is typically a chronic infectious disease caused by bacteria of the genus Mycobacterium. Mycobacteria are widely distributed in nature. The classical tuberculosis bacilli are mycobacterium tuberculosis var hominis, mycobacterium var bovis and mycobacterium avian. *Mycobacterium tuberculosis var human and mycobacterium var bovis* are the principal closely related mammalian pathogens. Atypical mycobacterial infections have also been reported in animals.

The three main species of tubercle bacilli occur most frequently in their respective hosts but cross infection do occur and various other species of animals are affected. The lesions of tuberculosis are the prototype of granulomatous inflammation. The tuberculosis granulomas are mainly cellular and its development is frequently designated or proliferates in contrast to the more exudative type of lesion it occasionally causes.

When tubercle bacilli are ideally implanted in tissues, they behave as relatively bland lipid rich foreign particle should be expected to do an instinct to foreign body reaction. Bacilli are phagocytosed by macrophages, and if the resistance of macrophages is adequate, the bacilli are eventually killed. If less immunity is there, the bacilli proliferate and the released from killed macrophages together with antigenic material which sensitized attracted T-lymphocytes. By the 20h day or so after exposure, by which time hypersensitivity is developing many bacilli are present; cytokine secretes by the sensitive t-lymphocytes cause the attraction proliferation and activation of macrophages which are derived mostly from blood monocytes. In the infected foci macrophage assume as epitheloid cells and these epitheloid cells have a larger vesicular nuclei and extensive pale cytoplasmic will defined borders. These epitheloid cells contain ingested bacteria and form giant cells of Longhan's type. These are multinucleated giant cells with the nuclei arranged in the periphery in the form of horse shoe. The admixture of epitheloid and giant cells form the centre of young tubercles. At the periphery is a narrow zone of lymphocytes, plasma cells and unaltered monocytes. As the lesion progresses, the tubercle develops fibrous tissue accumulation peripherally, and central necrosis. This reaction varies from species to species and from individual to individual as per the susceptibly to organism as well immune back ground of the individuals.

Encapsulating fibrosis is clearer in those individuals who have considerable powers of resistance, as tuberculosis grnaulation tissue over grow and dominate the lesion. The development of central necrosis gives to the tubercle a high degree of histological specificity. The necrosis is a product of cell mediated hypersensitivity and is of caseous character. The necrotic material is most commonly inspissataed

into yellowish cheesy mass, but may liquefy or calcify. Calcification is a characteristic development in some species of animals, but seldom observed in others.

The exudative type of lesion in tuberculosis usually develops acutely. The exudates are relatively voluminous and consist of fibrin and neutrophils as well as the mononuclear. Eventually the exudates clots and it too caseates. For exudative lesion occur rapid bacterial proliferation, presence of abundant reactive lymphocytes, and a site of localization is in easily distensible space lining tissue like lungs or pleural or peritoneal cavity.

There is every portal of turbcle bacillus entry. Infection occurs congenitally by way of umbilical vein, or post natal through alimentary, respiratory, genital or cutaneous routes. Growth of original tubercle takes place by centrifugal fashion and other places it spreads and further tubercles form. The new tubercle coalesces with old ones and form large lesions.

In a susceptible insensitive animal, the bacilli spread rapidly, along the lymphatics, macrophages may carry the organisms, to the regional lymph nodes where further tubercle develops. The combination of lesions in initial focus and in the regional lymph node is known as the primary complex of Ranker.

As lesion develop in the regional lymph node, the infection passes successively from one lymph node to another and eventually reach the blood and spread widely. Extensive haematogenous disseminating is due to the break down of lesion in blood vessels. The course of the disease after massive generalization is short, and the disease is then referred to as military tuberculosis. Spread can occur via natural passage such as ureters from kidney, from one bronchus to another by coughing, from lungs to the intestine. Rapid spread occurs in cavities like meningeal and serous cavities.

Most cases of bovine tuberculosis are acquired by inhalation or by ingestion. The tuberculosis in pulmonary areas usually starts at the bronchio-alveolar junction and extends into the alveoli so that it is initially sub lobular or lobular. The histological picture is typically a tuberculosis nodule. Multiple initial foci are seen, later they become enlarge coalesce and form large regions of caseating bronchopneumonia. These are in due course encapsulated and calcified. Cavitations may form in any of these lesions.

In adult cattle, primary infection is usually in the lung and is caused by inhalation of infected droplet nuclei. The primary lesions may be single or multiple and may occur in any lobe, but they occur predominantly in sub pleural location on the dorsal portion of the diaphragmatic lobes. Mediastinal and bronchial lymph nodes are affected.

The Tuberculous lesions slowly extend from bronchiolar-alveolar junction and extend into the alveoli. Histologically in lung typical tuberculous granulomas are seen.

The appearance of pulmonary lesions varies with their age and rate of progress. The earliest lesions aren't encapsulated, but caseation and calcification is present.

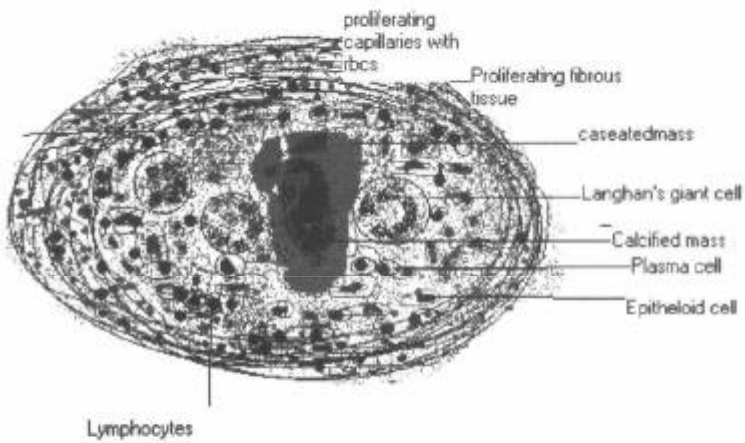
Depending on the rapidity and extent of spread, the lesions form a pattern of irregular caseous bronchopneumonia. Trachea and bronchi may be ulcerated.

When the infection is spread to the serous membranes either directs expansion of the original lesions, by lymphogneous extension from the lungs, by direct haematogenous dissemination, or by local expansion from a haematogenous focus in an adjacent organ. Once the Tuberculous process breaches the serosa, the bacilli are distributed by respiratory movements and may be widely implanted. Pleural tuberculosis is largely nodular, diffusely caseous or intermediate type. The affected areas of pleura, both visceral and parietal are thickened by fibrous granulation tissue. The characteristic lesions are nodular and tend to occur in clusters. They may be sessile are pedunculated and frequently combine to form cauliflower like masses. Initially these tubercles may be soft and later they may undergo calcification. Fibrinous deposits may be seen in between the nodules.

Generalization of infection can occur early in the course of the disease or later in the course of the disease. In late generalization, it is assumed that the immunity the animal has acquired has broken down, thereby permitting widespread. Generalization may be massive and widespread when large number of bacilli enters the blood stream or it may be more protracted with few bacilli entering the circulation. Haematogenous metastases occur or frequently in the lung.

Miliary lesions in lung are associated with a fulminating course of the disease. The lesions are typical small grayish tubercle which is translucent at first but soon become caseous and centrally calcified.

Histological structure of an epitheloid granuloma [Cross section of Tuberculous nodule].



Tuberculosis in horses:

Horses apparently possess a high innate resistance to tubercle bacilli, because of the disease is rare in them. Most infections involve *Mycobacterium bovis, and Mycobacterium avium and Mycobacterium tuberculosis var hominis* also produce localised

or generalised disease. Many of the bovine strains recovered from horses are of lowered virulence when tested in laboratory animals. The route of infection is almost exclusively alimentary. The primary complex is often incomplete, with large lesion in retropharyngeal or mesenteric lymphnodes. *Mycobacterium avium intracellulare complex* sometimes produce proliferative enteritis closely resembling john's disease in cattle.

The lesions of tuberculosis in the horse often diffuse from those in cattle. Whereas extensive caseation and calcification are typical of bovine tubercles, the equine tubercles have lardaceous appearance grossly resembling sarcoma. Caseation and calcification are rarely observed.

Histologically, the early lesion is a tubercle which consists of macrophages, epitheloid cells, and a few or many giant cells without peripheral zone of lymphocytes. As the lesion progresses, it develops more and more proliferative fibrous tissue in which ill defined tubercles are scattered. Bronchial lymph nodes are involved when lungs are involved and the corticomeduallary distinction in lymph node is lost.

Tuberculosis in Sheep and goats:

Sheep and goat do not appear to have any special resistance to tubercle bacilli, except to that of human type. It is usually caused by *Mycobacterium bovis or Mycobacterium avium*. The main route of infection is respiratory. The lesions are common in lungs.

Tuberculosis in Swine

Pigs suffer to all the three major types of Mycobacteria. The reflection o f incidence of tuberculosis is related in association with cattle or poultry or humans. *Mycobacterium bovis* produces generalised disease. *Mycobacterium tuberculosis var hominis* confines the infection to the local point of entry that is lymph nodes. Mostly wound infection, occasionally it gets through therespiratory tract. Primary nodules are found in the pharynx or in the intestine.

There are certain differences between the lesions produced by the bovine and avian types of bacilli. The bovine bacilli produce caseo-calcareous tubercles similar to those which occur in cattle, and the lesions are often surrounded by fibrous capsule. The avian bacilli produce lesions which are proliferative in nature and consist of tuberculous granulomatous tissue resembling lardaceous or sarcomatous lesions like that of horse. Caseation is not a feature of these lesions.

Pulmonary tuberculosis in swine is haematogenous and is usually of the miliary pattern. In some infections with the bovine bacillus there is extensive consolidation of the anterior lobes resembling grossly the caseous bronchopneumonia of cattle, but histologically seen to be a confluence of numerous haematogenous tubercles. In this form of pulmonary disease there may be a tuberculous tracheitis. Miliary

lesion in the lungs produced by the avian bacilli resembles dew drops, and there appears to be a characteristic tendency for these to spread along the subplerual and septal lymphatics which are beaded by small tubercles.

Tuberculosis in Cats and dogs:

Cats appear to be more susceptible to *Mycobacterium bovis* that to *Mycobacterium tuberculosis var hominis or Mycobacterium avium.*The route of infection in cat is by oral way.

Dogs are susceptible to *Mycobacterium bovis and Mycobacterium tuberculosis var hominis* and to a lesser extent to *Mycobacterium avium* infection. Dogs are more likely than cats to contract tuberculosis usually by inhalation in households with tuberculosis persons.

The lesions of tuberculosis in carnivores differ from those in other species. Typical tubercles are not so common and when they occur, caseation necrosis is not a prominent gross feature. More often there is nonspecific granulation tissue in which the macrophages are scattered at random and giant cells are rare.

The discrete tubercular granulomas that do occur are composed principally of epitheloid cells surrounded by narrow zones of fibrous tissue in which there are scattered small collections of lymphocytes and plasma cells. Necrosis is often present in the centres of larger granulomas. Giant cells are rare or absent.

In the dogs in the dorsal portion of the lobes, the lesion develops. They appear as firm pale building nodules of 1 to 3 cm in size. The cut surface is uniform but there is a central liquefaction and there is a tendency to fistulate on to the pleura to produce serofibrinous or seroharmoorhagic peluritis. Metastatic nodules in the lungs are usually few in number with an appearance similar to that of primary foci. The bronchia lymphnodes are regularly involved. Peluritis is common in dogs.

8. Hypostatic pneumonia

The porous nature of pulmonary tissue is especially conducive to hypostatic congestion, as a result of which oedema of the area is likely to develop. Tissue devitalized by these two circulatory disorders may well fall prey to inhaled upper respiratory pathogens which would be promptly destroyed in a healthy lung. Pneumonia that develops in recumbent patients in the lower part of the lung lobes occur in many terminal diseases.

9. Mycotic pneumonia

Mycotic pneumonia due to Aspergillosis

Inflammation the lung caused by a variety of fungi is called mycotic pneumonia. Various fungi that may invade the lung and cause pneumonia are *Aspergillus, Blastomyces, Mucor, coccidioides, and Cryptococcus.* Of these the commonest is the

fungi Aspergillus fumigatus in the poultry popularly called as brooder pneumonia.

Aspergillus fumigatus is ubiquitous and is found everywhere in nature. It is surprising that more causes of pneumonia caused by spores of the fungus and are found in the poultry litter and mouldy grain. Infection is by way of respiratory tract. Spores may be inhaled with the infected dust or may be aspirated from the mouldy grains. Especially in the hatcheries if the eggs collected from the dumpy deep litter floors and kept in incubators contribute the onset of the disease in chicks. Due to relative humidity of incubators these organisms grow in the shell and mortality in hatching itself is observed. In fact in dug eggs the percentage of hatchability is very poor and most of the embryos die in eggs it without hatching.

Aspergillosis in poultry

In brooder chicks also it is common. Spores may be inhale with the infected dust or may be aspirated from the mouldy grain. Since this affection is very common in brooder houses, it is called as **brooder pneumonia.**

Gross lesions are found in the trachea, bronchi and air sacs. Sometimes larynx is also affected. White or greenish, thick cheesy material is found in the affected areas. The spores after entering the terminal bronchiole and alveoli grow by budding and formation of septate hyphae. As a result a granulomatous bronchopneumonia develops and there is infiltration of neutrophils and macrophages. This focus expands and more and more lung tissue is affected.

Histologically the lesion is nodular. Central caseous material is surrounded by granulomatous reaction preferably with epitheloid cells, lymphocytes, and giant cells. Stained by PAS, sections reveal pink stained mycelia as well yeast like bodies.

Mycotic pneumonia in animals by Aspergillosis other than poultry

Aspergillosis can be a respiratory or placental disease in animals. Infections of either the upper respiratory tract are sporadic in all a species. Infection of the pregnant uterus and foetus has been found mainly in cattle. Secondary intestinal infections have been observed in cattle.

In horses the infection may develop as an implantation on the mucous membranes of the nasal cavity, sinuses, guttural pouches, and trachea bronchial airways, or it may be in the form of nodular bronchopneumonia.

When the fungus grows on a mucous membrane, they may be visible to the naked eye first as a whitish growth and later as a powdery felt like growth with a typical blue green colour produced by the conidia. These superficial colonies may develop after death, and the presence of the colonies of the fungus on a mucosa is not significant unless there is tissue reaction. The tissue reaction is characterized by necrosis surrounded by a zone of hemorrhagic inflammation. Breakdown of these lesions in the wall of the bronchi can result in Bronchiectasis cavities.

The pulmonary lesions typically occur in young animals as grey white nodules of 1 to 10mm in diameter, with a narrow hyperemic rim. The nodules develop around fungal colonies which proliferate in the terminal bronchioles. The fungal colony consists of long branching septate hyphae and is surrounded by a zone of neutrophils, macrophages and necrotic tissue. The nodule expands and compresses adjacent alveoli. The affected bronchioles contain plugs of purulent exudates.

In chronic cases where the animal resistant is more, the colonies composed of shorter radiating hyphae which branch freely near the outer ends. It appears as ray fungus fashion. Dissemination of the infection from the pulmonary lesions can occur. Of the many organs, including the meninges, in which metastases develop.

Mycotic pneumonia-Blastomycosis:

Blastomycosis is a disseminated or localised mycotic infection caused by Blastomyces dermatitidis. It is a disease of humans and dogs but also seen in cats, horses and other mammals. It is a dimorphic fungus; in cultures at room temperatures it produces mycelia growth, whereas in issue or culture at 37°C, it is yeast like. The fungal spores are 8-20μ in diameter with thick double contoured walls and reproduces by budding.

The animals get the infection from soil. In dogs it is seen in pups.

The lung is the most primary site of involvement and cutaneous infections are also seen. The pulmonary disease is a chronic one. Animal exhibit debility, chronic cough, exercises intolerance and terminal respiratory distress.

Grossly multiple grayish white nodules of various sizes are distributed throughout all lobes. Superficial nodules reduce elevation the pleura. When this does occur it is due to fistulation form a mycotic abscess. Most pulmonary nodule is of firm granulomatous tissue, but some undergo central abscessation or caseation and these may fistulate into a bronchus or on to the pleura.

Mycotic pneumonia due to Coccidioidomycosis

The disease is due to dimorphic fungi named as coccidioides immitis. There is zoonotic spread is there with the fungus. In arid regions, there is an association between the faeces of desert rodents and high concentrations of the fungus. Vegetation of the fungus occurs in soil after rains, and subsequently, large number of infective arthrocondia (spores) is disseminated widely in wind blown dust after the soil dries.

As already stated the fungus is dimorphic, in tissues the distinctive form is a spherule that is sporangium which measures between 10 to 20μ in diameter and has a thick double contoured wall. It is called sporangium because it reproduces in tissues by endosporulation; the endospores are globose and have 2 to 5μ in diameter and are released into tissues in large numbers when a spherule ruptures.

Mycelia are rare in animal tissues. On artificial media mycelia are seen. Reproduction in mycelia growth is by orthoconidial which are produced in a very large numbers along the hyphae. These arthrocondia are highly infective and easily detached from mycelial growth.

Coccidioidomycosis causes primarily infection of respiratory tract. Local trauma causes entry, subsequent abscess formation and it maybe distributed to blood and reaches the lungs. The high susceptibility of lung to the established infection can be demonstrated experimentally by intranasal insufflations of spores.

Cattle, swine, horses, sheep, dogs and cats are affected. The lesions are in the lungs and associate lymph nodes. Persistent lameness with fever and development of cutaneous nodules.

In lungs the lesions are of pyogranulomas. The grnaulomas are grayish white and usually nodular. There may be central caseation necrosis or liquefaction and in some cases calcification is also seen. Arthrocondia in initial stages provoke exudative reaction. The infiltrating cells are neutrophils surrounded by a zone of epitheloid cells mixed with a few giant cells. And lymphocytes. In cattle the granulomas contain corona of acidophilic clubs possibly epitheloid cells devoided of nucleus.

Cryptococcosis

Cryptococcosis is a sub acute or chronic disease caused by Cryptococcus neoformans and the organism is monomrophic, yeast like reproduces by single buds and is 4 to 8μ in diameter.

The *Cryptococcus neoformans* when injected into the mice these take up the infection. The yeast is surrounded by a wide capsule which is composed of mcuopolysaccharides. The capsular material is copious enough to give the lesion a mutinous texture, and it stains well with mucicarmine and positive of pinkish in nature which by periodic acid Schiff reaction as well blue with alcian blue stain. By negative staining with India ink or nigrosine in wet mounts, the refractile in nature of the organisms are seen.

The source of the infection is usually soil especially when the faecal matter from pigeons or other bird dropping are mixed with. Disease is sporadic.

Cryptococcus is natural saprophytes and only accidentally acts as pathogens in animals with impaired local or systemic immunity. Immunosuppression of the individual flares up the infection.

Infection is acquired in most instances by inhalation of contaminated dust. The respiratory tract is usually site of infection. The nasal cavity and lungs are affected.

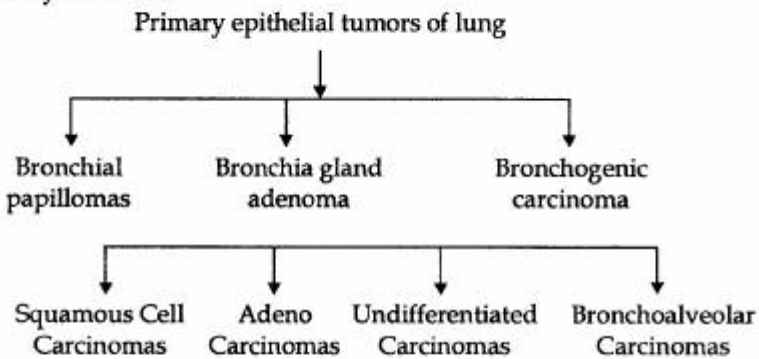
In lungs, skin, meninges and even in cattle incase of udder granulomatous lesions are seen. The granulomas consist of lymphocytes, macrophages and plasma cells. In nasal cavity the inflammatory lesions are not prominent because of the lack of

inflammatory response due to the immune suppression by the capsular polysaccharide. This results in lack of macrophages and as well less amount antigen antibody reactions.

Examined in sections stained by Haematoxyin and eosin, the fungi appear as typical yeasts surrounded by a clear halo produced by unstained cellular substance. The capsular substance immediately around the organism is often condensed into an acidophilic rim.

Neoplastic diseases of lungs

Primary pulmonary tumors are rare in domestic animals. Metastatic lesions are very common as the lung have vast circulation and seeds metastatic foci. Tumor emboli are very common.



Pulmonary adenomatosis of sheep is an infectious form of bronchio alveolar tumor with the behavioral characteristic of a low grade carcinoma. This has already been described. **Pulmonary carcinomatous (jaagsiekte)** occurs in many parts of the world. The characteristic histological lesions of pulmonary carcinomatous consist of multiple proliferative foci of cuboidal or columnar cells which line alveoli and for papillary projection into their lumina. The papillary proliferations involve both alveoli and bronchioles in many nodules.

Diseases of pleura and mediastinum

Congenital cysts

Congenital cysts may occasionally be found in the anterior mediastinum. Cysts of 1 cm or more in diameter can be seen grossly as thin wall structures containing clear, light yellow fluid. Fluid filled cysts in the caudal mediastinum are more likely to be of Brnchogenic origin and can be large enough to cause pulmonary insufficiency.

The author has observed number of cysts in the mediastinal region of cattle. These are lined by cuboidal to columnar cells and contained fluids and are encapsulated. Few workers opined that these are embryological error in origin and formed from primitive gut epithelium.

Pneumotharoax: Pneumotharoax refers the presence of air or gas in the pleural cavities. Air in the cavities allows the lungs to collapse to a degree proportional to the amount of air present. It is associated with emphysema, asthma and tuberculosis. An abscess cavity that communicates either directly with the pleural space or with the lung interstitial tissue may also lead to escape of air.

Pneumotharoax can be spontaneous or traumatic. Spontaneous pneumotharoax is rare. It may complicate any pulmonary disease which leads to rupture of parenchyma at the pelural surface. It is most often associated with rupture of emphysematous bullae. Less commonly it follows rupture of a cavitated abscess or pyogranulomas as that communicates with an air way, or rupture of parasitic cyst such as the fluke infestation with paragonimiasis.

Traumatic pneumotharoax is the result of accidental perforation of the thoracic wall or rupture of lung and visceral pleura. Traumatic pneumotharoax is a complication of biopsy of lung or due to resuscitation measures. The air enters into the thorax is slowly absorbed normally provided the lungs are not collapsed. It may complicate any pulmonary disease which leads to rupture of pulmonary parenchyma at the pleural surface.

Inflammatory lesions of pleura could be categorized as serofibrinous peluritis, suppurative peluritis, and hemorrhagic peluritis.

Noninflamatory conditions of pleura such hydrothorax, haemothroax and chylothroax.

Haemothorx is the presence of blood in the pleural cavities. It is most often due to the traumatic rupture of blood vessels, but it can also be caused by the erosion of the wall of a vessel by an inflammatory or neoplastic process. Even clotting disorders cause the Haemothorax condition. Hemorrhages are also due to highly vasuclarised tumors such as Haemangiosarcomas. Pleural tuberculosis in dogs, as well aneurysms developed due to Spirocerca infections in dogs.

Hydrothorax. It is the accumulation of oedema in the thoracic cavity. It is seen consequent to cardiac failure and in generalised passive venous congestion as well oedema due to nutritional deficiencies. It is usually bilateral. The fluid is clear, watery and ranges from almost colorless to light yellow. Large amounts of it present when there is widespread neoplastic involvement of pleural surfaces. When lymph vessels are obstructed by tumor emboli also hydrothorax results. Enlargement of thymus or cranial lymph nodes also produce hydrothorax. This is also seen in mulberry disease of pig, Alfa naphthyl thio-urea poisoning animals, and African horse sickness in horses.

Chronic hydrothorax causes pleural opacity because of active hyperplasia of meosthelial cells and fibrous lining of the under lying pleural connective tissue.

Chylothorax refers to the accumulation of milky fluid into the thorax. The fluid is

lipid rich lymph which can be distinguished from other turbid fluids by extracting of fat with fat solvents. Occasionally the source of chylothroax is traced to the rupture of thoracic or right lymphatic ducts.

Peluritis the inflammation of the pleura. It is peluritis is most commonly encountered abnormality. It is secondary to pneumonia. Other pathways by which pleura are affected are due to agents reaching the pleura by blood stream, lymphatic penetration from the peritoneal cavity, traumatic penetrating from the outside chest, or from the esophagus or from the abdominal viscous, such as traumatic reticulitis, or direct extension from mediastinal abscess or oesphagitis.

Abundant pleural effusion into the pleural sacs is designated as pyothroax or thoracic empyema. This is common in horses, in dogs and cats due to pyogenic organisms reaching the pleural cavity either by blood steam or through in contiguity to abscesses. This may be secondary to pneumonias. Variety of bacteria like streptococci, Escherichia coli, Klebsiella spp, Pateurella spp, pseudomonas, staphylococci and Mycoplasma are involved.

Neoplastic diseases of pleura: Primary pleural tumors are rare. The specific type is the pleural mesothelioma.

Mesothelioma arise from pericardial and peritoneal surfaces as well from the pleura also. These tumors are increasingly observed in cattle in India. This maybe due to inhalation of asbestos fibers as the bullocks working with these factories are involved.

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Chapter 4

Diseases of Digestive System

Digestive system-anatomical parts- Ingestion of food – Diseases of the oral cavity- Secondary cleft palate. Inflammatory terms used while describing the oral cavity – Bacterial Stomatitis – Diseases of teeth and dental tissue – – teeth classification in domestic animals – Structure of teeth – Histological structure of tooth – – Enamel – Dentine – pulp cavity – Brachyodont – hypsodont teeth – – Eruption of teeth, Dental formula of different animals including humans-Teeth of horse – Teeth of cattle – – Teeth of sheep and goat – – Teeth of dogs – Disorders of teeth in animals – – Pigmentation of teeth, Anodontia: Oligodentia, Polyodontia, Heterotopic Polyodontia, Odontogenic cysts – Periodontal disease - Diseases of buccal cavity and mucosa, Diseases of Salivary glands – Ptyalism – Salivary calculi (sialoliths) – Sialoadenitis – Oesophagus – Parasitic diseases of oesophagus Diseases of the fore stomachs – Tympanitis (Bloat) – Secondary tympany or free gas bloat – Foreign bodies in the rumen and reticulum, Reticulitis- Ruminitis – Lactic acidosis – Symptoms – Traumatic reticulitis – Foreign bodies in the forestomachs – Diseases of true stomach – Circulatory disturbances – gastritis – gastric ulcers – Chronic gastritis-Torsion, Sites and types of hernias – Parts of hernia, Caudal abdominal hernias, inguinal hernia – Scrotal hernia, Perineal hernias -Diaphragmatic hernias – Traumatic hernias – Femoral hernias – Liver function tests – Tests for bile pigments – Serum bilirubin – Liver and Biliary system – Developmental anomalies – congenital cysts – Pigment accumulation – Nutritional diseases-Hepatic necrosis – – Apoptosis – Cirrhosis – Portal or nodular cirrhosis, Alcoholic cirrhosis, Multinodular or Gin drinkers or Laennec's cirrhosis, Biliary cirrhosis (monolobular or hypertrophic cirrhosis)-parasitic cirrhosis – Pericellular cirrhosis – Ascites – – Cholangitis – Cholilithiasis, Pancreas – Neoplasia of pancreas diabetes mellitus – Type I diabetes called insulin dependent diabetes mellitus, juvenile – Type II diabetes - non-insulin dependent diabetes mellitus, adult onset diabetes – Insulin – peritoneal tumors.

Digestive system

The digestive system starting from mouth to anus with its accessory organs like liver, pancreas is fundamentally similar in all animals. But as per the need of the animal and the food it take, this system has been modified.

Thus in cattle and buffaloes (large ruminants), and in sheep and goat (small ruminants) starting from the mouth the organs have been modified to cope up

the grabbing of the food materials and their digestion. Thus the incisors of the upper jaw have been replaced by a dental pad, which will be helpful in mastication of the regurgitated food. The tongue especially in cattle and buffaloes has been modified in such a way that it acts a prehensile organ. Whereas in sheep and goats the lips act as a prehensile organ to grab the feed.

In ruminants the forestomach has been modified to become fermentative vat to cope up the cellulose digestion holding vast number of bacterial flora and fauna. In a day old calf or in a new born lamb, the stomach what we visualized is a simple stomach (abomasum), when the calf reached a month age or in lamb when it is more than a week, one can visualize the other three stomach namely rumen, reticulum and omasum coming up as offshoots or diverticula form the lower end of the esophagus where it dips into the abomasum. The well developed Caceum and colon also helps in the digestion of fiber.

Horse, though herbivore is a simple stomached animal. But for the digestion of the fiber, the vast caceum has been developed. The caceum runs into meters and holds vast capacity of the mass and helps in the digestion of fiber due to the flora and fauna. The lips act as a good prehensile organ in grabbing the food.

The dog is a simple stomached animal, but the intestine is voluminous to help in the digestion of the food material. The canine teeth have been developed in such a way, to catch the prey, dissect it and take it into pieces.

The pig is an efficient converter of the food, is having a well developed large intestines, the spiral colon, which runs into several meters. The snout is well developed and has good teeth with well developed canine teeth which act as a good prehensile organ in grabbing the food.

The elephant, herbivorous animal has a well defined digestion for fibers and the caceum has been developed for this to an enormous extent. The proboscis acts as a prehensile organ for ingestion of the food and fodder.

The camel having three stomachs only viz., rumen, omasum and abomasum and lacks reticulum. The lips act as prehensile organ in the procurement of feed.

In birds, the mouth cavity has been narrowed with the presence of beak, the esophagus having a diverticula known as crop which helps in the storage of food; due to absence of teeth, the nature has provided the bird another stomach, a muscular organ known as gizzard, apart from the true stomach namely proventriculus. The proventriculus secrets hydrochloric acid, digestive enzymes and the gizzard acts as a grinding organ with its encircled musculature, with a lot of grit inside. In order to make the body lighter, the intestines are shortened, with duodenum, jejunum, ileum, two caeca and rectum altogether measuring less than a meter in length. There is no definite colon.

Ingestion of food

The amount of food that an animal ingests determined principally by the intrinsic desire for food called hunger. The type of food that a person preferentially seeks is determined by appetite. The food to be taken is to be masticated (chewed) and to be swallowed. The teeth are admirably desired for chewing. The anterior teeth (incisors) providing a strong cutting action and posterior teeth (molars) for grinding action. In the human being as the jaw muscle working together can close the teeth with a force as great as 55 lbs. on the incisors and 200 lbs. of pressure/ square inch on the molars.

With this short study of physiology and anatomy background of intestines, we will examine the diseases of alimentary system of animals.

In general the alimentary tract is composed of oral cavity, esophagus, stomach, small intestine and large intestines. The oral cavity is composed of teeth, tongue, salivary glands, and tonsils. The mucosal surface of the oral cavity is lined by thick, stratified squamous epithelium which provides protection. Oral cavity is always flooded with saliva, which varies in composition from species to species and in the bovine often it is alkaline due to the presence of carbonates and in all the domestic animals saliva, an enzyme Lysozyme is present which is having an antibacterial action. Saliva also contains secretory antibody namely IgA which keeps the oral flora into a limiting number. These floras are aerobic and anaerobic bacteria, spirochetes and sometimes fungi. These flora fluctuates in number and kind and varies in response to factors such as presence of carbohydrates or protein substances, pH, oxygen tension, mucous and antibodies.

Diseases of the oral cavity

Examination of the oral cavity is the standard procedure during any postmortem examination. To obtain a clear view of the mucous membrane of the buccal or oral cavity, teeth, tongue, gums and tonsils, it is essential to split the mandible symphysis and separate the mandible as far as possible. A thorough examination of all structures will reveal not only local lesions but often those which may be due to systemic diseases.

First we discuss the congenital anomalies of the oral cavity. The development of normal face and the oral cavity requires the integration of many embryonic processes. Failure of the fusion of these embryonic processes resulting in facial clefts which involve the skin as well as the deeper tissue as well.

Primary cleft palate or palatoschisis includes developmental anomalies of the lips anterior to the nasal septum, columella and premaxilla. These anomalies, may be uni or bilateral and superficial or extend into the nostril. The defect arises from incomplete fusion of the fornto-nasal process with the maxillary processes.

Secondary cleft palate occurs wherein there is the failure of formation of hard

palate. The hard palate is formed, except for a small anterior contribution from the front-nasal process, by the bilateral in growth of the lateral palatine shelves from the maxillary processes. At the mid line they fuse with each other and with the nasal septum, and undergo intramemrbranous ossification, except in their posterior part, which becomes the soft palate. This results in communication between the oral and nasal cavities. Affected animals have difficulty and sucking milk may have nasal regurgitation, and usually die within the first few days of life from aspiration pneumonia. This has been reported in foals and calves. The cause is suspected to be due to ingestion of lupine plants in Friesian cows during gestation at 40 to 70 days. In lambs there is genetic tendency or due to ingestion of Veratrum californium plant leaves. Secondary cleft palate has been induced in piglets by feeding sows with plants of poisonous Hemlock during gestation periods from 30 to 45 days. Tree tobacco, a close relative of *Nicotine tobacum*, ingestion of which has been attributed for the incidence of cleft palate in newborn pigs when gilts were fed early in pregnancy. Palatoschisis in piglets has also been associated with consumption of feed contaminated with Crotalaria retusa seeds by sows during gestation. Primary and secondary cleft palate in dogs especially in German Boxer dogs appears due to a single autosomal recessive gene. In cats, it has been shown that when pregnant cats have been treated with griesofulvin, showed cleft palate.

Anomalies in the growth of jaws are quite common. Brachygnathia superior, shortness of the maxilla is an inherited breed characteristic among dogs and swine. It has been reported in the Large White or Yorkshire breed of pigs.

Brachygnathia inferior or micrognathia, shortness of the mandible, is a lethal defect in cattle and sheep. This is characteristic of long nosed dogs. This is called parrot mouth condition and is common in horses. Prognathism refers to an abnormal prolongation of the mandible. It is common in sheep.

Agnathism is a madibulo-facial malformation characterized by the absence of lower jaw due to failure of development of the first branchial arch and associated structures. This is common anomaly in lambs and also in cattle.

A lethal gross pharyngeal hereditary defect, termed bird tongue and caused by a simple, recessive autosomal gene has been reported in dogs. Hypertrophy of the tongue occurs as a congenital anomaly in pigs.

Epitheliognesis imperfecta is an anomaly causing widespread effects in cutaneous epithelium, and also affects the lining epithelium of the oral cavity, especially the tongue. The condition is characterized by irregular well demarcated red areas, from which the epithelium of the oral mucosa is absent.

Inflammatory terms used while describing the oral cavity

Stomatitis: This is a diffuse inflammation of the mucous membrane of the mouth. **Gingivitis** is the inflammation of the gums. Gingivitis with an ulcerative condition

of gums is Noma (necrotizing). **Glossitis** is the inflammation of the tongue. **Lampas** is the inflammation of the palate. **Chelitis** is the inflammation of the lips. If pharynx is affected it is known as **pharyngitis**. If tonsils are inflammed the conditions is known as **tonsillitis**.

Stomatitis: Stomatitis is a common affection noticed in animals and more often it is a symptom of some other disease. For this physical, chemical, bacterial, fungal and viral agents and a variety of common causes are responsible.

Grossly the lesions start as catarrhal inflammation of the mouth and pharynx with reddening and swelling of the mucosa, which is covered by small whitish spots known as apthous stomatitis. These whitish spots develop as ulcers in the latter stage.

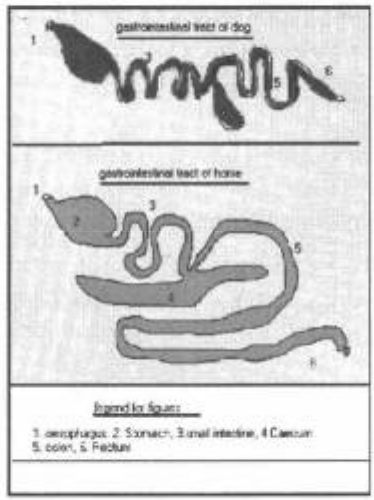
Vesicular Stomatitis is seen in foot and mouth disease in cattle, buffaloes and pigs and is due to calci virus.

Stomatitis is also seen in **contagious pustule dermatitis**. It is an acute readily transmissible disease of sheep and goats. The causative agent is a parapox virus. It is a zoonotic disease and human beings are also affected. The lesions occur on the lips, external nares, and also occur in the oral mucosa. Epithelial cells of the oral mucosa contain eosinophilic intracytoplasmic inclusion bodies.

Stomatitis is also seen in **bovine pustule dermatitis**. This disease is caused by a virus which is related to that of contagious pustular dermatitis. This occurs in young animals. The lesions are seen in the oral cavity. Raised pusutlar lesions occur on the hard palate, lips, muzzle and tongue and may extend to the oesophagus, reticulum, rumen and omasum.

Rinderpest affects the oral cavity and the causative agent is the Morbili virus. This is characterized by erosive or hemorrhagic lesions of the mucous membranes. It is a febrile disease. Cattle and buffaloes are affected. The oral lesion typically involves the inner side of the lower lips. The buccal papillae at the commisures and the ventral surface of the free portion the tongue are involved. Erosions are become ulcers and with diphtheritic mucosa, these ulcers appear is covered by bran like deposits.

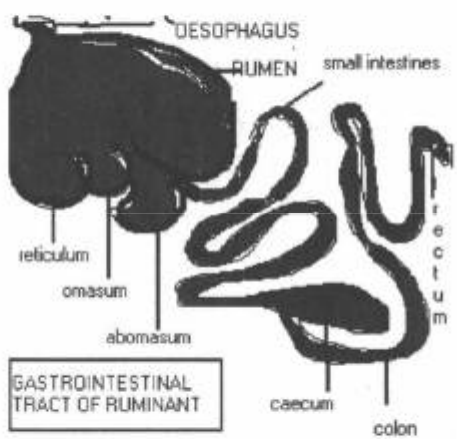
The lesions of oral mucosa involve the stratified squamous epithelium originating on the basal layer. Many epithelial cells undergo necrosis, the nuclei become pyknotic and fragmented and the cytoplasm shows coagulate appearance and is eosinophilic. Multinucleated syncitial giant cells are seen and these may have cytoplasmic or nuclear inclusions. The initial minute erosions enlarge and coalesce to form extensive large ulcers.



Comparative measurement of gastrointestinal tract and relative compartments in %.

Species	Stomach	Small intestines	Caceum
Ox	1	18	3
Horse	9	30	16
Pig	9	33	6
Dog	3	23	1

At birth abomasum is the largest compartment I young ruminants. If calves are not fed little quantity of roughage they will consume extraneous substances resulting in trichobezoars.



Two types of ruminants are there. The first type of ruminant contains rumen, reticulum, omasum and abomasum. The second type of ruminant is Tylopoda that is camel, llama. In this omasum is vestigial or absent and areas of cardiac glands open into ventral sacculated surfaces of reticulum and rumen.

Bacterial Stomatitis

Actinobacillosis: *Actinobacillus lignieresei* causes a deeply located infection and granulomatous inflammation of the oral tissues and the adjacent lymph nodes. Actinobacillosis infection is seen in cattle, buffaloes, sheep, goat and horses. The causative agent gram negative bacillus. There is suppurative inflammation of the tongue. It is chronic in nature. With the resultant suppurative inflammation, the tongue looks like a hard object hence is called as wooden tongue.

Histopathological examination revealsthe granulomas with central gram negative bacilli at the centre in the form of colonies and these are surrounded by a zone of palisade, eosinophilic club shaped structures which are enucleated histiocytes. These clubs are surrounded by granulocytes, macrophages, epitheloid cells and foreign body giant cells. A row of lymphocytes and plasma cells are also present. All this is surrounded by a fibrous tissue reaction. Whole this looks like suppurating granulomas with yellowish granules like masses. Infact these are called as sulfur granules.

Acitnomycosis: This is caused by a gram positive bacillus or filaments. This reaction gives to this lesion as ray fungus lesion. The gram positive bluish filaments are surrounded by eosinophilic gram negativeclubs. The gross lesions are grey-white, firm and fibrotic, irregular dense nodular mass which contain suppurating granulomatous as described previously with actinobacillosis lesions as sulfur granules. Lymph node involvement is common.

NOMA: It is an acute gangrenous Stomatitis. This is seen in human beings, monkeys, and dogs. The causative organisms are spirochetes and fusiform and other bacteria of the mouth. The lesions are necrotizing, progressive to gangrenous changes.

Ulcerative gingivitis: This is caused by spirochete-bacterial infections of the mouth. This is seen in humans and monkeys. The disease is seen in nutritional deficiency conditions. Acute inflammation causes painful gums, a fetid mouth dour, hemorrhages which occur with slight trauma and increased salivation. The lesions in acute, necrotising inflammation of the gingiva. Punched out, crater like ulcers in the interdigital gingival, and are covered by a grey pseudomembrane.

Tumors: Oral papillomas are common in young dogs and puppies. The causative agent is a virus. These are transmissible and multiple and occur in the buccal mucosa and on the tongue, palate, pharynx and epiglottis.

Clinically the disease is mild, and tumors persist for about 2 to 3 months, after which there is spontaneous regression followed by complete immunity.

Squamous cells carcinomas are common in the oral mucosa of aged dogs and cats. The carcinoma may begin in the tongue, gingival or tonsils. Tonsilar mucosa is affected commonly in dogs, whereas in cats tongue mucosa is involved. Clinical signs with carcinoma of the tonsils include attempts to regurgitate out saliva and interference with respiration or swallowing.

Grossly the tumors look like cauliflower masses. Histologially stratified squamous cells invade the lamina propria and submucosa or even underlying muscle. Epithelia pearls are common with keratin encircled into the inner side.

Malignant melanoma: Benign melanomas develop as back moles and develop rapidly into rapidly growing firm masses. They are seen in the pigment portions of the mouth of dogs of 7 to 14 years of age and they originate in the gums, buccal mucosa, palate or lips.

Histologially the neoplasm consists of epithelial or spindle shaped melanocytes. Most oral melanomas are malignant, and metastasize through lymphatics to regional nodes or by the blood to the lungs.

Diseases of teeth and dental tissue

The brief histology and embryology of the teeth is given to understand about the dental diseases of animals. Dental examination of teeth in animals usually done to determine the age of the animal under study.

Teeth develop from horseshoe shaped thickenings, in the oral ectoderm called dental laminae. Neural crest cell beneath the laminae induce formation of tooth buds, which generates the enamel organs. These epithelial structures grow into the underlying ectomesenchyme and organize it to form dental papillae, which they enclose like a cap.

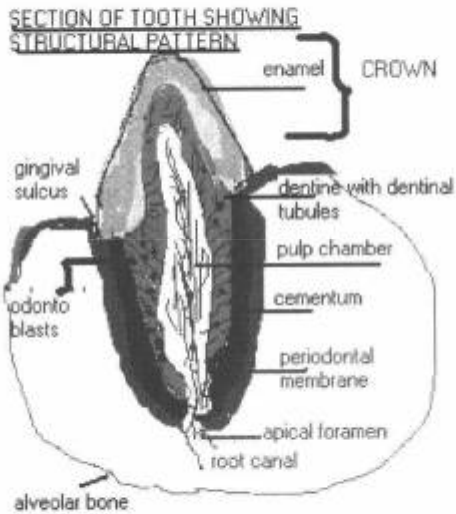
The inner enamel epithelium of the enamel organ induces differentiation of odontoblasts from the mesenchyma of the papilla. Odontoblasts produce dentin, which in turn induce enamel formation by the inner enamel epithelium. Formation of dentin is essential for formation of enamel. The free edge of enamel organ extends beyond the enamel dentin junction, and this extension is called epithelial root sheath.

Mesenchymal cells from the dental sac differentiate into cementoblasts and deposit cementum on the dentin. Teeth of domestic animals are divided into two forms, namely simple teeth and complex teeth.

Structure of teeth

The structure of teeth as follows.

The three hard tissues of teeth are dentin, enamel and cementum. The number of teeth in upper jaw and lower jaw varies with the species and age of the animal. This is written in the form of dental formula. The dental formula of different species of aged animals is given in the table.



Histological structure of tooth

Histologically a tooth contains enamel, dentine, cementum and pulp. The tooth also can be divided into the crown, which is the portion that protrudes out of the gum into the mouth, and the root which is the portion that protrude into the bony socket of the jaw. The collar between the crown and root where the tooth is surrounded by gum is called neck.

The crown is visible part of the tooth that is the portion above the gums. The body of teeth is embedded in the alveolar socket of the bone. The enamel is the hardest substance of the body and is glistening and covers the crown. Next to the enamel the body of tooth consists of dentine. The body of tooth is divided either into a single or two or three roots. The root is the portion embedded in the socket (alveolus) of jaw bones. The root, made up of dentin is covered by cementum and no enamel covering is there. The root is maintained rigidly within the alveolar socket by the firm, fibrous periodontal ligament.

Enamel is epithelial in origin and encircles dentine beyond the plane of gum. It is the hardest substance found in the body. The outer surface of the tooth is covered by a layer of enamel that is formed prior to eruption of tooth by special epithelial cells called ameloblasts. Enamel contains 5% organic matter and 95% mineral. It is produced by tall columnar ameloblasts of the inner enamel epithelium. Enamel is produced in the form of prisms or rods, cemented together by matrix. Mineralisation begins as soon as it is formed and it is a two stage process. Enamel is hard, dense, brittle and permeable and is translucent and white. Ameloblasts are very sensitive to environmental changes. Formation enamel ends before tooth eruption.

Chemically it has calcium phosphate in the largest quantity and also considerable amounts of organic substances. Enamel is composed of large and very dense crystals of hydroxy apatite with adsorbed carbonate, magnesium, sodium, potassium and other ions embedded in a fine mesh work of very strongly and almost completely insoluble proteins fibers that are similar in physical character but not chemically identical to that of keratin of hair. The crystalline structure of salts makes the enamel hard, much harder than dentine, the special protein fiber mesh work; around 1% makes the enamel resistant to acids, enzymes and corrosive agents. This is one of the most insoluble proteins so far found in nature. Histologically, enamel is composed of enamel rods or prisms, which are minute crystals of inorganic material embedded in organic one. The calcified organic cementing substance between each rod is named as inter-rod or interprismatic substance.

The bulk of tooth is composed of dentine which contains a higher percentage of inorganic material than bone but lesser than enamel. Similar to bone it has collagen fibers in a calcified ground matrix. Dentine is made up principally of hydroxy apatite crystals similar to those in bone but much denser. These are embedded in strong network of collagen fibers. The major difference between bone and teeth is that teeth do not contain osteoblasts, osteoclasts or spaces of blood vessels or nerves. Instead it is deposited and nourished by layer of cells called odontoblasts which line in its inner surface all along the wall of the pulp cavity. The calcium salts in dentine make it extremely resistant to compression forces, while the collagen fibers make it tough and resisting to tensional forces that might result when teeth are stuck by solid objects. The cells, odontoblasts are responsible for deposition of dentine. It covers the pulp cavity and presents all through out the life. Dentine is light yellow and consists most of the tooth. It consists of 35% organic matter and 65% mineral. Thus its composition is similar to that of bone. Dentine is produced by odontoblasts. Dentinal tubules are visible in histological sections. Near the bulb dentine is innervated and the dentine is acelllular. Odontoblasts normally are active throughout life.

Cementum which is also like bone both histologically and chemically covers dentine at the root of the teeth. Cementum may be cellular, containing the cells, cementocytes which are similar to osteocytes or they may be free from cells named as acellular cementum. Cementum is avascular, bone like substance, produced by cementoblasts; and it contains 55% organic and 45% inorganic matter. The pulp cavity is composed of connective tissue and richly supplied with blood vessels. It has also both myelinated and non-myelinated nerve fibers. The gingiva or gum is the oral mucous membrane which is firmly connected with the periosteum of the alveolar bone at its crest and also with the surface of the tooth by the epithelial attachment. The dentin of Brachyodont teeth is covered by cementum wherever it is not covered by enamel. Cementum is more resistant to resorption than to bone.

Table : Showing Comparative correlation of chemical composition of bone and teeth

Salt	Bone ash % composition	Teeth (Dentine)
Tricacium phosphate	15.0	13.2
Calcium carbonate	8.0	4.6
Magnesium phosphate	0.5	0.8
Others	0.5	0.6
Calcium alone as%	35.0	27
Chlorides	1.0	0.06

Table. 7 Composition of bone of cattle

Stage	water	fat	protein	Ash
At birth	6.53%	2.30%	16.19%	13.76%
At 3 months	4.92%	13.30%	20.0%	16.20%
At 4 years	3.21%	17.72%	21.0%	26.34%

Tooth could be classified as Brachyodont and hypsodont. Brachyodont teeth are seen in humans, carnivores and swine. In these animals the tooth enamel is restricted to the tooth crown. In hypsodont teeth, enamel extends far down on the roots, and is invaginated into the dentine to form infundibula. Hypsodont teeth are present in the herbivore mainly the molars are covered by cementum.

The large domestic herbivore have a teeth meant for rotating and grinding for mastication. The teeth have a high, flat masticating surface and undergo physiological friction. Therefore, there is need for continuous eruption. The distinction between the crown and root is less obvious than in simple tooth. As in the simple tooth, the dentine occurs closest to the dental pulp. Enamel is deposited abundantly against the dentin, not only on the crown, but it extends also deep into the alveolar socket along the tooth root. Unlike the simple tooth, cementum is adherent to the enamel layer, so that dentin, enamel and cementum make up the hard dental substance on both crown and root. Another feature of complex teeth is in the folding which occurs on the masticator surface. A deep indentation (funnel shaped passage) lined by enamel and filled with cementum is called the infundibulum.

Eruption of teeth

During infancy or in young calf the teeth begin to protrude upward from the jaw bone through the oral epithelium into the mouth. Number of theories has been put forward for eruption of teeth. The most likely theory is the growth of teeth root as well of the bone underneath the tooth progressively shoves the tooth forward. During early embryonic life a tooth forming organ also develops in dental lamina for each permanent tooth that will be needed after the deciduous or temporary teeth are gone. These tooth producing organs slowly form the permanent teeth that are needed when temporary teeth are gone. These tooth

producing organs slowly from the permanent tooth. When each permanent tooth is fully formed, it pushed through the bones of the jaw. In so doing so it erodes the root of the deciduous tooth and eventually causes it to loosen and fall out. Soon thereafter the permanent tooth erupts to that place of the original one.

Metabolic factors in the development of tooth: The rate of development and speed of eruption of teeth can be accelerated by both thyroid and growth hormones. Also, the deposition of salt in the early stages of tooth forming is affected considerably by various factors of metabolism such as availability of calcium and phosphate in the diet, the amount of vitamin D is present and the rate of parathyroid secretion. When all these factors are normal, dentine, and enamel will be correspondingly healthy, but when they are deficient, the calcification of teeth may also be defective so that the teeth will be abnormal throughout life.

Dental formula of different animals including humans

Species	Ini-t	Cani-t	Pre-t	M-t	Tot-t	Inci-p	Cani-p	Pre-p	M-p	Tp
Humans, upper jaw	2	1	-	2	5	2	1	2	3	8
Lower jw	2	1	-	2	5	2	1	2	3	8
Cattle Upper aw	0	0	3	0	3	0	0	3	3	6
Cattle Lower jaw	4	0	3	0	7	4	0	3	3	10
Horses Upper jaw	3	0	3	0	6	3	1	¾	3	10/11
Lower jaw	3	0	3	0	6	3	1	3	3	10
Swine Upper aw	3	1	4	0	8	3	1	4	3	11
Lower jaw	3	1	4	0	8	3	1	4	3	11
Dog Upper jaw	3	1	3	0	7	3	1	4	2	10
Lower jaw	3	1	3	0	7	3	1	4	3	11
Camel Upper jaw	1	1	3	0	5	1	1	3	3	8
Camel lower jaw	3	1	2	0	6	3	1	2	3	9

In: Incisors, Cani: canines, Pre: Pre molars, M: Molars, Tot-t: Total Temporary, P: Permanent, Tp: Total permanent

Teeth of horse

Teeth of horse: The horse, mule and ass normally have 6 incisors teeth consisting of two central, two lateral and two corner teeth.

Eruption of deciduous incisors teeth; Birth to 1st week, Ist teeth, 2nd after birth from 4 to 6 weeks, 3rd pair from 6 to 9 months. Decidous premolar of Ist, 2nd and 3rd pairs come after birth up to 2 weeks.

Eruption of permanent teeth; Incisor of 1st pair at 2 and half years; incisors of 2nd pair at 3 and half years and incisors of 3rd pair at 4 and half years. Canine will start erupting at 3 and half to 5 years after birth. Premolar of first pair will come at 5 to 6 months and premolar of 2nd will come at 2 ½ years and premolar of 3rd pair will come at 3rd year and premolar of at 4th year. The first molar start coming at 9 to 12 months; 2nd pair at 2 years and molar of 3rd pair at 3 and 1/2 to 4 years.

Incisor teeth: They are 6 in number in the upper and lower jaws;they are found in the front of the mouth in each jaws. The temporary incisors differ from the permanents in that each of the former possesses a definite neck. The temporaries are smoother, whiter and smaller. When both temporary and permanent teeth are present into the mouth, it is not usually difficult to differentiate between them. The temporary incisors have several ridges and shallow grooves. The permanent upper incisors often have two well defined grooves on the labial surface. The lower permanent incisors have one distinct groove only.

Canine (dog teeth): These are four in number and one on each of the jaws and in the right and one in the left. The canines are present only in male animals. The canine teeth are comparatively simple, showing no folding of enamel.

Molars (cheek teeth); These are 6 or 7 in each of the four jaws; according whether wolf teeth are or are not present. The first three permanent molars are called premolar. Each tooth has got a complicated folding of enamel which bears some resemblance to the capital letter B.

Infundibulum; Each permanent incisor carries on its table a dark depressed ring known as the infundibulum. At 8 years of age, infundibulum will disappear from all the incisors.

Galvayne's groove: This is a well marked longitudinal groove in the lateral surface of upper incisor 3.

Teeth of cattle

The incisors are absent from the upper jaws of cattle, their place being taken the dental pad. The incisors in the lower jaw are slightly movable in a forward directon. The incisors are chisel shaped and do not have flat tables and an infundibulum as in the horse. The incisors are described as central, medial, lateral and corners. The canine are absent in cattle. The premolars and molars are also more less chisel shaped and progressively increase in size from first to last. The premolars and molars have well formed grinding surface.

Incisors on the lower part of jaws specially first and II pair will erupt before birth itself. Temporary incisors of 3rd and 4th pair will erupt within 1 to 2 weeks after birth of the calf. Temporary 3 pairs of premolars on lower and upper jaw erupt after birth at around 3 weeks.

Permanent teeth of 1st, 2nd and 3rd pair of incisors will come 1 to 3 years after birth.

4th pair will come after 3 and ½ years to 4 years. The 3 pairs of premolar will come into surface within 2 to 3 years after birth. The first pair of molar will come at 5 to 6 months and 2nd pair at 1 to 1 and half years and 3rd pair at 2 to 2 and ½ years. At 5 years of age the teeth are slightly worn along their cutting edges and at 6 years the teeth are slightly worn along their cutting edges and the surface of each reach half way across the upper surfaces of teeth and a portion the root is exposed. At 10 years of age, the greater part of the crown worn from the teeth. Only little cup shaped pieces of enamel remains and at 12 to 14 years of age only stumps of the teeth remain and the teeth are widely separated from each other.

Teeth of sheep and goat

In sheep and goat, the 1st, 2nd, 3rd and 4th pair of incisors of temporary nature will erupt before 3 to 4 weeks after birth. Premolars of 1st, 2nd and 3rd pair erupt before 4 weeks after birth. Permanent teeth of first pair of incisors will come within one year and 3rd and 4th pair will come within 3 years. Premolar of 1st, 2nd and 3rd pairs will come within one and 1/2 year to 2 years. The molars erupt especially first a pair between 3 to 4 months and 2nd pair at 9 to 12 months and 3rd pair at 1and 1/2 year to 2 years of age. At 2 and ½ years the 4th pair of permanent incisors cut through the gums. The 4th pair of permanent incisors come into wear at 3 year 3 months and the sheep is full mouth at this age.

Teeth of sheep in dogs

Appearance of teeth at various ages: at birth: At birth no incisors are present. At 3 to 4 weeks of age one pair of temporary canine erupt. At 4 to 5 weeks of age one pair of temporary incisors and first three temporary molars cut through the gums. At 4 months of age the central and lateral permanent incisors appear. At 5 to 6 months of age the corner permanent incisors cut through the gums. Two pairs of canine appear. The 1st, 2nd, 3rd and 5th cheek tooth appear at 6 to 8 months of age the pair of 6th cheek teeth appears in the lower jaw only. At one year of age the incisors are in full wear. At 2 years of age the end of the crown appears uniform in outline. At 4 years of age the incisor shows definite line of wear.

Disorders of teeth in animals

Pigmentation of teeth: Normal enamel is white and shiny, but normal cementum is off white to light yellow and normal dentin is slightly darker yellow. In fluorotoic conditions, the enamel is hyperpalstic and is discolored yellow. Discolored dentin consequently discoursed teeth occurs in congenital porphyria or pink tooth of bovines). Dentin maybe coloured brown by puplpal heaemorrhages as gray green in putrid puplpitis and yellow in icterus. Calves born that have been given injections of tetracycline in pregnancy show after the birth discolored teeth. Tetracyclines are toxic to ameloblasts in the late differentiation and early secretion stages and, at high dose rate may produce enamel by hypoplasia. Black discoloration of ruminants' cheek teeth is extremely common and is caused by impregnation of

mineral salts with chlorophyll and coprophyrin pigments from herbage.

Anodontia: Absence of teeth. This is seen I cow, camels and this disorder is due to a sex linked gene.

Oligodentia: Fewer teeth than normal. Occurs sporadically in horses, cats and dogs and also an inherited trait in dogs.

Polyodontia: Excessive teeth. This is common condition in humans. The incisors are involved. This is seen in brachicepahlic dogs.

Heterotopic Polyodontia: It is an extra tooth or teeth outside the dental arcade.

Odontogenic cysts are epithelium lined cysts seen in oral cavity. Dentigenrous cysts are by definition cysts which contain part or all of teeth which often is malformed. This is seen in horses, sheep and in calves.

Dental attrition: This is due to repeated mastication. Sharp molars are common in sheep, goats, cattle and buffaloes. This is due to wearing of the one side part of the teeth. Abnormal wear due to abnormal chewing is caused by voluntary as in painful conditions, or mechanical impairment of jaw movement. Certain vices such as crib-biting in horses produce abnormal wear.

Caries

Caries is a decay of teeth wherein enamel is decalcified followed by softening and discoloration. This is a disease of monogastric animals and too those depending on the simple carbohydrates. Humanscommonly suffer with this as they consume lot of carbohydrates. Occasionally dogs too suffer due to intake of imbalanced and inadequate diet. The affected teeth have, usually had one or more depressed areas which are black or brown in colour.

For caries to occur three theories have been proposed. One is acidogenic theory, the second one is a proteolytic theory and the third one is proteolysis chelation theory.

Acidogenic theory: Here presence of microorganisms and production of acid in the mouth are the factors in the genesis of caries. For the decay of teeth, a cavity is produced. This is due to formation of acid by bacteria existing in the mouth. These bacteria produce enzymes which break down carbohydrates into simple sugars (glucose), further these sugars are broken down into lactic acid and pyruvic acids, acetic and butyric acids . These acids soften hard enamel, leaving an entrance through which bacteria enter the tooth and create a cavity.

Proteolysis cavity theory: According to this theory, certain gram negative bacilli produce an enzyme, sulphatase, which attacks the proteins causing the rods to tumble down. The enzymatic reaction releases sulfuric acid and this acid and other acid S disintegrate the calcified rods, thus creating cavity.

Proteolytic chelation theory: _According to this theory enamel is a unified structure consisting of a chelate complex, linking the organic and inorganic components. Caries is brought about by proteolysis and chelating, occurring simultaneously.

For the starting of dental caries, plaque formation is essential. Some bacteria are able to stick to teeth on mucosal surfaces. Attachment to teeth is not direct but rather to a coating of sticky macromolecules, mainly proteins, the dental pellicles. Most bacteria transform sucrose into detrains which are particularly sticky. They are layered on the pellicle to form a matrix but allows further adherence of other organisms. The result is formation of dental plaque. This is also known as dental calculus or dental tartar. It is formed by the deposition of mineral, mainly from saliva, the dextrans as said above and the dead bacteria.

In horses and dogs, calculus is predominantly calcium carbonate. Calculus is often found in the old dogs and cats occasionally in horses and sheep, and rarely in other species. Calcium on horse teeth is chalky and can be easily removed. In dogs, it is hard, firmly attached, and often discolored. Redbrown to black calculus with a metallic sheen develops in pastured sheep and goats. It usually involves all the incisors, principally on the neck of the buccal surface. In caries there is damage to the dentin. The opposed surfaces of the adjacent teeth may be more frequently affected. Enamel flakes occur which are yellow stained spots on the enamel. The affected teeth are shaky and are very painful and so interfere with mastication. Caries is frequently seen in fluorine poisoning and in dietary mineral disturbances.

Malocclusion; Malocclusion is usually caused by a heredity abnormality that causes the teeth of one jaw to grow to an abnormal position. In malocclusion, the teeth cannot perform normal grinding or cutting action adequately. Occasionally malocclusion causes abnormal displacement of the jaw causing such undesirable affects as pain in the mandibular jaw or deterioration of the teeth.

Puplpitis

The dental pulp is derived from dental papilla. It is surrounded by odontoblasts and dentin, except at the apical foramen, through which vessels and nerves pass. Pulp is a loose syncitium of stellate fibroblasts. It contains histiocytes and undifferentiated mesenchymal cells. The latter are odonotblastic precursors.

The apical foramen is narrow and this disposes to vascular occlusion, ischemic necrosis of pulp and death of tooth. Very mild puplpitis may heal, but usually it terminates in necrosis, suppuration or gangrene.

Inflammation of the pulp may extend to the periodontium and jaws. Periodical abscesses and osteomyelitis of jaws are complications of pulpitis. Pus in antrum is a common complication in dogs and in human beings consequent to the puplpitis. Clipping the tusks of piglets trimming the incisor teeth of sheep also results in puplpitis.

Periodontal disease: This is the common chronic disease of humans and animals. Periodontal disease begins as gingivitis associated with sub-gingival plaque, and may progress through gingival recession and loss of alveolar bone to chronic periodontitis and exfoliation teeth.

Diseases of buccal cavity and mucosa:

1. **Pigmentation:** Melanotic pigmentation is normal and is common in most of breed of animals and increases with age.
2. **Circulatory disturbances:** Congestion and edematous swelling of the tongue and buccal mucosa are specific lesions of blue tongue of sheep.
3. An acute congestion and ulceration is seen in chronic uremia cases in dogs.
4. Heaemorrhages in buccal mucosa indicates septicemia, and large ones may accompany local inflammation and trauma.

Diseases of Salivary glands:

The common salivary glands in the animals are parotid, sub-mandibular and lingual glands. The most common conditions of the salivary glands are affecting the function. Ptyalism means increased secretions of saliva and aptyalism means reduced secretion of saliva.

Aptyalism occurs in a variety of conditions including heavy metal poisoning, poisoning with organophosphates, encephalitis and most often with Stomatitis. Decreased secretion of saliva, aptyalism accompanies fever, dehydration and salivary glands affecting in a variety of bacterial and viral diseases. Aptyalism occurs in foot and mouth diseases, rabies and variety of viral and bacterial infections.

Salivary calculi (sialoliths)

Salivary calculi (sialoliths) are present in the ducts of salivary glands. These are composed of largely calcium carbonate, and the nidus may be of dead cells. Most of the sialoliths is usually single and cylindrical and they may be quite large. Most of them lodge at the orifice and cause some degree of salivary retention, glandular atrophy, and a predisposition to infection and further inflammation.

Ranula are they cystic distension of the ducts of the salivary glands that are present in the floor of the mouth. These present a smooth, rounded prominence with a blush tinge and fluctuations. The contents maybe serous or of a thicker, tenacious mucous. Rupture of duct or a gland to an epithelial surface results a permanent fistula as the continued flow of saliva prevents normal restoration. Accumulation of salivary secretions in single or multiloculated cavities adjacent to duct is now referred to as salivary mucocoele or sialoceole. Small mucocoele not exceeding 0.5 cm. in size, are occasionally observed on the side of the bovine tongue.

Cysts of other origin: Cysts of other origin do occur in the mouth region. Cysts of the thyroglossal duct are mid line and are distinguishable readily when they

contain thyroid follicles.

Sialoadentitis: Inflammation of the salivary glands. Submandibular glands are commonly affected in dogs and cats. Inflammation of zygomatic gland in dogs is a cause of retrobulbar abscesses. Sialoadentitis is seen in bovines with viral infections like rabies and malignant catarrhal fever. In rabies there is focal lysis of glandular lining, and mononuclear infiltration is seen in between the glands. Negri bodies are present in the ganglion neurons. Mumps virus infects the salivary glands of both human and dogs. Sialoadenitis occurs in vitamin A deficiency in calves and pigs.

Neoplasms of salivary glands are rare in all species. Tumors arising in the glandular tissue are usually adenomatous in type.

Diseases of Oesophagus:

Oesophagus: Inflammation of the oesophagus is known as oesophagitis. Erosive and ulcerative oesophagitis is a common finding associated with viral diseases. Rinderpest, malignant catarrhal fever. Bovine popular Stomatitis, infectious bovine rhinotracheitis cause focal esophageal ulcers.

Reflux oesophagitis

Reflux oesophagitis: Reflux oesophagitis is thus most common in dogs and cats as a sequel to surgery involving general aneaesthesia, though it may follow chronic gastric regurgitation or vomition may cause. In swine and horses, it may be associated with ulceration of squamous esophageal portion of the stomach. In dogs it is associated with hiatus herniation.

Thrush or mycotic oesophagitis

Thrush or mycotic oesophagitis; this is caused by *Candida albicans*

And is seen in piglets and weaner swine, in which the lesions may involve squamous mucosa of the entire upper alimentary canal. The condition is secondary to other intercurrent problems, including antibiotic therapy and esophageal gastric reflex.

Ingluvitis is the inflammation of the crop. Thrush of the crop is also common in poultry consequent to indiscriminate feeding with antibiotics. This is due to the growth of fungus *Candida albicans*. The mucosa of the oesophagus resembles turkey towel appearance and is thickened due to the inflammatory lesions and fungal elements.

Choke

It is obstruction to the oesophagus. Impaction of the oesophagus is seen with large or inadequately chewed objects such as potatoes, corn cobs, apples, bones, masses of grain or fibrous ingest and infact the author has observed in a bovine there was choke consequent to the lodgment of big stones. This often occurs

where the esophagus deviates or it slightly restricted normally, at the area over larynx, the thoracic inlet, the base of the heart and immediately anterior to the diaphragmatic hiatus.

Consequent to choke there is pressure necrosis and ulceration of the mucosa, which may progress to perforation. Sharp objects, such as bones are most likely to cause perforation. Perforation of the thoracic oesophagus is a complicated one leading to sepsis and with resultant contents falling on to the pleural surface and peluritis. The cervical esophagus may be perforated by sharp objects such a wire or needle penetrating form the exterior surface of the skin.

Removal or dissolution of an obstructing object may be followed by scaning of the segmentally ulcerated oesophagus, resulting in the narrowing of the lumen, stricture or stenosis. A vascular anomaly that may constrict the oesophagus includes persistence of both rightly and left aortic arches, persistent of right ductus arteriosus, aberrant left or right subclavian artery. The site of stricture with its narrowed esophageal lumen is readily identified at necropsy.

Choke is seen consequent to the paralysis of muscles oesophagus in rabies and veterinarian's infact manipulate mouth of bovines leading to exposure to rabies infections.

Dyspahgia: Difficulty in swallowing. The disorder of swallowing is a major signs of esophageal disease. Swallowing is a complex and highly coordinated physiological act which will be followed into three phases. Pharyngeal dyspahgia could be recognized in diseases such as Stomatitis, glossitis or hyoid bone disease or due to rabies or due to brain abscesses or in the blue tongue.

Parasitic diseases of oesophagus: Sarcosporidia of striated esophageal musculature is common in cattle, buffaloes, sheep and goats. Esophageal Sarcocysts appear as ovoid thin walled nodules of less than 1 cm long projecting from the esophageal musculature. Sarcocysts in esophageal muscle normally incite little or no local inflammatory reaction and are of no significance only larvae of gasterophilus species may be temporarily attached to the caudal pharyngeal and cranial esophageal mucosa and to the mucosa carni to the cardia in horses.

Spirurid nematode of the genus *gongylonema* may be encountered in stratified squamous mucosa of the upper alimentary tract including oesophagus, in ruminants and wine. *Spirocerca lupi* is a Spirurid nematode which parasitises the esophageal wall of canine and some other carnivores. The normal site for the adult nematode is in large, thick walled cystic granulomas in the submuosa of the caudal portion of oesophagus or gastric cardia, where one or more pink worms surrounded by purulent exudates are found. A fistulous tract to the esophageal lumen is usually present, through which the tail of the female worm may protrude, and which provides the outlet for ova to the gastrointestinal tract. In some animals with *Spirocerca lupi* neoplasms develop in the wall of the oesophagus grnaulomas, and

the granulomas contain highly reactive pleomorphic fibroblasts with large open nuclei and numerous mitotic figures. Neoplasms arising form such lesions have cytological characteristics typical of fibro sarcoma and osteosarcomas with local tissue invasion and in many cases, pulmonary metastasis.

Diseases of the fore stomachs

The fore stomachs are the constituent parts of the ruminant digestive system. These are the rumen, reticulum, omasum and abomasum. Abomasum is the true stomach and resembles the mammalian counterpart of the other animals. The rumen, reticulum and omasum are the simple diverticula of oesophagus. Thus in the ruminant in the early stages of life i.e., in case of calf below a month and in the case of lambs below one week, the well developed stomach only is the abomasum. These diverticula of rumen, reticulum and omasum appears as if small leaves sprouting from the plant.

The adult ruminant having a weight of 800 kg animal holds around 400 liters of fluid in the rumen. If one visualizes the anatomical structure of the fore stomachs, the oesophagus dips directly into the rumen, but the ventral surface is in direct contact with reticulum, which is against in contact with omasum. The esophageal groove which forms a fold of reticulum, omasum and abomasum can be easily visualized in young claves. In adult ruminants, the elevated musculature could be seen, linking the esophageal groove. In fact it can be stimulated in the adult animal by administrations of low dilutions of copper sulfate solution in the form of drench. The picture of rumen, reticulum, omasum and abomasum in situ has been depicted in the figure.

The physiological configuration of dipping oesophagus into rumen is such solid particles of heavy nature first fall into reticulum, instead of rumen and less dense particles will enter the compartment of rumen. The rumen has been divided into dorsal and ventral compartments. Thus the fibers will enter into dorsal sac of rumen, churned by the ruminal motility which will be 2 to 3 per minute.

The cardiac end of oesophagus which dips into the rumen having sensitive fibers traveling in the vagus, responsive to scratching reflex. Thus the fibrous material that scratches the cardia of rumen initiates ruminal contractions.

The ruminal papilla in the newborn is rudimentary, which gives the mucosa relatively smooth and pale appearance. Subsequent development of the ruminal papillae depends mainly on the type of diet fed. Little or no growth of papillae occurs in animals as long as they are fed milk. Animals on rations containing adequate levels of roughage develop long, slender, regular, and white to grey ruminal papillae. Histologically the normal papillae are covered by a thin layer of keratinized squamous epithelial cells.

The pathogenesis of morphologic variations in the ruminal papillae depends on several factors. These include they type and proportion of volatile fatty acids

evolved in the ruminal contents, the pH, and the proportion and the coarseness of roughage fed. Hyper and parakeratosis occurs when ruminants are fed rations containing adequate levels of coarse roughage that is approximately at 15% level. Animal and vegetable hairs cause damage to the ruminal papillae and cause and also bring about mild ruminitis and micorabscesses in the ruminal wall.

Tympanitis (Bloat)

It is abnormal accumulation of gases in the rumen resulting in over distension of it which in turn contributing for the pathogenesis of the disease.

The accumulation of gas in the rumen is normal. Rumen is a fermentative vat. It is under tight anaerobic condition. The gases produced in the rumen are methane (CH_4)-26.76%, H2S-0.01%, Nitrogen (N_2) -7.00 % and CO_2- 65.35 %, O_2-0.56%. These gases are exhaled out by a process of eructation, through mouth. The number of eructation's per minute is 1 to 2. In the normal rumen the amount of gases produced per hour are around 40 liters with 70 kgs of ruminal content, 2 litres of gas is produced/mt in a 500 kg animal.

Ruminal motility is therefore used as an index of digestive function in the ruminant. The plain muscle of the forestomachs has no intrinsic contractile power, depending on the nerve stimulation namely vagus. Food enters into the forestomachs, divides into layers, upper layer of the free gas and a lower layer of fluid with suspended particles.

Population of bacteria is around 10^9 cells/gm. of ruminal fluid. Methane is formed by reduction of CO_2 by methanogenic bacteria; methane forms the bulk of the total gas produced in the rumen.

The physiological configuration of dipping oesophagus into rumen is such solid particles of heavy nature first fall into reticulum, instead of rumen and less dense particles will enter the compartment of rumen. The rumen has been divided into dorsal and ventral compartments. Thus the fibers will enter into dorsal sac of rumen, churned by the ruminal motility, which will be 2 to 3 per minute.

The cardiac end of oesophagus which dips into the rumen having sensitive fibers traveling in the vagus, responsive to scratch reflex. Thus the fibrous material scratch of cardia of rumen initiates rumen contractions.

The ruminal papillae in the new born are rudimentary, which gives the mucosal relatively smooth and pale appearance. Subsequent development of the ruminal papilla depends mainly on the type of diet fed. Little or no growth of papillae occurs in animals as long as they are fed with milk. Animals on ration containing adequate levels of roughage develop long, slender, regular, and white to grey ruminal papillae. Histologically the normal papillae are covered by a thin layer of keratinized squamous epithelial cells.

The pathogenesis of morphologic variations in the ruminal papillae depends on several factors. These include the level, type and proportion of volatile fatty acids liberated in the ruminal contents, the pH and the proportion and the coarseness of roughage fed. Hyper and parakeratosis occur when ruminants are fed rations containing adequate levels of coarse roughage (approximately 15%). Animal and vegetable hairs cause damage with resultant mild ruminitis and micorabscesses in the ruminal wall.

Tympanitis (bloat): Abnormal accumulation of gases in the rumen resulting in over-distension of it which in turn contributing for the pathogenesis of the disease. It is due to failure of eructation and elimination of gases. Before discussing complete pathology of bloat ruminant bloat, we will discuss about the physiological response rumination.

Rumination is physiological process confining to the ruminant consists of phases of mastication swallowing, regurgitation of bolus, remastication and reswallowing. Here we will discuss the ruminal physiology first to understand the pathology. Ruminant will grab as much material available at one stroke and regurgitate the material into mouth and swallow it again. This is called rumination. Rumination thus consists of four processes namely regurgitation, remastication, re-in salivation and redeglutination. Animals may spend around 8 hours per day for rumination.

If the same material is coming into the mouth of the monogastric animal it is called as vomitus. The lack of involvement of abdominal muscles in increasing abdominal pressure in the ruminant is a primary characteristic that distinguishes regurgitation in ruminant from that of vomiting of monogastric animals.

In the new born calf the rumen and reticulum together are about one half as large as abomasum. In 10 to 12 weeks, the abomasum is about one half as large as the rumen and reticulum combined. At the age of one and half years, the four compartments have reached their permanent relative sizes, the rumen accounting for about 80% of the stomach capacity, reticulum for about 5%, omasum at about 7 to 8% and the abomasum to around 7 to 8%. The rumen communicates freely with reticulum over the rumino-reticular fold. From the cardia to the reiculo-omasal orifice extends the peculiar esophageal or reticular groove. In well developed cattle, it is around 7 to 8 in length. The ruminoreticular groove can be stimulated even in the adult animal by ingestion of copper sulfate so that the medicaments can be directly passed on from the oesophagus to the abomasum. In fact in calves, the suckling reflex makes the stimulation of esophageal groove so that the milk from the oesophagus directs enters into abomasum. The ruminal contraction is 1 to 2 per minute, whereas reticular contractions are 79 to 100 per hour while eating, 47 to 80 per hour while ruminating.

Rumen is a variable fermentative tub with number of flora and fauna staying in it. The muscular activity of rumen makes the churning of the contents easily. The ruminal movements are around 1 to 3 per minute. Ruminal motility is an index of

positive function in the ruminant.

The remasticated bolus of food fill be churned by ruminal action, will be acted by the bacterial flora and fauna. Cellulose digestion takes place. Free volatile fatty acids will be liberated, and will be absorbed into the blood. The common volatile fatty acids liberated by ruminal digestion are acetic, butyric and propionic acids.

The digesta will enter into the reticulum, from there into the omasum and abomasum and passes on into the intestines. The ruminal movements are 2 to 3 per minute. They start from the reticulum and moves into the posterior sac of rumen. These can be freely visible from the flank.

Thus in a normal animal active ruminal movements will help in mixing of the food and eructation reflex helps in the exhalation of gases produced under fermentative reactions. Failure of these mechanisms results in abnormal amount of gas production in rumen and consequent tympany methane is produced by reduction of CO_2 by methanogenic bacteria. These gases are the common products of microbial fermentation of carbohydrates and proteins and results from the actin of many kinds of gram negative saprophytic bacteria and protozoa presented in the ingested material.

Pathogenesis of Bloat: As already stated Tympanitis of rumen or bloat consists of accumulation of excessive quantities of gas in the rumen. Normally ruminant animals get rid off gas produced in the rumen by eructation.

The tympany could be classified as primary ruminal tympany or frothy bloat and secondary tympany or free gas bloat.

The frothy bloat is characterized by accumulation of abundant foam. The foam consists of gas bubbles and the digesta. Thus the free gas produced in the rumen is not being exhaled out but being trapped in the form of foam containing gas bubbles. Gas bubbles or foam occurs due to the substances that lower the surface tension and float freely in the water.

The foam producing factors are multiple. The formation of foam is dependent on soluble proteins, which are present in legumes. These soluble proteins are released from chloroplasts. These proteins are degraded by the ruminal flora and rise to the surface where they are denatured, become insoluble and stabilized as foam.

Increase in the viscosity of ruminal contents also increases the foam. Proteins present in the plant products also contribute to the viscosity of ruminal fluid and act as foam stabilizing agent.

Saliva is also an antifoaming agent. When secretions of saliva decreases foaming results. Cows that have a high susceptibility to bloat produce saliva. Succulent and high concentrate feed reduced salivary secretions thus increasing the viscosity of ruminal contents.

The composition of saliva also affects the frothy bloat production. Combination of salivary bicarbonates with organic acids such as citric, malonic and succinic acids which are present in high levels in legumes, results in the production of large amounts of CO_2 enhancing the bubble formation.

Normal salivary proteins increase the viscosity, whereas mucin reduces the viscosity. Increase of saline producing bacterial also contributes for the foam properties and bloat production. The buffering action of saliva may raise the pH of ruminal contents above the range at which soluble proteins are most likely to produce stable foam. The saliva prevents formation of bloat or froth. In cattle consuming 215 liters of water per day, the saliva addition is 178 liters, i.e., 83% of water entering the stomach was provided by salivary secretions.

Cattle that have a high susceptibility to bloating have higher levels of chlorophyll that originate from chloroplasts, and have more density of particulate matter in rumen, higher rate of ruminal contents that produce gas production compared to cattle that do not bloat. High and low susceptibility to bloat can be temporarily transferred between animals by exchange of total ruminal and reticular contents.

Rations high in concentrate and low in roughage not only reduce salivary secretion but also change the ruminal microflora.

The substances that are produced form the grasses such as cyanides, and fodder that encourage production of phosphatase also results in inhibition of ruminal motility, which is added factor in the forth production.

Secondary tympany or free gas bloat

Secondary tympany or free gas bloat: This is usually an acute condition. The causes are physical or functional defect in eructation of gas produced by normal ruminal fermentation. The frequent causes are internal or external obstruction of oesophagus or esophageal groove by tumor, papillomas, or foreign body and esophageal stenosis. Reticular adhesions, abscesses, peritonitis or tumor masses that interfere with contraction of forestomachs can result in bloat. Other factors to be considered are Organophosphourous intoxication, vagal nerve damage. In the calves it is due to consumption of large amount so milk, which escape the esophageal groove and flow into the rumen, where it putrefies because of digestion by proteolytic bacteria. Even animals that have fed too much succulents, there is a tendency for bloat formation, because minimal amount of fiber is required for scratching the cardia for eliciting the ruminal response. Even animals fed rations that have too much roughage may have recurrent episodes of bloat. Indigestible roughage accumulates in the rumen and reticulum where intake of digestible nutrients) starch and sugar) are inadequate. As a result the rumen is dilated and ruminal and reticular contractions stops and eructation reflex also will be stopped.

The cause of death in bloat is probably the combined effects of increased abdominal pressure on the diaphragm inhibiting respiration. The shunting of large volumes

of blood away from the abdominal viscera results in anoxia and consequent respiratory embracement. Consequent to intra-abdominal pressure that is compressing of blood in the posterior vena cava which results in the redirection of blood flow from the caudal areas of the animal. The blood is shunted through the lumbar veins, into the longitudinal vertebral sinus, from there to the intercostals veins and to the hemiazygos or costocervical veins.

Lesions: The bloated animal is often found dead and distended with gas; blood exudes from the orifices. Due to over distension of rumen the carcass often roles on its back and assumes a saw horse posture. The blood is dark and cots poorly. Subcutaneous heaemorrhages are prominent in the neck and trunk. There is marked oedema, congestion and heaemorrhages of cervical muscles and lymph nodes of head and neck. Esophageal mucosa is congested. The tracheal mucosa is hemorrhagic especially anterior to the thoracic inlet. This lesion is path gnomonic feature to bloat and this should be differentiated from number of other diseases including Rinderpest and hemorrhagic septicemia in cattle and buffaloes under Indian conditions.

Blood clots are frequently seen in the bronchi and paranasal and frontal sinuses. The lungs are compressed into the anterior thorax by the bulging diaphragm. Paleness of liver is observed. Lymph nodes and muscles of hind legs are pale. There is marked subcutaneous oedema particularly of vulva and perineum. When postmortem is done immediately after the death of the animal, there will be lot of foamy ruminal contents is seen. Inguinal and diaphragmatic rupture may occur after death.

Foreign bodies in the rumen and reticulum: Cattle and buffaloes are not selective grazers. This makes them as disadvantageous animals in grabbing the food. Amazing variety of foreign bodies starting from barbed wire, hair pins, stones, rubber derived products, now-a-days the plastic bags, gunny bags and a variety will observed in rumen, reticulum. Sheep are largely immune because of their more selective eating habits. Foreign bodies are rarely found in the rumen of goats, despite their reputation for indiscriminate feeding habits. It is possible that many of lighter and smaller foreign bodies are regurgitated.

Foreign bodies consisting of larger of hair or wool *(trichobezoars)* or plant fibers *(phytobezoars or concretions)* are also observed in the ruminants. The author has observed hair balls in two adult buffaloes at postmortem in the rumen. They are just like tennis balls. Hair balls as per the literature are most common in younger ruminants. The hair being swallowed after licking, particularly by animals deprived of dietary fiber. They may have some other foreign bodies as a nucleus and contain proportion of plant fibers, the whole mass concreted by organic substances and inorganic salts.

The hair balls are not usually harmful. Similarly the phytobezoars. Being smooth, these are not important unless regurgitated to lodge in the esophagus or passed

on to obstruct the reticulo-omasal orifice, the pylorus or the intestine which is infrequent.

Reticulitis: Inflammation of the reticulum is called as reticulitis. This is very common condition in cattle and buffaloes. As already discussed, that cattle and buffaloes are notoriously lacking the alimentary fineness, a deficiency that allows an amazing variety of foreign bodies, prehend with food, to be deposited in the forestomachs. When sharp objects perforate the reticulum, the condition is known as traumatic reticulitis.

Traumatic reticulo-peritonitis and its complications: As already stated perhaps the cardia of esophagus opening is such that solid objects fail into the reticulum and reticulum is situated as the lower portion of the forestomachs. Anterior surface of the reticulum is in contact with the diaphragm. Thus a sharp object like pieces of wire or a nail of 2 " or more in length, which is present in reticulum will cause the pathogenesis. Incomplete perforation of the wall is usually without significant effect, although in some cases a suppurative or granulomatous inflammation develops in the wall of the reticulum, with minor overlying peritonitis. The perforation occurs mostly in the anterio ventral direction due to the frequent reticular contractions. This is being precipitated by the increased intra-abdominal pressure of late pregnancy and parturition. The foreign body may advance to perforate the diaphragm and pericardium, resulting in traumatic pericarditis. A ventral penetration may result in sub peritoneal and subcutaneous assesses near the xiphoid. Rare perforation of one of the larger regional arteries may result in sudden death from hemorrhage. Sudden death may also occur if there is penetration of the myocardium or rupture of a coronary artery.

Penetration of the thoracic cavity may occur without perforation of the pericardium and causes pneumonia and peluritis. Right lateral deviation of the penetrating agent causes involvement of the wall of the abomasum. Even in some cases liver or spleen will also be penetrated. This result in metastatic abscesses into the liver. Traumatic pericarditis with suppurative pericarditis is also very common under Indian conditions. With this disease good lactating cows will died with complications. When the vagus nerve is affected due to traumatic reticulitis, vagus indigestions common. There is persistent ruminal atony or irregular motility and gradual onset of bilateral abdominal distension.

Ruminitis: Inflammation of the lining epithelium of the rumen is the cause of ruminitis. Inflammatory lesions of rumen occur in number of viral diseases, includes, Rinderpest in cattle and buffaloes, in infectious bovine rhinotracheitis, bovine popular Stomatitis, contagious ecthyma of cattle and blue tongue of sheep. Accidental urea poisoning and with acid indigestion caused by carbohydrate overload (lactic acidosis).

Lactic acidosis

Lactic acidosis (ruminitis and acidosis caused by carbohydrate overload): ruminitis and ruminal acidosis is common in ruminants. Under Indian conditions the author has seen several cases of this when cattle, sheep and goats are in access to large heaps of grains and thereby consuming them in large quantities. Primary tympany exists and the condition is usually fatal or followed by several complications.

Pathogenesis: Ruminal acidosis usually follows with the ingestion of excess carbohydrate in the form of grain, bread and other nuts. It is peculiar in villages in India after parturition to get good lactation yield from milk cattle and buffaloes are frequently fed with finely grinded horse gram, black gram. This leads to development of acidosis in these animals.

There is a wide variation in the amount of carbohydrate necessary to kill an animal, because tolerance to rations high starch does develop. Shortly after the ingestion of toxic amounts of carbohydrates, the ruminal pH begins to fall. The decrease in pH during the first 8 hours is mainly due to an increase in dissociated volatile fatty acids. Then large amounts of lactic acid are generated as this is the end product of Embden Meyerhoff pathway in the anaerobic cycle.

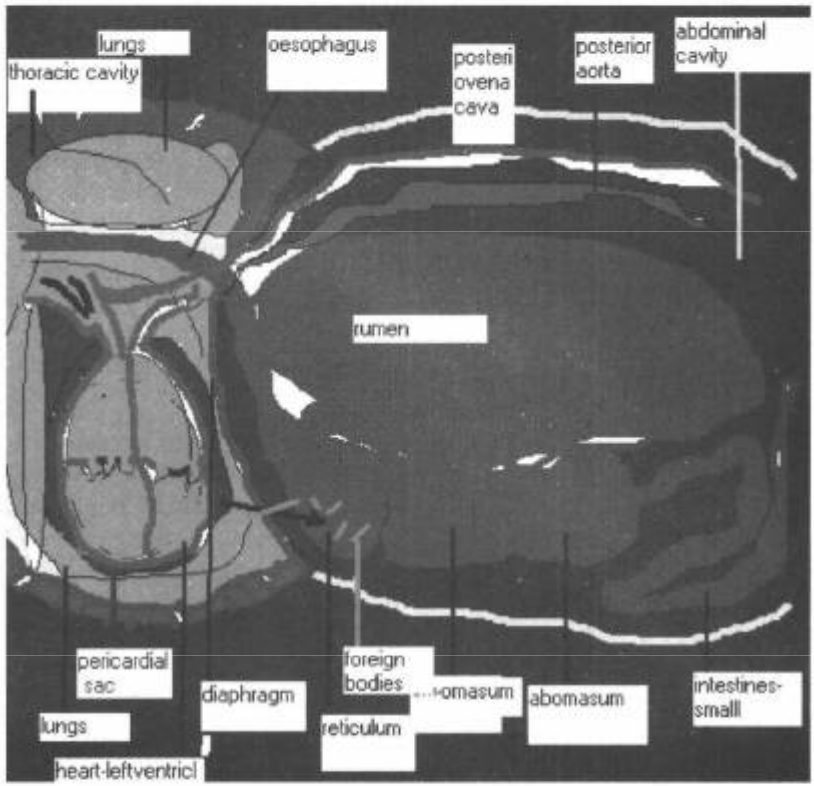
The normal pH of ruminal fluid in cattle and sheep varies between 5.5 and 7.5 depending on the diet. Normally at this pH the bacteria are usually of gram negative in nature. When the pH is falling down, the protozoa die and these gram negative bacteria also die. There is rapid proliferation of streptococci mainly Streptococcus bovis and as a result liberal amounts of lactic acid is produced by these bacteria. When the pH is reached from 4.5 to 5.0 the number of streptococci decreases and lactobacilli proliferate.

Symptoms: As the ruminal pH drops, ruminal atony develops. Reticulo ruminal motility also stops due to inhibition of vasovagal reflex. There is cessation of salivary secretion so that the buffering effect of saliva is absent.

When lactate of rumen increases, the osmotic pressure of ruminal fluids increase resulting movement of fluid from the blood to rumen. There is reduction in plasma volume, haemoconcentration, anuria and circulatory collapse. The osmolarity of ruminal fluids is increased, there is haemoconcentration and dehydration. High concentrations of lactic acid cause chemical ruminitis and development of mycotic ruminitis.

Traumatic reticulitis

This is a very common condition in older cattle and as well in heavy lactating cows. Cattle are not selective grazers. The indiscriminate habit of taking materials make them to susceptible to variety of traumatic injuries one of this is the traumatic reticulitis. As the ingested object falls down first into the reticulum which is the lower most portions of the stomachs.



PATHOGENESIS OF TRAUMATIC PERICARDITIS AND RETICULITIS IN CATTLE

Foreign bodies in the forestomachs

As already told cattle are notoriously lacking in alimentary fitness, a deficiency that allows an amazing variety of foreign bodies, prehended with the food, to be deposited in the forestomachs. Sheep and goats are largely immune because of their more selective eating habits. Foreign bodies are rarely found in the rumen of goats, despite their reputation for indiscriminate feeding habits. In consequence, a large proportion of adult cattle, and very goats or sheep have foreign bodies in the rumen and reticulum but rarely in the omasum. It is possible that many of the lighter and smaller foreign bodies are regurgitated.

Foreign bodies consisting largely of hair or wool trichobezoars may also form younger ruminants, their heir being swallowed after licking particularly by animals deprived of dietary fiber. Plant fibers, phytobezoars are also common in ruminants. They deposit on the organic nucleus and encircle them and form rounded balls. Being smooth neither phytobezoars nor trichobezoars is important unless they obstruct to the oesophagus or passed on to obstruct the reticulo-omasal orifice,

the pylorus or the intestines. Nails and hair pins and barbed wire always cause traumatic reticulitis and traumatic reticulo-pericarditis and bring about considerable number of animals death especially in high yielding lactating cows. A mixed bacterial flora containing clostridia is responsible for causing mucosal trauma. The seqelae to penetration by sharp objects in adult cattle is traumatic reticulo-peritonitis.

Traumatic reticuloperitonitis and its complications: Perforation of the forestomachs by foreign bodies virtually always is penetration of the reticular wall by sharp foreign body, usually a piece of wire or a nail. Incomplete perforation of the wall is usually without significant effect, although in some cases a suppurative or granulomatous inflammation develops the wall of the reticulum, with minor overlying peritonitis.

A ventral penetration may result in sub peritoneal and subcutaneous abscesses near the xiphoid. Rare perforation of one larger regional artery may result in sudden death from hemorrhage and sudden death may also occur if there is penetration of the myocardium or rupture of a coronary artery. Penetration of the thoracic cavity may occur without perforation of the pericardium and causes pneumonia and peluritis. Right lateral deviation of the penetrating agent causes involvement of the wall of the abomasum. It is unusual for the liver or spleen to be penetrated, but metastatic abscesses in the liver are common.

As soon as the foreign body penetrates the serosa, a local fibrous peritonitis develops, which later leads to dense adhesion of variable extent between the reticulum and adjacent structure. Further progression of the foreign body is ordinarily slow and produces a canal surrounded by chronic granulation tissue and containing, besides the foreign body,ingesta, purulent exudates, and detritus. The common bacteria commonly active in the tract are *Actinomyces pyogenes*, *Fusobacterium necrophorus* and a variety of putrefactive type. In many cases a foreign body cannot be found because it has rusted away or been withdrawn into the reticulum.

Traumatic pericarditis is a less common sequel now, perhaps because so many of the initial penetration are diagnosed and the foreign body so many of the initial penetration is diagnosed and removed surgically.

One of the variants in the usually pattern of migration of the foreign body is penetration of the side of the reticulum, leading to a suppurative inflammation in the grooves between the reticulum, omasum and abomasum. Although, the acute local peritonitis causes immediate cessation of ruminal movements, a persistent ruminal atony or irregular motility and gradual onset of bilateral abdominal distension, inappetance, and decreased milk production may stop. Clinically, this is referred to as vagal indigestion, and at postmortem there are very characteristic changes in the stomach. In the vagus indigestion, the abomasum may be distended and impacted with dry ingesta, presumably because of functional pyloric stenosis

or abomasal stasis. The omasum in this condition can be very large and impacted with dehydrated ingesta.

Ruminitis caused by acidosis and carbohydrate overload or lactic acidosis has already been discussed.

Parasitic diseases of forestomachs: Flukes belonging to the family para-amphosotmatidae are usually found in cattle and sheep. These reddish plump droplet shaped fluke are about the size of the papillae between which they reside in the rumen, where they are non-pathogenic. The immature flukes of amphistome cause immature amphisomiasis in duodenum causing inflammation and death in cattle, sheep and goats.

Diseases of true stomach

Haematemesis, Melena or anemia may signify gastric bleeding. Systemic states such as uremia and endotoxemia produce characteristic gastric lesions in canines and horses.

Physiology and anatomical features of true stomach: In the horse and pig, a clear smooth white or yellowish oesophageal region of stomach is present. It is covered by stratified squamous epithelium. Chronic inflammatory infiltrates and lymphoid follicles are normally present in the lamina propria and sub-mucosa of the cardiac gland mucosa abutting the esophageal region. The cardiac gland zone is grayish in colour. This occupies half of the body of the stomach. In the dog, cat, and ruminants cardiac glands are limited to a narrow zone at the cardia or omasal opening. Cardiac glands are branched tubular structures, limited almost exclusively columnar mucous cells. The fundic or oxyntic gland acid secretory mucosa in the horse and pig is reddish brown and slightly irregular but not highly folded. More prominent longitudinally originated rugae or plicae are present in the dog and cat, and in the abomasum. Gastric secretions undiluted by ingesta in the dog or cat normally should be <pH 3. Abomasal pH is around < 3.5-4.0. Tall columnar mucous cells cover the gastric surface, and line pits or foveolae. The neck of the oxyntic gland below the isthmus is lined by pyramidal, cells which produce intrinsic factor. Interspersed are inconspicuous mucous neck cells, mainly in the upper neck, and scattered endocrine cells. In the base of the gland, pepsinogen producing zymogen or chief cells is concentrated.

The pyloric mucosa forms slightly pitted or irregular surface in the distal portion of the stomach; it extends further cranially along the lesser than the greater curvature. The tubular glands of the pyloric mucosa open into deep gastric pits, which may extend half the thickness of the mucosa. The glands relined by pale mucous cells, with interspersed endocrine elements manly gastrin G, and D somatostatin cells.

The parietal cells secrete HCl in response to stimulation by histamine, acetyl choline and gastrin.

Acid production during the gastric phase of secretin is depressed by the negative feedback effect of acid in the antrum possibly through the inhibitory effect of somatostatin on the G cell below the pH 3. Acid, fast and hyerosmolarity solutions in the proximal small intestine also inhibits acid secretions perhaps by the mediation of neural reflexes and secretin, gastric inhibitory polypetides, epidermal growth factor or other enterogastrones. Prostaglandin E2 also inhibits acid production by parietal cells; the chief cell is probably susceptible cell to the same general stimuli for secretions as is the parietal cell.

The gastric mucosal barrier to acid back diffusion and auto digestion resides largely in the single layer of ovular and surface mucous cells. Integrity of the gastric mucosal barrier implies continuity of the mucosal surface epithelium. The capacity of these cells to maintain tight junctions to migrate rapidly to fill defects, and possibly to secrete mucous and bicarbonates is central to protecting the gastric mucosa against progressive injury by insults arising in the lumen. Prostaglandins cause vasodilatation and increased blood flow in addition to inhibiting acid secretion. The high metabolic rate of gastric mucosa requires high blood flow to maintain an intact functional surface epithelium. The peptides, epidermal growth factor, originating in salivary glands, and transform growth factor Alfa, produced locally in gastric mucosa also appear protective in that they may promote cell proliferation and migration to fill defects and suppress acid production.

Gastric mucosa is freely permeable to hydrogen ions and has little innate buffering cpacity. Cardiac glands mucosa in the pig and pyloric mucosa secretes bicarbonate in considerable quantities and normally resisting acid attack. Fundic surface mucous cells also actively secrete bicarbonate into a thin, unstirred layer of surface mucous. Bicarbonate and mucous secretion by mucous cells is stimulated by PGE2.

Gastric dilation and displacement: In the horse it is often a secondary effect of obstruction of the small bowel, or colic with ileus. Primary gastric dilatation in horses is a sequel to consumption of exceeds fermentable carbohydrate, sudden access to lush pasture, or excessive intake of water. Dilatation associated with intake of fermentable feed. Ingesta may swell through absorption of saliva and gastric secretion. Evolution of gas and organic acids, including lactic acid, by bacterial fermentation of carbohydrate, occurs in the cranial portion of the stomach. An influx of water flows as the result of increased osmotic pressure in the stomach, contributing to increased distension and to systemic dehydration. Animals suffering for any time with acute gastric dilatation of this type may develop laminitis. Gastric rupture may follow primary or secondary dilation of the equine stomach. Rupture occurs usually along the curvature. Death ensues as a result of shock and acute peritonitis.

Gastric dilation and volvulus in dog occurs due to aerophagia and problems associated with eating. The accumulation of CO_2, food and fluid in the stomach causes the organ to dilate and alter its abdominal position, so that its long axis rotates from a transverse left right orientation to one paralleling that of the abdomen.

In swine gastric volvulus is common in those pigs that have been fed with feed after a long gap of starvation. This is to excitation of pigs.

Circulatory disturbances: Hyperemia of gastric mucosa occurs with ingestion of chemicals which usually also cause superficial erosion and necrosis. Focal hyperemia may be related to local irritation of the mucosa by foreign bodies and with focal acute viral lesions of the abomasum of cattle. Congestion of mucosa can occur in conditions causing portal hypertensions, including cirrhosis and shock in the dog. Uraemic gastritis is associated with signs of haematemesis, and Melena. In such animals the mucosa is thickened and deep red black.

Histologically the lamina propria between glands is oedematous and there increased mast cells. Calcification of muscular oats of arterioles and mucosa wherein parietal cells are seen. Gastric hemorrhage is common in hemorrhagic septicemia of cattle, anthrax and other septicaemic and viremic diseases. In theilerosis of cattle and buffaloes, punched out ulcers and heaemorrhages in gastric mucosa are common.

Gastritis

Inflammation of stomach is called as gastritis and is very common in domestic animals. It may be primary consequent to irritants or may be secondary to number of parasitic, bacterial, viral and parasitic infections. The stomach is a veritable, sounding board of emotions and when one considers the bombardment it suffers from neurogenic, secretory and hormonal stimuli not to mention exogenous irritants of every sort and description, the wonder that any one has a healthy digestion (Body- text book of human pathology).

Gastritis may be acute or chronic.

The causative agents are physical, like overfeeding with frozen foods, coarse material eating, faulty dentition preventing mastication and resulting in roughages entering into stomach, foreign bodies taken in food may traumatize stomach mucosa, spoiled mouldy, fermented hay and silage and too sudden changes of feed.

Chemicals like caustics and corrosive chemicals like mercury, lead, copper, arsenic and phosphorus. Toxic plants, Uraemic conditions, feeding easily fermentable foods liberates irritating substances which produce gastritis, feeding heavily fatigues animals has the same effects produce irritation of stomach, feed is not easily digested, stagnates, ferments and produce irritation, stress conditions wherein adrenaline is produce large quantities which is responsible for gastritis. This is seen in nervous dogs and in calves separated from mothers and in human beings.

Acute gastritis may be catarrhal, fibrinous, suppurative, hemorrhagic or necrotic depending on the cause and their severity.

Acute hemorrhagic gastritis characterized by gastric injury with grossly heaemorrhages and necrosis with inflammatory processes is seen in most of the septicaemic, viremic Rinderpest, malignant catarrhal fever, blue tongue, infectious bovine rhinotracheitis and haemoprotozoan diseases. Mycotic gastritis is common in pigs. Fungal hyphae are present in submucosa and venules and arterioles are also invaded, causing thrombosis and hemorrhagic infarcts. Mycotic abomasitis is common in calves due to viral infections like infectious bovine rhinotracheitis and endotoxemia or septicemia associated with Escherichia coli or salmonella infections.

Parasitic gastritis is common in sheep and goats and cattle, due to members of genera *Haemonchus contortus, Mecistocirrus digitatus, trichostrongyles axei, Trichostrongylus colubriformis, Ostertagia spp*, Cooperia spp, cause chronic gastritis with associated mucosal hypertrophy and atrophy of the lining epithelium of fundic gland and dilatation of glands. Especially Haemonchosis and *Mecisterocirrus* are large abomasal blood sucking storngyles.

Members of the genera *Physaloptera* and *Gnathostoma* are found in dogs, where *Physaloptera* cause focal ulceration and Gnathostoma cause sub mucosal inflammatory cysts containing suppurative exudates and worms. In cats *Physaloptera* spp may attach to mucosal ulcers, whereas *Gnathostoma* spp are found in nodule in gastric wall.

In the horse *Habronema muscae, Habronema micro stoma and Habronema mega stoma* found on the mucosa are associated with ulceration of stomach. Apart from these parasites both of the genus *spp*, are also found attached to small erosions and ulcers in the esophageal and glandular mucosa.

In swine the spirurids spp, *Ascarops strongylina, Physocephalus* sexalaus are associated with mild gastritis. Hyostrongylus rubidus cause chronic gastritis and wasting in pigs. *Gnathostoma spp* maybe embedded in the inflammatory cysts of submucosa.

Chronic gastritis in animals has usually the same cause as the acute but operating for a longer time. Sometimes it maybe secondary to chronic gastric dilatation and hepatic cirrhosis. Partial anemia in the former and passive hyperemia in the hepatic cirrhosis decreases the local resistance thereby facilitating infections. The gastric mucosa usually is thickened and covered with tenacious viscid glassy mucous. Mouth of glands are occluded resulting in retention cysts.

Histologically there is desquamation the epithelium with increased interstitial connective tissue and this is the cause of exaggeration of mucosal folding. Hyperplasia of gastric glands and hyperplasia of muscle fibers with infiltration of inflammatory cells and hypertrophy of mucosa with evidence of lymphocytic nodules are seen. The mucosa is thrown into folds and hence the name polypoid gastritis.

Gastric ulcers

Gastric ulcers are common among animals. Calves are more often affected. Usually gastric ulcers run an acute course, heal promptly and become chronic in few cases as in man. Small superficial defects are known as erosions. Gastric ulcers rarely perforate in animals unlike in humans.

Factors implicated are hyper secretion of acid include abnormally high basal cell secretion, possibly associated with an expanded parietal cell mass, as a result of increased tropic stimulation by gastrin. Increased histamine levels associated with mastocytosis or mastocytoma also cause acid hyper secretion and ulceration.

Ulceration due to compromise of mucosal protective mechanisms is attributed to non-steroidal anti-inflammatory agents such as aspirin, phenylbutazone and indomethacin. The ulcerogenic properties of these drugs reside partly in direct toxicity to the gastric epithelium, and partly in their effects on prostaglandin metabolism. Orally administered non-steroidal anti- inflammatory agents which are weak organic acids, such as aspirin have a direct deleterious effect on the stomach. In the acid gastric lumen, unionized lipid soluble acetyl salicylic acid readily coarse the surface cell membrane. At neutral pH within the cell it ionized, damaging the cell metabolically, permitting back diffusion of acid and incipient ulceration. Ulcers induction by this agent is secondarily attributable to depression of prostaglandin synthesis. This they block by interfering with the cyclooxygenase catalyzed conversion of arachidonic acid to the prostaglandin endoperoxides, PGG2, PGH2. In the stomach, prostaglandin mediated vasodilatation, modulation of histamine induced acid secretion, and other protective effects may be impaired. Phenyl butazone may also have direct toxic effect on vascular endothelium in the mucosa, which compromises circulation and precipitates ulcer.

In humans antral gastritis associated with Campylobacter pylori infection and duodenal colonisation with this agent, may be associated with development of duodenal ulcers. Reflux of duodenal contents containing bile salts has been implicated in the induction of gastritis and gastric ulcer. Acid back diffusion into the gastric mucosa and morphologic damage has been caused by application of bile salts. Lipid solubility of bile slats and associated damage to surface cell membranes may mediate these effects. Alcohols also lipid soluble compounds, alter permeability of gastric mucosa and permit diffusion of acid. Lyso-leicithin formed when pancreatic lipase hydrolyses lecithin in bile also increases gastric mucosal permeability.

Gluco-corticoid and stress have been implicated in the genesis of ulcers. Severe gastric hemorrhage or ulceration may occur following neurosurgery, trauma to the spinal cord, and burns. Steroids decrease reparative gastric epithelial cells turnover, and by stabilizing membranes may decrease the availability of arachidonic acid for prostaglandin synthesis. These effects may predispose to

development of ulcer when combined with other insults. Reduced mucosal perfusion or ischemia may be a principal factor interacting in stress associated ulceration. Ischemia will result in hypoxemic compromise of surface cells. In combination with the effects other insults this may initiate mucosal permeability and back diffusion of acid. Neutralization by blood borne bicarbonate of acid diffusing into the mucosal also may be reduced in ischemia. Peptic ulcers are common in domestic animals mostly in cattle.

Perforation of gastric or duodenal ulcers may lead to massive hemorrhage or release of gastric contents into the abdomen.

Ulcers are often to occur under stressful circumstances, as in recently weaned and veal calves, post parturient cows, animals with concurrent disease such as abomasal displacement or mastitis or after transporation. Lactic acid and histamine entering the abomasum from the forestomachs in animals poorly adapted to high concentrate ration may contribute to muscle damage. In calves' consumption of straws, shavings or other roughages contribute for abomasal ulceration. Abomasal ulceration is also seen in theilerosis of cattle as well infiltrating lymphosaromas.

Ulcers in pigs are due to stressful husbandry practices, high dietary copper levels, feeding of whey, starchy diets, low in protein, and high levels of dietary unsaturated fatty acids and administration of finely ground ration shave been found to be ulcerogenic. Ulcers are common in oepshageal portion where dips into the stomach. Swine with gastric ulcers have abnormal fluid stomach contents. Those with hemorrhagic ulcers may have red brown gastric contents or massive hemorrhage into the stomach with large blood clots in the lumen, and thrombosed vessels with blood adherent to the base of the ulcers and in its exposed bleeding points. Melenic content will often be in the intestine, and the colon may contain firm black pelleted faeces. Carcasses of animals which bleed with gastric ulcers are pale in colour. Gastric ulcers in pigs heal by re-epithelisation and such lesion usually become scirrhous, puckered and contracted as the ulcer closes from the periphery and scarring may be visible from the serosa.

Chronic gastritis occurs with gastric trauma, abomasal and gastritis parasitism and in some viral infections of large animals, where it may be associated with sub acute superficial irritation or erosion, a stable gastric ulcer, gastric venous infarction, clostridia and mycotic gastritis, or some systemic viral infections.

Campylobacter (Helicobacter) pylori, has been associated with acute and chronic type of gastritis in human beings especially with peptic ulceration. Braxy or brad sot is an acute abomasitis of sheep and less commonly, calves, due to infections with *Clostridium septicum.*

Torsion: Stomach torsion is usually observed in old dogs. The stomach is twisted around the oesophagus. The causes are due to sudden movements like jumping and rolling, especially when the stomach is full. With the oesophagus as the axis,

the heavy stomach rotes clockwise. The twist closes both the opening to stomach and so gastric tympany develops with resultant dyspnoea. In some cases the stomach may rupture. As the blood vessels are compressed, there may be congestion and hemorrhage. The contents of the stomach are blood stained.

Rupture of the stomach: This is common in horses and is due to Tympanitis and dilatation. Such causes as trauma and violent gastric contractions are also responsible for this.

Dilatation of the stomach: The causes are excessive accumulation of gas or food as in overeating of grains and due to accumulation of excessive fermentable foods in stomach.

The accumulation of gas and feed makes the stretching of stomach wall and intense pain will be felt by the animal. Dilatation of the stomach causes vomition. Loss of fluid results in fatal dehydration and alkalosis. Rupture results due to the stretching of muscle fibers and death occurs due to shock.

Dilated stomach presses on other organs, especially on the diaphragm and lungs results in dyspnoea and congestion.

Malpositions

Herniation: Herniation of the stomach into the thoracic cavity, either through the hiatus esophagi, or at the hiatus cruri is common in man and animals. The herniation into the thoracic cavity is alsocommon in animals met with automobile accidents.

Abomasal displacements: Abomasum is displaced from the normal position either to the left or to the right. But the left sided displacement is more common, in which it comes to lie between the rumen and left abdominal wall. The greater curvature of the body of the abomasum which is more mobile slips under the ventral ruminal sac.

Causes: This condition is met with more frequently after parturition. It is suggested that during pregnancy the rumen may be lifted by the expanding gravid uterus and the abomasum may slip under the rumen. After parturition, when the uterus recedes the rumen is dropped to its normal l position, when it traps the abomasum. Atony of the abomasum due to feeding large quantities of concentrated feeds is a contributory cause for the condition to continue without any tendency at correction. Atony of the may be caused by the inhibitory effects of high fat or protein feeds. Post-parturient disease like milk fever, mastitis, metritis and ketosis may cause atony the abomasum. Abomasal displacement has been met with in cases treated surgically for chronic indigestion. In such cases the incisions made are the weak spots where the abomasum may slip through. Violent activity like jumping in oestrous may be a cause in non-parturient cases. A heredity predisposition may exist.

Symptoms: The symptoms manifested are vague and are like those of chronic indigestion anorexia alternating abnormal appetite. Animal exhibits pain in the abdomen and ruminal tympany develop. Animal loses it weight rapidly, is listless, dull and has a tucked up appearnace. The dung is scanty but sot. Mild ketonuria is present. Abnormal sounds may be heard at the level of Para lumbar fossa.

Due to pressure and compression the normal function of the abomasum is interfered with. Due to displaced abomasal position, the function of the esophageal groove is affected.

Diagnosis: Displacement of abomasum must be differentiated from chronic acetonemia, traumatic reticulitis, vagus indigestion, diaphragmatic hernia, pyelonephritis and lymphomatosis.

Hernia: Hernia is the protrusion of abdominal viscera either through natural or artificial opening. Hernia of intestines is commonly seen in calves, dogs and pigs.

These hernias may be classified as internal or external; natural or artificial; temporary or permanent that is reduced versus incarcerated or irreducible hernias. Hernias could also be classified as a protrusion of an organ or part through a defect in the wall of anatomical cavity in which it leis or into a subsidiary compartment of that cavity. The majority of hernias involve protrusion of abdominal contents through part of abdominal wall, diaphragm or perineum.

Sites and types of hernias

Anatomical area	Types of hernias
Cranial abdominal (ventral and lateral)	Umbilical, traumatic, incisional
Caudal abdominal	Inguinal, scrotal, femoral
diaphragmatic	Peritoneal, pericardial, hiatal or traumatic
perineal	perineal

Parts of hernia: Parts of hernia include hernia ring, or neck, the sac and the contents. The neck or ring is the actual defect in the limiting wall, e.g., tears in the diaphragm. The sac comprises the tissues that cover the hernia contents.

Signs of herniation: Swelling is noticed, resulting from the separation of muscles and intrusion of abdominal contents.

Congenital hernias: The abdominal wall is formed in the embryo by the migration of cephalic, caudal and two lateral folds. These four folds meet at umbilicus, where the yolk sac is continuous with the developing mid gut. During its elongation the mid gut enters the umbilical cord but return to the abdominal cavity well before parturition.

The umbilical aperture in the foetus allows passage of the umbilical blood vessels, the vitelline duct and the stalk of allantois. After the structures are disrupted at birth this opening normally closes rapidly. If closure does not occur, a defect remains in the ventral side line, forming the umbilical hernial ring. Depending on the size of the ring, the hernia may contain falciform ligament, omentum or small

intestine. Genetic defects wherein polygenetic threshold character is there. Improper transaction of umbilical cord at birth may result in failure of the umbilical ring to close normally. If the mid gut fails to return to abdominal cavity, the condition is described as cord hernia. Failure of any folds to properly migrate results in an impholocoele, in which are large defect is present around the umbilicus and the viscera are covered only with a layer of amnion and chorion. Umbilical hernia has been seen wherein rectal abdominal muscles are hypoplastic. Umbilical hernia is most frequent in pigs, foals, calves, pups and depends on persistence patency of umbilical ring. Incarceration of enclosed intestine is uncommon.

Herniation through a natural foramen occurs mainly in horses. In aright to left incarceration in the epiploic foramen a portion of small intestine, usually distal jejunum and ileum, may pass down into the omental bursa and become incarcerated, if the normally short and slit like epiploic foramen of Winslow is dilated for any reason.

Omental hernia occurs, when a loop of intestine passes through a greater or a lesser omentum. Mesenteric hernia is due to passage of intestine through a tear in the mesentery. These are probably traumatic defects and usually involve the mesentery of the small intestine, but occasionally that of colon.

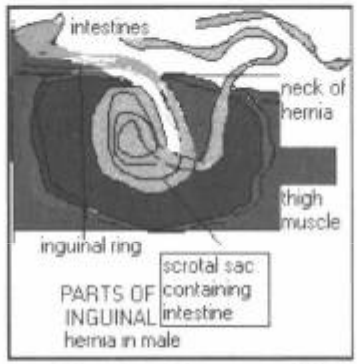
Caudal abdominal hernias: These are scrotal, inguinal and femoral hernias. Indirect hernias involve the abdominal viscera entering the cavity of vaginal process, which forms a hernial sac. Direct hernias pass through the inguinal rings adjacent to the normal evagination of vaginal process.

An inguinal hernia results from a defect in the inguinal ring through which abdominal contents protrude. Males are more susceptible than female to developing congenital hernias.

The passage way for the vaginal process with the spermatic cord, in the male or the round ligament of female, through the opening in the caudoventral abdominal wall is called the inguinal canal. In both sexes, the genital branch of the genito-femoral nerve, artery and vein and the external pudendal muscles, vessels pass through the caudomedial aspect of these canals. The inguinal canal is a saggital slit between the abdominal muscles connected by the external and internal inguinal rings. The internal inguinal ring is bounded medially by rectus abdominus muscles, cranially by the caudal edge of the internal abdominal oblique muscle, and both laterally and caudally by aponeurosis of external oblique muscle and inguinal segment.

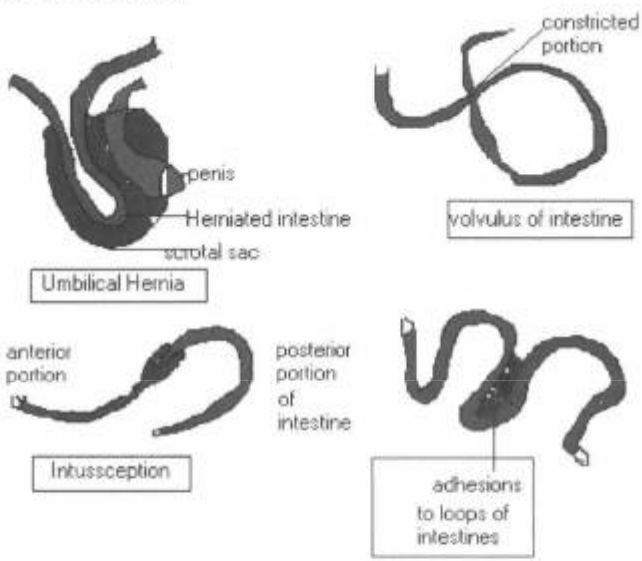
Anatomical defect in the inguinal area is important. Majority of inguinal hernias appear in the oestral or pregnant bitch. Ex-hormone imbalance has been directly linked to inguinal hernia formation in male and female mice. Weakening of the abdominal wall maybe due to altered nutritional or metabolic status of the animal. Obesity may predispose the animal to inguinal hernias.

Inguinal hernia may evolve to scrotal hernia when the herniated viscera pass down the inguinal canal. The internal or deep, inguinal ring remains patent in intact male, but its diameter and tendency to herniation in the neonate may be inherited.



Scrotal hernia: Trauma may be related to scrotal hernia formation. The hernia may be unilateral or bilateral. The intestine slide into the tunica vaginalis along the inguinal canal in contact with the spermatic cord. The testis may undergo thermal atrophy when in contact with the intestine.

Indirect inguinal hernia is by far the most common form, occurring as a congenital problem in the young of many species, as an acquired problem in older animals. Although the size of the inguinal rings may be a factor in neonates, there is usually no apparent cause in acquire cases. The herniated viscus passes through the inguinal and vagnial rings within the vaginalis sheath, coming to lie in the scrotum inside the cavity of the tunica vaginalis. If there hernia is scrotal, there may be degeneration of the testicles.



SCHEMATIC DEPICTION OF MAJOR CAUSES OF INTESTINAL OBSTRUCTION

Direct or false, inguinal hernia may also develop in males, especially horses. The displaced viscous does not pass within the cavity of the tunica vaginalis, but outside it, in a subcutaneous position.

Femoral hernias may develop as an outpuching of peritoneum through the femoral triangle along the course of the femoral artery. They contain omentum and small intestine.

Perineal hernias occur principally in old male dogs in association with Prostatic enlargement. They are precipitated by weakening of perineal fascia and muscles from some unknown cause, possibly hormonal. They occur in females. Retroperitoneal pelvic fat bulges through a defect between the coccygeus medialis muscle and the anterior border of anal sphincter. There is usually loss of support to one side of anal ring. Concomitant with the loss of strength of muscles of pelvis, the rectum deviates, and the prostrate and bladder may move into the pelvis.

Diaphragmatic hernias: A diaphragmatic hernia is a protrusion of abdominal viscera through the diaphragm into the thoracic cavity. Poorly developed central tendon of the diaphragm and in congenital defects develop in utero when diaphragm's embryonic segments fail to fuse.

When an animal experiences a sudden powerful bow against the abdominal wall, there is abrupt increase in the intrabdominal pressure. The flexible diaphragm is pushed violently cranially and if the glottis is opened the lungs deflate, resulting in a large pleuro-potential pressure gradient. The diaphragm disrupts at its weakest points, allowing the abdominal contents to enter the thorax. There is a faulty development of septum transversum, permitting peritoneal and pericardial communications.

Hiatus herniatus: A hiatal hernia is defined as the protrusion of herniation of nay structure through the esophageal hiatus of diaphragm into the thorax.

The diaphragm develops from six embryonic segments. The largest section is transverse septum, which migrates from the cervical regfion. There are three places where viscera pass through the diaphragm. The venal caval hiatus, the aortic hiatus and oepshageal hiatus.

Traumatic hernias: Hernias caused by trauma usually lacks a peritoneal covering to hernial contents and hence have been called false hernias. False hernias are common in flank. These are exacerbated by hyperadrenocorticism and diabetes; and also ventral hernia during parturition.

Incisional hernias: It is serious postoperative complications of abdominal surgery; prolonged postoperative vomiting or coughing excited barking and severe obesity are the exciting causes.

Femoral hernias: Femoral hernias are characterized by protrusion of flat or

abdominal contents through a defect in the femoral canal. The femoral opening in the caudal abdominal wall is composed of two separate areas confined within the limit of the inguinal ligament and pelvis caudal lateral to the inguinal canal. The muscular lacuna contains the femoral nerve within the substance of ilio-psoasmuscle. The vascular lacunae containing lies craniomedial to the muscular lacuna and contains the femoral artery, veins and saphenous nerve. Each lacuna is separated by ilio-pecitneal arch composed of iliac and transverse hiatus. The transverse fascia also surrounds the femoral forming the funnel shaped femoral sheath. Herniation most likely occurs in a potential space. Caudomedial to femoral vessels known as femoral canal. Femoral hernias in man are primarily due to an anatomical weakness in the borders of the femoral canal. Hormonal metabolic or heredity causes may also play a role.

Anomalies of intestines

Segmental anomalies of intestines namely stenosis that is in complete occlusion of the lumen, atresia is the complete occlusion. The atresia may be a membranous, where simple membrane or diaphragm obstruction is there or it may be a cord atresia, where the blind ends of gut are joined by a cord of connective tissue or blind end atresia in which a segment of gut and possibly the corresponding mesentery is missing.

All these type of anomalies are produced by ischemia to a portion of intestine. As the intestine grows with the developing foetus, they form coiled loops which herniate into the umbilicus. In later stages of foetal development, the intestines withdrawn in anterior to posterior direction, from the umbilicus into the abdomen. During this phase any ischemia to intestines results in segmental anomaly. Even the palpation of the embryo result in pressure on the amniotic vesicle prior to 42 days of gestation.

The segmental anomalies of intestines are stenosis, atresia. Stenosis implies incomplete obstruction of the lumen; complete occlusion is referred to as atresia. Atresia coli are the most common segmental anomaly of the intestine in domestic animals. It is seen particularly in the spiral colon of Holstein calves and in the large and small colon of foals.

Atresia ilei is most prevalent in calves and rare in foals, lambs, piglets and pups. Atresia jejuni in Jersey cattle and atresia ilei in Swedish High land cattle are inherited lethal autosomal recessive traits. Animals fail to pass faeces after birth.

Atresia anii (imperforate anus) is the most common congenital defect of lower gastrointestinal tract. This is commonly seen in calves and pigs and is hereditary.

Short colon, probably the result of abnormal rotation of mid gut and failure to lengthen during foetal life, has been reported in several dogs and cats.

Hypoplasia of the small intestinal mucosa with short villi and sparse crypts has been reported in foals with failure of passive transfer of immunoglobulins.

Persistent Meckel's diverticulum is an anomaly of the lower smaller bowl, and is mainly in swine and horses. It is derived from the omphalo-mesentric duct which is the talk of the yolk sac. This duct is normally obliterated before the end of the first third of pregnancy. Rarely may it be retained in post natal life as a patent tube extending from the anterior mesenteric side of the intestine to the umbilicus. In horses, it is around 10 cm. in diameter and is associated with impaction.

Rectal prolapse is seen in swine, sheep, and cattle. It may occur in any animal which has prolonged episodes of tenesmus or straining only the mucosa or all layers, may be involved in the prolapse.

Intestinal obstruction involves the upper or middle small intestine. It may be due to segmental atresia or due to acquired stenosis due to pathological processes arising within the wall of the intestine. Foregin bodies of all kinds are commonly found such as strips of cloth or string or now day's plastic bags, which are undegradable, will find a way to digestive tract. In horses the obstruction is due to enteroliths

Enteroliths

Enteroliths are usually seen in the colon of horses. These stones consist of chemically magnesium ammonium phosphate, which are deposited concentrically around a central nucleus, a foreign body such as nail, wire, stone or particle of a food. They vary greatly in size and weigh as much as 10 kgs. They are usually smooth.

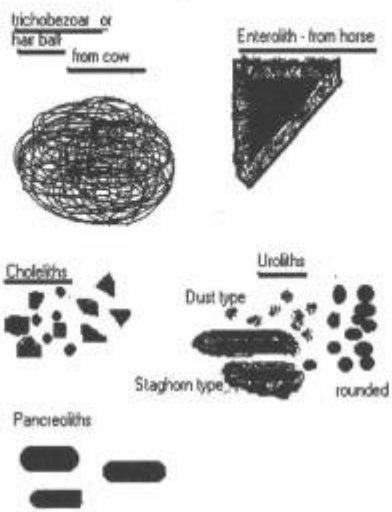


Fig. Showing various types of liths (stones) including enteroliths

Pathogenesis of enteroliths: When animals are faced on wheat or bran which are rich in magnesium phosphate, intestinal calculi can occur. Normally magnesium phosphate is dissolved by gastric juice and then absorbed in the intestines. On the other hand when excessive amounts are fed to an animal, and that too to one suffering from chronic catarrhal gastritis in which gastric juice is not secreted,

much of the magnesium phosphate reaches the intestine in an undissolved state. This combines with ammonia that is formed from the decomposition of protein to form triple phosphates. This triple phosphate crystallizesaround foreign bodies like a grain of sand, a piece of metal or undigested plant fiber.

The followings are the contributory factors, disturbances in the colloid protection of dissolved salts; change in the bacterial flora with altered fermentative conditions, sluggish intestinal movements.

Enteroliths may sometimes attain a large size and weigh as much as 10 kgs.

Enteroliths do not form in the small intestines because

1) The movement of food is too rapid, which does not permit deposition of salts and formation of calculi.
2) Bacterial decomposition of proteins to form ammonia does not takes place in the small intestines.

Phytobezoars: (Phyto: plant) (Bezoars: concretions) these are food balls. These arise from plant fibers and awns which are impregnated with triple phosphate and rolled into balls. These have a velvety surface, are light in weight and are brown in colour.

Trichobezoars (Piliconcretions): Hair Balls: Hair balls are found mostly in the rumen. This is due to the licking of hair kind consequent ingestion. The hair is rolled into balls during ruminal contractions. Mucous of rumen form a smooth coat over such balls.

The enteroliths, phytobezoars, and trichobezoars are usually of nonconsequence unless they obstruct the passage, when, sometimes, even rupture may occur. Cattle may regurgitate a food ball into the oesophagus which may be choked. Most often these concretions are found only at postmortem.

Enteritis

Enteritis is the term denoting inflammation of the whole of the intestinal tract. The inflammation of colon is called colitis that of caecum typhlitis and of rectum proctitis. Since enteritis occurs along with gastritis. Gastroenteritis is a frequent condition occurring in domestic animals. Causes are many and varied and they include bacteria, viruses, protozoa, rickettsia, helminthes, fungi, chemicals, disturbed metabolites in ruminants..Venous congestion as in portal hypertension and congestive cardiac failure, toxins of clostridia, coliforms, toxins of the fungi, mouldy feeds and avitaminosis are contributory.

Based on the nature of exudates and the changes produced in the intestinal tract, enteritis could be classified as catarrhal, hemorrhagic, fibrinous, suppurative and necrotic. The enteritis is depending on the duration of inflammation either as an acute one or chronic one. After birth no part of gastrointestinal tract is sterile.

Several hundred species of bacteria in habit the stomach and intestines. Bacterial populations are least in the stomach and upper small intestine of ruminants and carnivores, being limited by the acid gastric environment and peristalsis. The anaerobes and facultative anaerobes mainly *Escherichia coli*, increase to about 10^7/ gm of content in the lower small intestine, and total bacterial populations in excess of 10^{10} or 10^{11}/gm content are present in caecum and colon.

Prominent among bacteria are coliforms, lactobacillus, strict anaerobes, include bacteriodes, fusobacterium, clostridium, eubacterium, streptococci.

Normal flora acts as a barrier to colonisation by pathogens through several means. Secretions of proteins such colicins, production of acetic acid and butyric acid by the anaerobes are contributory in the pathogenesis. Host factors influencing gut flora include composition of diet, perisatalisis, Lysozyme, lactoferrin and gastric acidity.

The enteric microbial flora promotes the development of population of immune cells as well as inflammatory cells in the lamina propria by antigenic stimulation. *Escherichia coli* have the capacity to attach to the epithelium of small intestine by pilli, permitting colonisation. Production of secretory diarhoea is a characteristic feature with these strains.

Salmonella are entero toxic and also enteroinvasive. As a result of invasive nature it stimulates acute inflammation and cause extensive mucosal damage due to production of verotoxin. Severe mucosal damage causes heaemorrhages.

Mucosal invasion by Mycobacteria will produce granulomatous enteritis, lymphangitis and lymphadenitis.

Intestinal mucosa can be a site from embolic establishment of circulating bacteria and subsequent ulceration.

Parasitic diseases of ruminants (Fore stomachs)

Infection by nematodes, trematodes and cestodes

Gongylonema spp. occurs in the epithelium of rumen (buffaloes and cattle, sheep and goats). Flukes of family *paramphostomatida*e are found in cattle and sheep in India. These reddish, plump mulberry shaped flukes of 2 to 6 cms. stay in the rumen occasionally in the reticulum. When ingested metacercaria encyst on herbage give rise to immature flukes in the duodenum, such the duodenal mucosa and cause considerable damage leading to severe enteritis resulting in death of animals. The common flukes are *Paramphistomum cervi, Microbothrium, explanatum*). The last one is an adult fluke and is usually found in the bile ducts. Apart from the *Fischoderius spp. and Cotylophoron Cotylophoron* are also involved.

After 3 to 5 weeks, in the small intestine, the worms normally migrate forward, through the abomasum, to establish and mature in the reticulo-rumen. However

if massive infection occurs, growth in small intestine is retarded and flukes may resist for months in the duodenum, prolonging the course of disease.

Morbidity and mortality is considerable in the affected flocks.

Animals are depressed and in appetent. Fetid diarrhea develops usually within several weeks of infections and may contain immature flukes. Big ruminant side within 2 to 3 weeks, whereas small ruminants die within 5 days.

Postmortem findings consist of emaciated carcass, oedema of subcutaneous tissue, abomasal folds and mesentery and fluid in the body cavities. On opening intestines immature flukes penetrate deep intestinal wall is seen. Occasionally they will perforate the gut and found free in the abdominal cavity. Mucosal surface of duodenum is thickened, corrugated and covered with mucous.

In histological sections, larval paraamphistomes are found deep in the lamina parpria, ocassionaly in submucosa and sometimes in Brunner's glands. These will be found sucking mucosa into acetabulum with their suckers. Erosions or ulceration of mucosa and hyperplasia of mucosal glands with interglandular infiltration of mononuclear is the common feature.

Gastrointestinal helminthosis

These fall broadly into the category of trematodes, cestodes and nematodes.

Trematodes infections of the intestine of domestic animals are not common, except in sheep and goat where immature amphisomiasis is common.

Paraamphistomes infections are common in ruminants and cause significant intestinal disease. The adults of the *genera, paramphistomum, Cotylophoron, calicophoron, gastrothylax, Fischoderius* occur in the forestomachs of ruminants. Infection is most common in warm temperate to tropical countries. In the rumen, the reddish pear shaped adult flukes with their characteristic anterior and posterior suckers.

When ingested, metacercaria encysted on herbage give rise to immature flukes which inhabit duodenum, where massive infections may cause severe enteritis.

After 3 to 5 weeks in the small intestine, the worms normally migrate forward, through the abomasum to establish and mature in the reticulum and rumen.

Calves and lambs with intestinal paramphistomiasis are depressed and in apparent. Fetid diarhoea develops and faeces may contain immature flukes.

In sections, small **larval para-amphistomes** are found deep in the lamina propria, occasionally in the submucosa and sometimes in Brunner's glands. The disease is called as piti in India as immature amphisomiasis.

Coccidial enteritis

Sheep, goat, cattle, buffaloes suffer with Eimeria infections. These coccidia multiply

in intestines. It begins with the infection of cells, usually the intestinal mucosa, by sporozoites released from a sporocyst in the lumen of gut. One or more cycles of asexual division, schizogony or merogony follows and the merozoites produced infect other cells, forming another generation of meronts or transforming to sexual stages, gamonts. Gamonts subsequently develop into nonmotile female macrogamonts and motile male forms or micorgamonts. A non motile zygote is produced by the union of micro and macrogamonts from oocysts. Oocysts after the rupture of the cells, thrown into faeces. Members of genus Eimeria are homoxenous, sexual and asexual development taking place in a single host.

Coccidiosis in sheep and goats: At present, about a dozen species of coccidia are found in each of sheep and goat species. Eight species of coccidia present and these do not cross infect sheep and goat. Coccidiosis in these species is a disease of young animals. In sheep, giant schizonts of around 300 ì in diameter develop in cells deep in the lamina propria. Endogenous development of coccidium cycle is common. Terminal ileum is affected. Small second generation schizonts evolve, and infect other glands in the same area and these areas are subsequently become infected by gaematocytes.

Affected areas of gut are oedematous and thickened, and there may be focal congestion or heaemorrhages in the mucosa. Giant schizonts may be seen and even these can be seen though the serosa.

In sections schizonts and gamonts are in may or in most cell lining glands in affected areas. Neutrophils and macrophages many accumulate in response to merozoites released from ruptured giant schizonts.

Infected epithelial cells appear some what hypertrophied, with eosinophilic cytoplasm and prominent brush borders. Often these coccidia infected cells do not rapidly slough at postmortem in contrast other uninfected cells.

Why mass of infected cells apparently persist ironically in infected animals without clinical disease is not clear. However plaques and polyps may be the result of mitogenic stimuli from progamonts, the immature stages in cryptic epithelium, which appear to divide by binary fission, in synchrony with infected host cells.

In animal during the peak of infection, virtually all cells lining caecal and colonic glands in many areas are infected by small schizonts, gamonts or develop in oocysts. If destruction is wide spread, and the animal survives sufficiently long, their mucosa may ulcerate to the level of the muscular is mucosa, and begins to granulate. In areas where lining of patchy glands which have been relatively spared are lined with hyperpalstic epithelium, mainly in an attempt to regenerate the mucosa.

In sheep and goat, *Eimeria chritersnsi* has a developmental cycle which involves giant schizonts to nearly 300 m across in the endothelium of the lacteal villi in the middle small intestine. The more mature of these may detach and appear to lie

free in the lacteal, dilating the villi. Second generation schizogony and gametogony occur in the epithelial cells lining the crypts and villi, mainly in the small intestine 4 to 6 meters below the abomasum. Gamonts are usually below the host cell nucleus. In heavy infection in the crypts or villous unit is infected. There is an acute focal reaction around the schizonts that is ruptured. Diarhoea develops clinically affected intestine is congested and oedematous. Numerous pale white or yellow foci form a few millimeters to a cm. in diameter, often visible for most of serosa, are present as slightly raised plaques on the mucosa of small bowel. These foci are areas of intense infection and these may in focal cryptal and villous epithelium and is infected by gamonts and developing oocysts, and have been dubbed as oocysts patches. The faeces are rarely bloody.

Nodular polypoid structures, sometimes pedunculated, and about 0.3 to 1.5 cm. in diameter, are encountered in the small intestine of mucosa of sheep and goats. These masses comprise hypertrophic crypt villi units, in which every epithelial cells is infected by mainly gaematocytic stages of coccidia. Adjacent mucosa appears normal and uninfected. The term pseudoadenomatous has been used to describe these polypoid lesions. Plaques and polyps may be the result of mitogenic stimuli from progamonts, the immature stages in crypt epithelium which appear to divide by binary fission in synchrony with the infected host cell. Aspect to the microvillus surface of the enterocytes usually between villi in folds on the villous surface or occasionally in crypts of Lieberkuhn. Relatively resistant oval cysts are passed in the faeces, and transmission is by the oral-faecal route.

When the host parasite relationship has been disturbed disease sets in. In young dogs and cats, intermittent or chronic diarhoea, may persist for several months. The stool is soft, pale, mucoid and greasy. Poor hair coat is seen. Steatorrhoea, malabsorption of vitamins is seen.

Amoebiasis

Amoebiasis: *Entameoba histolytica* is the cause of Amoebiasis in humans, non-human primates and in dogs, cattle and cats. Infection in donkeys is sporadic, probably acquired by exposure to cysts in faeces from infected humans. Dog is a dead end host does not pose any public health hazard. Amoeba causes colitis. Number of factors including diet and immune status of the host, and virulence of the organisms influence the pathogenicity. Amoebae secrete several factors which are enterotoxic or cytotoxic and pathogenic strains are erythrophagocytic. Amoebae attract and lyses neutrophils which may exacerbate local tissue damage. They also release a factor which inhibits macrophage motility and generally they suppress macrophage functions.

Amoebiasis in dog is associated with diarhoea and dysentery. The disease seems more common or severe in animals with concomitant trichuriasis or ancylostomiasis infections.

Established ulcerative amoebic colitis has a flask shaped ulcer, the narrow zone

of neck passes through the mucosa, and the broad base is the submucosa. Amoebae may attain the deeper tissue via mucosal blood vessels or lymphatics. Amoebae may be present commonly in small clusters in necrotic debris or in adjacent viable tissue, frequently not involved in inflammatory reaction. Amoebae in tissue, often surrounded by clear halo, may be spherical or irregular, with extended pseudopodia and are a6 to 50 ì in diameter. The nucleus has a central dense karyosome and peripheral chromatin clumps. The cytoplasm may appear foamy can contain remnants of RBCs in phagolysosomes, and contain glycogen which makes cytoplasm PAS positive.

Giardiasis

Giardiasis species are flagellate protozoa which inhabit the small intestines of a wide range of vertebrates. It appears that three morphologically distinct groups exist, each with a relatively wide host range.

Giardia duodenale infection is common in humans. Giardia from humans is infective for wider range of mammals (dogs, cats, cattle, sheep, goats and horses). Giardia trophozoites are pyriform in outline, 10 to 20 ì long and 5 to 15 ì wide and 2 to 4 ì thick and convex on the dorsal surface. The concave ventral surface is modified by the presence of a disk, which functions in attachment. A pair of nuclei, two axonemes, two medial bodies and four pairs of flagella are present.

The organism applies their ventral contact with spine. This is a commensal but capable of opportunistic invasion of tissues injured by other disease. With invasion of anaerobic organisms, this produces necrotising lesions. In cattle and buffaloes mucoid diarhoea is a characteristic feature.

Eventration

Eventration is displacement of the portion of the gut usually the small intestine, outside the abdominal cavity. Acquired event rations, result from trauma, the bowel may protrude through lacerated vaginal fornix or through ruptured averted bladder.

The large colon of the horse comprises a loop of capacious bowel joined along its length by the short mesocolon and folded upon itself at the sternal, pelvic and diaphragmatic flexures. The loop is fixed only at its base, by the caecum, the transverse colon and the mesenteric root. Its volume and lack of attachment make the large colon prone to displacement or torsion.

Left dorsal displacement of colon, variously known as entrapment of the colon by nephro-splenic or phrenico-splenic ligament or by the suspensory ligament of spleen is also encountered as a cause of obstruction and colic in horses.

Herniation through natural foramina occurs mainly in horse. In right to left incarceration in the epiploic foramen, omental herniation occurs when a loop of intestine passes through a tear in a greater or lesser omentum. Mesenteric hernia

is due to passage of intestine through a tear in the mesentery. Pelvic hernia, sometimes referred to as gut tie occurs in young ruminants following castration.

Torsion is a twisting of intestines on its axis.

Volvulus is a twisting of the bowl on itself as occur when it passes through tear in the mesentery. These conditions seen in horse more frequently may also be met within other animals.

Causes: 1. Violent movements as in rolling and struggling, 2. Violent peristaltic movements, 3. Foreign bodies and enteroliths by their weight make the part heavy and aid in it swindling around other parts, 4.Accumulation of gas makes the part bulge and twist around other viscera.

Torsion occurs more often in the small intestines, which have long mesentery attachment. In the horse, the right colon is fixed by ligaments and so torsion occurs in the left and transverse colon. In the cattle torsion of the caecum is more common. The changes that occur in torsion are acute passive congestion leading to oedema, haemorrhage, gangrene, peritonitis and death.

Intussception is telescoping of a portion of intestines into another usually the anterior into the posterior, and occurs mainly in the jejunum and caecum in dogs and cattle. Along with the portion of intestines, its mesentery also is dragged along and so there is compression of thin walled veins resulting in acute passive hyperemia.

Grossly the affected part is dark red or bluish and swollen. Usually gangrene and peritonitis supervene terminating in death. In some stray cases the invaginated portion may be sloughed off, healing occurs by granulation tissue. Epithelium covers the scar. But at the site of scar, circular stenosis may form. Death in volvulus and other intestinal displacement results in acute anemia which may occur due to extensive heaemorrhages into the intestine and peritoneal cavity. Asphyxia and heart failure due to compression of lungs and heart by pressure on the diaphragm by excessive gas formation. Rupture of intestines and stomach leading to peritonitis and absorption of toxic products. Toxemia due to the absorption of toxins from decomposed food and bacterial growth.

Incarceration of the intestine is trapping of the intestine internally from pressures on its external surface. Incarceration occur due to adhesion of intestine to other abdominal organs, the loop of intestine may pass through the epiploic foramen of the Winslow, occasionally a persistent urachus may cause incarceration, similarly an adherent to the uterus may cause this condition. Similarly an adhesion to the uterus may cause this condition and when the bowl passes through a fissure of the mesentery, congenital or acquired incarceration may supervene.

Prolapse : Prolapse of the rectum the rectum protrudes through the anus. The causes are straining, irritation, abdominal pressure, diarhoea increased peristalsis

and constipation. Grossly the rectum is bright red in colour, will be found hanging through the anus. It may be oedematous and some becomes gangrenous. The changes are similar to those for incarcerated intestines. If not attended to early, the prolapsed rectum will be pecked by animals and predators and birds with injuries and haemorrhages.There is extensive swelling fecal matter cannot be voided. Ante mortem prolapse can be distinguished by postmortem prolapse in the latter there is absence of congestion.

Liver function tests

The liver is an organ of many diverse metabolic activities, and any assessment of its functional status dependent upon its ability to perform a specific metabolic function. A number of tests have been devised for the detection of alteration in liver function. All liver functions tests may be classified according to the type of hepatic function Liver function tests may be categorized as follows.

1. Tests dependent primarily on hepatic secretion and excretion of bile pigments, clearance of foreign substances.
2. Tests dependent upon specific biochemical functions, namely protein metabolism tests, carbohydrate metabolism tests and lipid metabolism attests.
3. Tests dependent upon the measurement of serum enzyme activity, namely transaminase and alkaline phosphatase.
4. Tests for bile pigments.

Serum bilirubin

The determination of total bilirubin and conjugated bilirubin (cholebilirubin) in serum could be determined by van den Bergh test. The test is used on the ability of bilirubin to couple with diazo reagent to form a characteristic red violet pigment. Since unconjugated bilirubin is insoluble in water and the diazo reagent is in an aqueous solution, the detection of unconjugated bilirubin requires the use of a substance in which both bilirubin requires the use of a substance in which both bilirubin and the Diaz reagents are mutually soluble that in alcohol. The addition alcohol is not required for the coupling of the conjugated bilirubin to the diazo reagent since they are both soluble in water. This constitutes the direct reaction. The accepted method for the van den Bergh test requires the addition alcohol to a mixture of a diazo reagent and serum in order to of measure of total bilirubin.

The total bilirubin values in cows are 0.31 mg/dl, in calf 0.70 mg/dl, in pig 0.20 mg/dl, in dog 9.10 mg/dl, and in horse 1.25mg/dl.Direct reacting bilirubin in cow is 0.18 mg/dl, in calf 0.40 mg/dl, in pig o.10 mg/dl, in horse 0.37 mg/dl an din dog 0.07 mg/dl. Urobilinogen is absent in urine in dogs in liver diseases, due to decreased bacterial action on bilirubin in the intestines. Only conjugated bilirubin complexes are detected in the urine, as the unconjugated bilirubin does not normally pass glomeruli filter. The concentration of the bile pigment

(unconjugated) in the urine is directly proportional to the degree of biliary obstruction whether Intrahepatic or extraphepatic.The BSP clearance test is a widely used index of hepatic function in domestic animals. When injected intravenously, the dye is taking up rapidly, concentrated by the liver, and excreted into the bile. The rate of BSP disappearance and the percentage of retention in the dog are independent of dosage between a 5 and 20 mg/kg of body weight. In dogs less than a 5% BSP retention at 30 minutes has been accepted as normal. Prolonged BSP retention in dogs has been in hepatic lipidosis with centrilobular necrosis, and in a variety of liver damage causes. Delayed BSP retention may also be observed in conditions that reduce hepatic blood flow. Such conditions include cardiac deocompensation, severe dehydration and shock. This test is also useful in horse. Hepatic disorders can be detected as in dogs. Even in cows the BSP clearance technique is sufficiently sensitive to detect the presence of hepatic necrosis or fibrosis in cattle.

Indocyanine green has also been recommended for use in the dog.

Liver elaborates 22 distinct proteins that will be present in plasma out of which albumin and globulins are important. Total serum proteins can be estimated by refract meter, Biuret method. Rapid screening tests like sodium sulfite concentration of 14, 16 and 18 g%, detecting less than 500 m, between 500 to 1000 mg and more than 1500 mg% /dl of immunoglobulins in serum.

Since the liver is the major site for production of coagulation factors, advanced liver disease may affect some coagulation test results. Prothrombin synthesis can be tested as liver produce this protein which is essential for clotting.

Alterations in serum enzyme activity due to malfunctioning of the liver occur as a result of three processes. An elevation of enzymes due to disruption of hepatic cells as a result of necrosis or as a consequence of altered membrane permeability. Included in this group are the enzymes alanine aminotrnasferase (SGOT), Asparate aminotrnasferase (SGPT) and lactic dehydrogenase.

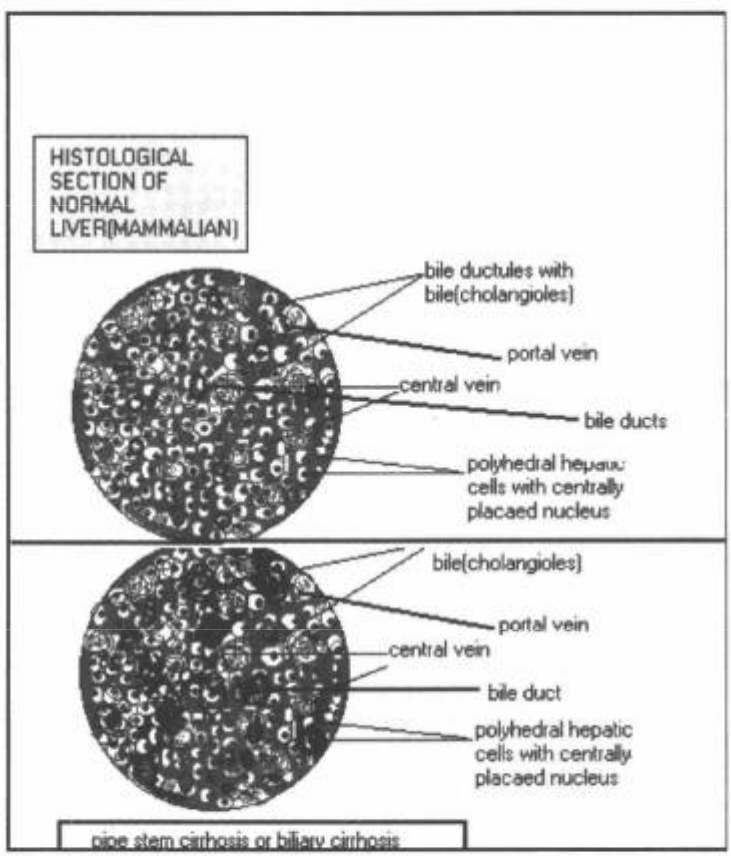
SGPT a test level are food in detecting liver increases in dog, cat and primates. SGOT levels are not a sure indication of liver damage, as this elevation of enzyme is seen in skeletal and cardiac muscle damage also.

Liver and Biliary System

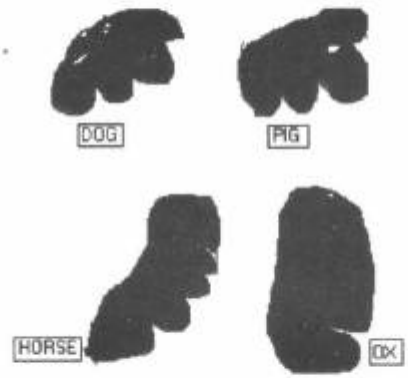
The metabolic function of the liver seems almost infinite in variety and complexity. The functions of liver are synthesis of carbohydrates, proteins and fats and inter-conversion of these substances. Thus livercells do involve in glycogenesis, protein synthesis and liponeogenesis. Liver cells are endowed with a variety of enzymes to do these metabolic activities. It secretes the bile and excretes variety of substances that are not needed for the body. It detoxifies several substances that are taken into the body starting from the chlorophyll to that of a paracetamol tablet or an antibiotic. As a general rule the liver is more important in detoxification

of those compounds which are non polar; more water soluble substances are more likely to be directly excreted by the kidneys.

The dynamics of the liver cell population in health and disease are interwoven with dynamics of its blood supply. Mammalian liver has a Double blood supply, one coming from the hepatic artery and the other supply is from the portal venous system. The portal vein, draining the splanchnic area, contributes most of the large volume of blood perusing the liver. Normally, approximately two thirds of hepatic blood flow is of portal in origin. Blood from the stomach and duodenum passes preferentially to the left lobe and that from the jejunum and ileum passes to the right lobes. The volume of portal blood flow is determined largely events in the splanchnic circulation. If the volume of hepatic blood is increased to a portion of liver, that portion will hypertrophy and reduction in the volume of hepatic flow leads to atrophy of deprived segments of liver.



View of caudal surface of liver of domestic animals



the median planes are indicated. The liver is assymetrical, less so in the dog, more so in the pig and horse and most in the ox, in which the bulk of the organ is displaced to the right. Note the absence of gall bladder from the horse liver. gall bladder indicated in green colour

The traditional functional subunit of liver is the hepatic lobule. It is hexagonal structure. The unit depends of liver on its afferent blood vessels and efferent bile ducts. The central of lobule is the central vein, branch of hepatic veins in turn of the branch of posterior vena cava. Periphery of the lobule is occupied by portal triads, consists of portal vein, bile duct and a hepatic artery. Sinusoidal spaces connect the portal vein to that of central vein. The cells that line the sinusoids constitute important components of the liver. Kupffer cells, representative of the monocyte macrophage system line all along the sinusoids. The hepatic cell, which is polyhedral I nature at one side is surrounded by sinusoidal space and the other side by the Biliary canaliculi. Kupffer cells are in the sinusoidal lumen, in contrast to the hepatic cells, line the space of Disse, secreting bile and other substances. The sinusoidal spaces are also lined by specialized endothelial cells with special transport functional arranged in a highly fenestrated sheet, thus giving sinusoidal plasma directs to the space of Disse. Thus the fluid in Disse space between the endothelium and the cell membrane of the heptocytes is equivalent to rather dilute plasma.

Liver is a parenchymatous organ and having mass. The mass is relatively fragile. When liver tissue has been damaged, the damaged tissue is intimate contact with the blood; this affects the haemostasis of the blood clotting cycle as well as is leasing large amounts of hepato-cellular debris into the circulation, the hepatic sinusoidal bed holds large quantities of blood and this volume is subject to large variations according to different conditions. As liver stores much of nutrients damage to liver resulting in malnourishment and starvation of the animal.

The term hepatic failure means loss of normal hepatic function as a result of either acute or chronic liver damage. However, all functions are not lost at the same time. The consequence of hepatic dysfunctional and failure include cholestatsis and jaundice hepatic encephalopathy, a variety of metabolic disturbances vascular and homodynamic changes and photosensitisation.

Developmental anomalies: Congenital cysts of liver occur in all species. Intrahepatic congenital cysts are probably derived from embryonic bile ducts. The main bile ducts and the interlobular branches in the portal triad are probably derived from the proximal portion of the hepatic analge. It also seems that many more embryonic choangioles are formed than are actually necessary. Accordingly cystic bile ducts may raise by failure of fusion of inter and intralobular portions of by failure of superfluous chalonagio cells to involve, or by establishment of the ducts stem with subsequent development of localised zones of atresia. The number, size and degree of lobulation of cysts are quite variable. The walls of connective tissue are lined by a flattened or cuboidal epithelium. The content is clear and serous. Serous cysts are occasionally found attached to the capsule on the diaphragmatic surface as seen in calves, lambs and foals. Congenital polycystic Biliary anomalies or of endodermal in origin.

Biliary atresia: Anomalies of the extra hepatic biliary system include absence of gall bladder and absence or atresia of one or more ducts. In carnivores, bile duct atresia may lead into only to jaundice, but also by vitamin D deficiency rickets due to inability to absorb fat soluble vitamins. Congenital atresia of biliary tract has been reported in lambs and calves in Australia.

Congenital vascular shunts: These include abnormal anastomotic connections between the hepatic artery and the portal veins, and the proto systemic shunts, which are between the portal vein and other systemic veins.

Displacement, torsions and rupture: Most displacements are caudal, so that the margins of the liver come to be much behind the coastal arch. Congenital or acquired displacements in ventral and diaphragmatic hernias are common. Usually only on lobe goes into the thorax with other viscera. Torsion of individuals obese, usually the left lateral occurs in swine and dogs, and the resultant infarction causes death through shock or hemorrhage. Rupture of liver occurs commonly as the result of trauma, because the organism fragile relative to its mess. Rupture of liver is very common in fowls especially in layers in fatty liver hemorrhagic syndrome, which may be of dietetic in origin. Liver rupture is often clinically noticed, since quite large ruptures may disturb liver functions. Moderate blood loss from capsular rupture is followed by first by rapid coagulation, then firbinolysis of the most of the free clot. In ruminants, infection with clostridia organisms leads to death of animals. Parasites that penetrate the capsule because numerous small hemorrhages but seldom lead to significant heaemorrhages. Liver rupture has also been noticed consequent to acute hepatitis, Amyloidosis, severe

congestion fatty degeneration and secondary neoplasms.

Telangectasis: Telangectasis is a cavernous ectasis of groups of sinusoids that occur in all species but is particularly common in cattle. Telangectasis occur throughout the liver as dark red areas, irregular in shape but well circumscribed and ranging from pinpoint to many centimeters in size. On cutting they appear as cavities from which the blood drains to reveal a delicate network of residual stroma and strands of atrophic hepato cytes. This is also common in older animals.

Peliosis hepatitis: This term has been used for a long time to designate focal blood filled spaces in the liver in humans, these lesions of unknown cause and was originally described in tuberculosis patients and as well with therapy of various steroids. This begins as a diffuse periportal sinusoidal dialtation and develops in cattle poisoned by plants of the Piemlea gaenus. Since these changes are found in these animals in spleen and in other organ with sinusoidal microcirculation it seems than the lesion may be adaptive to progressive dramatic increase into total blood volume. The liver may resemble a huge, blood filled sponge. The animal dies of a combination of haemodilution anemia and circulatory failure.

Passive venous congestion: This is due to an elevation of pressure in hepatic veins and venules relative to the pressure in portal venules. This may be due to congestive heart failure, or partial obstruction of large portal veins, or obstruction of posterior vena cava by abscess or neoplasm. In the early stages, the liver is swollen, dark and bloody on section. The congested liver elaborates lymph and these clots on the liver capsule, and the lobes may be stuck together by way of fibrin, which often blood tinged. Histologially there is uniform sinusoidal engorgement, with accompanying distension of fluid in veins, portal triads and capsule. Around the central veins and the liver lobule there is an extensive fibrosis, and this gives liver a nut Meg appearance and this is known as cardiac fibrosis.

Hepatocellular degenerations

Hydropic degeneration and cloudy swelling occur in number of diseases starting from mild intoxication to hypoxia. Any of the membranous compartments of the cytoplasm can be involved; thus hypoxia may produce lysosomal and mitochondrial vacuolation, whereas toxins that bind to endoplasmic reticulum may cause that organelle to take up large volumes of water. Hepato-cellular hydropic change has been seen in hyper-adrenocorticoidism or due to gluco-cortiocids administration. Grossly the liver is enlarged, pale tan and in long standing cases, may have scattered fatty hyperpalstic nodules. The cytoplasm of the cells contains space with poorly demarcated edges; the cells are swollen and the nucleus is often displaced in central position. The hydropic changes that are seen in gluco-cortiocids administration and with mild irritants are reversible. The changes seen with aflatoxin and other toxic chemicals could be regarded as earliest signs of necrosis.

Feather type of degeneration is seen in cases of cholestatsis. The cells are swollen and vacuolated and crossed by affine protoplasmic work that is brown with bile pigment.

Haemosiderin deposits are seldom sufficient to give gross discoloration. The pigment is detected microscopically as yellowish or brown crystal chiefly in the Kupffer cells. The ferric iron component of this pigment can be demonstrated by staining with Prussian blue.

Haemosiderosis should be distinguished from haematin, which is produced by the action of formic acid on haemoglobin following prolonged postmortem intervals, and is usually regarded as a histological artifact. Haematin is also an iron containing pigment but the iron is in the reduced ferrous state and does not stain with ferricyanide. Haematomas however be found in Kupffer cells and macrophages in small amounts.

The chemical relationship between some melanins, Liofuchsin and ceroid can be difficult to determine, and the latter two pigments tend to be disintinguished more by their origins and associations than by their structures. Ceroid is associated with peroxidation of fat deposits, and Liofuchsin is the term give to small, golden granular deposits derived from the lipid component of membrane of organelles. Liofuchsin accumulates in hepatocellular lysosomes and indicated senility or some other cause of reduced membrane repair.

Bile pigmentation may impart on olive green colour to the liver in diffuse obstructive biliary disease or intra-hepatic cholestatsis. Histologically conjugated bile pigments may distend bile canliculi,which when stand out microscopically as greenish-yellow stellate lakes between the Hepatocytes.

Haemochromatosis is rare in animals but has been observed in cattle exposed to high levels of iron in pasture and water and also in sheep. The liver is enlarged and brownish with a diffuse fine nodularity and the hepatic and adjacent lymph nodes are also darkened. Large amounts of iron are present in the hepatic parenchyma, the biliary epithelium and the cortex of lymphnodes, and lesser amounts are present in broad fibrous septa. The iron is stored predominantly in lysosomes.

Pigments of parasitic origin are seen particularly associated with flukes. In schistososmiasis the liver may be grayish in colour due to the accumulation of black pigment in Kupffer cells.

Fatty liver; the bulk of hepatocellular triglycerides are detained for the synthesis of low density lipoproteins which are secreted into the plasma and are more readily utilized by most tissues than are the fatty acids. Some of the lipid absorbed from the gut is presented directly to the liver as relatively water soluble, short chain fatty-acids after transfer to portal blood. Long chain fatty acids after absorption as triglycerides are cleaved by endothelial lipase into free fatty acids,

which may be either transported to the liver as albumin complexes or incorporated in adipocyte triglycerides.

The assembly of lipo-proteins takes place in the cisterna of the glandular endoplasmic reticulum, and any damage to the membrane of this structure or to the Golgi apparatus is likely to inhibit the rate of lipo-proteins synthesis. This sort of disturbances seems to be the basis of fatty liver in toxic liver injury. The amount of fat present in the earlier stages of degeneration is usually such more than can be appreciated histologically. The fat accumulates in small globules in the cytoplasm, and these show little tendency to fuse. The nucleus is not displaced, but maybe distorted. In the more severe and long standing degree of hepatic lipidosis most of the parenchyma cells are involved, probably as a result of fusion of globules, each cell usually contains a large globule, which alters the contour of the cell and displaces the nucleus. Fat is also present in the epithelium of the bile ducts. Fatty changes of this degree requires some time to develop and therefore implies a relatively mild cellular injury such as might result from nutritional and metabolic imbalances rather than from toxic or anoxic insult. With these severe degrees of degeneration the liver is moderately or greatly enlarged, of a uniform light yellow colour. The edges are rounded and the surface is smooth. Cut surface is uniform, greasy and without acinar pattern. Section of severe fatty liver floats in water or fixative.

Pigment accumulation: Variety of coloured substances is accumulated in the liver parenchyma. These are bile pigments, haemosiderin, melanin and the dark excreta seen in liver fluke infestations.

Nutritional diseases: Liver possesses the enzymes which cause biotransformation of a variety of endogenous or exogenous substances for elimination from the body. This process can also bioactivitate some substances to a more active form, thereby causing hepatic injury. During biotransformation lipid soluble compounds are made water soluble to facilitate their excretion into bile or urine. During phase I, polar groups are added to a compound or existing polar groups are exposed by oxidation, hydrolysis or reduction. In phase 2, the product of phase I is conjugated to glucoronate, sulfate or other groups. This water soluble form is then excreted in bile or urine.

Biotransformation: Algae contain preformed toxins, these are heapatotoxic, and Pyrrolizidine alkaloids are converted to pyrrole esters by the hepatic mixed function oxidase system. These react with cytosolic and nuclear constituents. Due to their anti-mitotic activity, which prevent cell division but not DNA synthesis? This is also seen with aflatoxicosis and nitrosamines.

Certain bacteria release deconjugated toxins, which are bioactivated in the liver.

Copper poisoning in sheep is the peculiar acidity of liver for copper, coupled with the very limited rate at which the species can excrete the element in the bile. The

mitotic rate increases, there is a hepatocellular necrosis. The liver is slightly soft and swollen, and deep orange. The bile is dark and granular and the spleen is engorged, dark and soft.

Drug induced hepato-toxicity, this causes massive hepatic necrosis. Sever peri acinar hepatic necrosis has been associated with the use of the anthelmenthetic mebendazole in dogs; hepatic failure appear within 2 weeks after exposure. Drug induced hepatic necrosis is due to severe allergic phenomenon, which are characterized by granulomatous infiltrates containing eosinophils.

Hepatic necrosis

Hepatocytes may be killed by toxic insult, activity of microorganisms or inflammatory cells or by nutritional deficiencies and severe metabolic disturbances including hypoxia. The Hepatocyte with its massive complement of membranous organelles is therefore highly vulnerable to free radical damage. These generated free radicals bring about destruction of lipoprotein membranes of organelles of hepatic cells and in turn death of Hepatocytes. Apoptosis is seen in a wide variety of hepatic cells ranging from toxicities to immunologically mediated inflammations. Apoptosis has become the accepted designation for the process whereby single cells are removed with minimal disturbance of the tissue of which they are a part. Apoptosis begins with sudden condensation of the cytoplasm and nucleus of cells that is alive and still metabolically active. Within short interval the cytoplasm is shredded away as a membrane bound fragments containing normal organelles and these fragments are rapidly engulfed by neighboring cells and by macrophages provided if they contain no nuclear material. The important distinctions of apoptosis from necrosis that at no stage do the apoptotic cells burst and release their content to the extracellular environment. There is no heaemorrhages or fibrosis or inflammatory response during apoptosis.

Focal necrosis is very common in post mortem specimens of liver. Focal necrosis is seen nearer to the portal areas. Focal necrosis occurs in many infections and parasitic larval migrations or bacteriaemic infections. The focal necrosis may be the outcome of a Kupffer cell reaction as seen in salmonellosis or of bacterial embolism as in Pasteurellosis.

Peri acinar necrosis or massive necrosis of liver cells is seen in variety of acute toxic, viral and bacterial infections. The necrosis may extend to the large portal areas. Midzonal necrosis, selective intoxications like CCL4 may produce mid zonal necrosis. Periportal necrosis is seen in a variety of toxins including mycotoxins. Massive necrosis is necrosis of considerable number of cells in a lobule. Para central necrosis is a peculiar type of necrosis which is wedge shaped occurring on one side of the central vein. Saw dust liver (Telangectasis); in well fed young cattle, at postmortem focal necrosis of the liver is common. The animals do not manifest any symptom while alive. The foci of necrosis may few or many and appear to the naked eye as saw is sprinkled on to the liver.

Histologically the lesions consist of hepatic cells which have undergone coagulative necrosis and infiltration of lymphocytes and neutrophils. These spots are of fibrotic type due to inflammatory reaction. Perhaps the irritant might have reached through the portal veins into the liver hence, the fibrotic appearnace in a sprinkled way.

Cirrhosis

Cirrhosis of liver is a condition of chronic non-suppurative hepatitis characterized by fibrosis, degeneration and hyperplasia of hepatic cells (regeneration). The stimulus for the fibroblast proliferation is due to some irritant, which is chronic and severe enough to produce degeneration and necrosis of the parenchyma.

The meaning of cirrhosis is actually derived from Latin term karyo means yellow colour. What is equally good is also equally bad proves with regenerating capacity of liver. Even if 2/3rd of liver has been destroyed it could be regenerated. But regeneration of liver is not perfect, because of the rapid proliferative response of fibrous tissue, which is cheaper which makes the hepatic cells throttled by encircling them, resulting in disorganization of hepatic structure.

The irritant may reach the liver through the portal veins, hepatic arteries and bile ducts. Based on the route of infection cirrhosis could be classified as portal or a nodular cirrhoissis, centrilobular cirrhosis, and that of Biliary types (monolobular or hypertrophic cirrhosis). Other forms of cirrhosis are pericellular cirrhosis, pigment cirrhosis, Glissonian cirrhosis and parasitic cirrhosis.

For a pathologist looking through the slides of cirrhosis of liver stained by either Haematoxyin and eosin or van Gieson stained sections gives a panoramic view, especially that of the latter stain where the mature collagen gives a pink or a red colour. Cirrhosis is the end stage phenomenon consequent to the insult to liver tissue. Because this is the result of several different hepatic diseases, it is termed as end stage liver disease. There is the total absence of normal lobular architecture. This may be due to loss of hepatic parenchyma, maybe duet to condensation reticulin network or formation of tracts of fibrous tissue.

1. Portal or nodular cirrhosis: Any agent that enters into the gut after absorption reached the liver. Among this toxic plants like *Crotalaria sagitalis* in horses, senecious family plants in horses, cattle and sheep, plants containing high selenium contents in horses, pitch in tar paper, repeated exposure to chloroform carbon tetrachloride and phosphorus.

Pathogenesis: When the irritant is conveyed via the portal vein, changes are noticeable first at the periphery of the lobules that is the area next to the portal tract. Due to the action of the irritant, degenerative changes are seen in the hepatica parenchyma; these degenerative changes may of hydropic, fatty and are severe enough to the death of the cells. This results in the stimulation of the connective tissue in the interlobular septa, infiltration of lymphocytes and macrophages. Among with the connective tissue new blood vessels are formed. These irregular

blood vessels anastomose with the network of portal veins as well as with the branches of hepatic artery. Thus anterio-venous shunts results and so ischemia of some parts of the liver occurs leading to further hepatic necrosis. Along with these changes, hyperplasia of the surviving cells takes place, replacing those that are destroyed. But the connective tissue which is young and cellular in the early stages becomes mature and fibrous, and then contrast, interfering with blood circulation. The decreased blood supply interferes with the proliferation of the hepatic cells and so hyperplasia does not progress further.

In the new fibrous tissue especially seen in the portal areas, new bile ducts are formed. These are not functional, lacking in outlets and so stasis of bile occurs.

As the fibrous tissue grows into the liver lobule, the hepatic cells become atrophied due to pressure and lack of nutrition. The central vein becomes narrowed due to the pressure of fibrous tissues stopping the out flow of blood, thereby rendering the irritant to stay longer in the liver. Growth of fibrous tissue into the lobule divides the parenchyma into the small islands of hepatic cells, known as pseudolobulation.

Varieties of ingested substances that reach intestine induce portal cirrhosis. Thus starting from drugs, alcohol in the case of human beings and a variety of toxic principles present in plants that are being ingested by the animals are responsible for causing portal cirrhosis. Among the plants are Crotalaria sagitalis, senecious plants.

The toxin, CCL4 incidentally which acts a drug for the control of liver fluke and certain other parasites, and as agent for dry cleaning in cleaning clothes on ingestion produces necrosis as well fibrosis of liver. Here membranous lipo-peroxidation occurs resulting in evolution of highly reactive radicals due to misocrosomal transformation.

Aflatoxin at the dose rate of 1 ppm And 3 ppm in rabbits the author with low does of observed, periportal bile duct proliferation, the hepatic cells in this zone showed hepatocytomeglay and karyomegaly. Fibrous tissue proliferation was evident when rabbits fed more than two weeks and the liver architecture has completely destroyed. After four weeks, the liver cells reorganize themselves and ductules or in the form of acinus. At around third week of feeding with 1 ppm, all lobules showed hydropic degeneration of the cytoplasm. At 3 ppm levels by second week hydropic degeneration of lobular parenchyma was evident and liver lobules showed regenerative nodules and intensive cholangiocellular proliferation. Diffuse fibrous tissue proliferation throughout the lobule is evident.

2. Alcoholic cirrhosis: Multinodular or Gin drinkers or Laennec's cirrhosis: Alcohol in liver is broken down mainly by oxidation of alcohol dehydrogenase in the cell sap. Ethanol ($CH_3.CH_2OH$) on Oxidation by Alcohol dehydrogenase forms $CH_3.CH.OH$ (Acetaldehyde). This results in the generation of hydrogen ions and

reflects an increase of NADH with a resultant change in the oxidation-reduction potential.

Some alcohol is also metabolized by smooth endoplasmic reticulum by microsomal ethanol oxidizing system. In chronic alcohol intake microsomal enzyme systems are increased at the cost of others. Hepatocyte fat metabolism is disturbed. Mitochondria are damaged by alcohol. As a result there is lipogenesis, accumulation of fatty acids, mainly because the NADH:NAD redox changes inhibit their oxidation via citric acid cycle and also damaged mitochondria also responsible for inhibiting oxidative pathways. There is increased L-glycerophsphates coming from alcohol, resulting in trapping of fatty acids in the hepatocytes, and these may be fed back to circulation resulting in hyperlipedemia. Among alcoholics 5 to 15% develop cirrhosis.

If the irritant enters the liver through the hepatic artery, changes of damage are first noticed in the tissues of portal canal and inter-lobular connective tissue. The feature is lymphocytic infiltration and proliferation of the connective tissue.

One feature in cirrhotic liver is the newly produced fibrous tissue acts an irritant, thus even the original irritant is removed or destroyed cirrhosis, progresses with more and more fibrous tissue formation until the condition terminates fatally.

Gross examination of the liver shows hard and firm liver. The surface is uneven and nodular. In early stages, the organ appears to be normal. But as the condition progresses due to atrophy of the parenchyma and contracting of fibrous tissue the liver may be reduced in size. The liver becomes yellow colour due to stasis of bile.

The architecture of the liver is lost, and the hyperplasia that is present gives nodularity to the organ (hob nail liver). The nodule lacks central veins and is usually greenish in colour due to stasis of bile, which cannot be excreted since the newly formed bile ducts lack an outlet. Stasis leads to deposition of bile pigment. On section, the liver cuts difficulty due to dense fibrous tissue proliferation. While cutting of peculiar grating sound can be heard. Histological examination reveals, increase in fibrous tissue in and around the lobules. In the portal areas presence of new bile ducts and mononuclear infiltration is seen. Pseudolobulation is evident. In some lobules central veins are absent or placed eccentrically.

The liver parenchyma shows various stages of degeneration, cloudy swelling, fatty degeneration and even frank necrosis. Regenerating nodules are seen and nodules containing these regenerating cells are plump, robust and stain more intensely.

Though the exact cause of cirrhosis is still obscure, it is thought that deficiency of vitamin B-complex and lipotropic factors, especially chronic alcoholic develop this. Lack of vitamin B complex and lipotropic factors results in high fatty liver, the fat globules literally occupying the cell cytoplasm pushing the nucleus to a

side. Along with this infiltration there is proliferation of the fibrous tissue which is infiltrated by chronic inflammatory cells. The bulging cells, pressing on the sinusoids produce ischemia resulting in necrosis of the parenchyma. New capillaries form and invade the lobule and connect the central vein with the portal vessels. The penetrating fibrous tissue divides the parenchyma into small lobules. Some surviving cells proliferate and form nodules. Contracting fibrous tissue makes the liver smaller and hence atrophic cirrhosis results.

3. Biliary cirrhosis (monolobular or hypertrophic cirrhosis)-parasitic cirrhosis: This type of cirrhosis is seen in animals due to cholangitis, due to pressure on bile ducts from tumors on the head of pancreas, presence of choleliths in the bile ducts, obstruction of Biliary passages by flukes like *Para-amphistomum explanatum, Fasciola gigantica* and *Fasciola hepatic* in bovines, *Fasciola hepatic* in sheep and goats, *Chlonorchis sinesis,* Chinese liver fluke in humans, *Ascarids* in pigs. Infestation of flukes is due to ingestion of metacercaria. Excystment occurs in the duodenum. The young flukes penetrate the intestinal wall and cross the peritoneal cavity attaching here and there to suck blood and penetrate the liver through its capsule; a few no doubt pass in the portal vessels or migrate up the bile duct. They wander in the liver for a month or more before settling down in the bile ducts to mature, which they do in 2 to 3 months.

Grossly the liver is enlarged and the surface is either smooth or finely granular. It is greenish in colour. The bile ducts are dilated and tortuous. They project on to the surface and one can recognize them grossly in cut sections as the thickened ones reasonably named as clay-pipe cirrhosis. The mature flukes are present in the larger bile ducts and cause cholangiohepatitis. The typical appearance of pipe stem to the ducts so that the connective tissue in addition to mineralisation largely surrounded by granulation tissue. These ducts make a grating noise when cut with the knife. The bile ducts contain dirty dark brown fluid of a mucinous or of tough consistency, formed from degenerated floccular material of bile, pus, desquamated cells and clumps of flukes and small masses of eggs which are dark brown. The liver lobes are indurated, atrophied and irregular.

The pathogenesis produced by *Dicrocoelium dendriticum* or lancet fluke are those of cholangiohepatitis and is less severe than that produced by Fasciola hepatica. The dilated cuts are darkened by the flukes and their eggs.

Opistoorhcid fluke are parasitise bile ducts of canines. These live in the liver for as long as the host lives. Chronic cholangiohepatitis and severe. Biliary fibrosis is seen.

Histologically the connective tissue encircles the individual lobules, hence is being called as monolobular cirrhosis. There is great infiltration of connective tissue with chronic inflammatory cells. Newly formed non functional bile ducts or cholangioles are also found. Hepatic cells show degenerative changes in the cytoplasm. Jaundice in the affected animal is common. Ascites is also commonly observed.

A variety of helminthes, cestodes, nematodes and trematodes and even in the degenerate arachnid Linguatula serrate produce inflammation of liver and bile ducts. The initial lesions produced by wandering larvae are traumatic. Sinus tunnels penetrate the parenchyma and often breach the capsule. In the tunnels there are free red blood corpuscles, degenerating Hepatocyte, and eosinophils as a reaction to parasitic invasion. Bordering the tunnel is a narrow zone of coagulation necrosis of parenchyma with infiltrating neutrophils at the margin. In due course necrotic area heals by extensive fibrous tissue invasion.

In sheep *Cysticercus tenuicollis,* produce interstitial hepatitis lesions. In pigs larvae *Ascaris suum* and *Stephanurus dentate* produce similar interstitial hepatitis. *Ascarids* produces distinctive interstitial hepatitis popularly called as milk spotted liver.

Migration tracks left by larval strongylus are common under the liver capsule in young horses and are probably related to the dense discrete spots that are found on the diaphragmatic surface of the liver. Larvae of Ascaris suum in calves also produce migrating tracks. These provoke granulomatous inflammation.

Stilesia hepatica and *Thysanosoma actinoides,* the fringed tape worm produce inflammation in bile ducts.

4. Pericellular cirrhosis: In this condition the fibrous tissue encircles each and every hepatic cell. This is due to extensive destruction of liver cells. This is seen especially in aflatoxicosis in cattle and buffaloes. This picture may be seen in the far advanced stages of multi and monolobular cirrhosis.

5. Pigment cirrhosis: This is seen when Haemochromatosis where excess iron has been stored in liver either due to enzyme deficiency or abnormal metabolism of iron controlling enzymes. The histological and gross appearance wherein portal triads are extensively surrounded by fibrous tissue and encircled by fibrous tissue. This is also maybe iatrogenic wherein excessive iron has been injected into the animals.

6. Glissonian cirrhosis: The cirrhotic areas are found under the Glisson's capsule of the liver, that is directly underneath the serosa of liver. Inflammation of Glisson's capsule as result of peritonitis or bacterial infection extends to the adjacent liver parenchyma. The fibrous tissue is seen under shorter distance beneath the capsular surface.

7. Cardiac or centrilobular or congestive cirrhosis. This is a nut meg liver or cardiac cirrhosis due to chronic venous congestion resulting from cardiac lesions as seen with vegetative endocarditis, right valvular stenosis or incompetence. The changes are due to anoxia and consequent degeneration of liver cells. The liver cell dies to anoxia and replaced by dense fibrous tissue. There is later tin in the liver and the typical nodularity of liver with shrunken appearance is common.

Effects of cirrhosis:

Ascites and congestion: Due to disturbances in portal circulation.

1. Ascites i) due to increased hydrostatic pressure in portal veins-flow of blood through liver is hindered due to compression and distortion of the portal and hepatic veins as well as sinusoids by the regenerating nodules. The effect is more in portal cirrhosis since the number of such nodules is greater in this condition than in the biliary type. I) Decreased colloid osmotic pressure since there is decreased production of plasma proteins, particularly albumin.iii) Hormones are not inactivated by damaged liver. In health the liver inactivates the mineralcortiocids of the adrenal and the anti diuretic factor of the posterior pituitary. But if these are not inactivated more of sodium chloride is reabsorbed and with it more of water is also reabsorbed, resulting in conservation of more fluid in the body and so ascites results.
2. Varicosity of esophageal veins -sometimes resulting in rupture and so haematemesis occurs.
3. Spleenomegaly
4. Gastroenteritis with resultant chronic venous congestion of abdominal viscera.
5. Caputus medusa in man that is dilatation of the cutaneous veins around the navel and is seen distinctly in white skinned people.
6. Loss of inactivation of hormones, and toxins. I) Estrogens normally are inactivated in the liver in the male. But in hepatic cirrhosis this does not occur and so gynecomastia and testicular atrophy occur. I) Toxins exogenous or endogenous are normally detoxified by the liver. If this is not done, the toxin affects the Brain, producing degenerative changes resulting in walking disease in horses.
7. Jaundice-due to pressure on the bile capillaries by the compressed cord cells that is by fibrous tissue. So there is obstructive jaundice resulting in digestive disturbances. Bleeding due to deficiency in production of prothrombin.
8. Anemia -since iron and B_{12} cannot be stored which are essential for the production of RBCs.
9. Vitamin A deficiency since vitamin A cannot be stored in the liver.

Cholangitis: Inflammation of bile ducts is called cholangitis. In liver fluke infection cholangitis is met with and cause irritation of the spines and the cuticles of the parasites as well as the toxins liberated by them. The lumen of bile ducts is dilated and its wall is thickened due to fibrous tissue proliferation around it. These ducts stand as thick cards. In some cases due to calcium deposition, these may be feeling hard also.

Grossly the mucosa is thickened and form papillary projection into the lumen. The lumen contains parasites. Histologically infiltrationof the all by inflammatory

cells like macrophages, lymphocytes and mucous is seen. The fibrous tissue that proliferates around the walls of the bile ducts may extend to a short distance into the parenchyma in the liver. Cut section of parasites cellular debris some mucous is even in the lumen. The fibrous tissue that proliferates around the walls of the bile duct may extend to a short distance into the parenchyma of the liver. Occlusion of bile ducts may give rise to obstructive jaundice.

Cholecystitis is the inflammation of the gallbladder. This is rare condition in animals. Infection is usually ascending and forms the duodenum. Stasis of bile by the presence of foreign bodies that is parasites concertinos or by pressure on the biliary duct by pancreas is other causes since the retained bile is itself irritant. *Escherichia coli* and *salmonella* are frequently found in the bile secretions.

Choleliths: stones in the gall bladder.

Cholilithiasis: A disease condition where presence of gall stones in the gall bladder. These are found mostly in cattle. The gall stones may be found in the gall bladder or bile ducts and is due to the presence of liver flukes. Bile ducts are more affected due to presence of frequency of parasitic involvement.

Gall stones are mixture of cholesterol, bilirubin, bile salts calcium and organic matrix. Grossly these may be dark brown or yellowish green in colour. There maybe numerous small stones or a few large ones in the gall bladder. The larger ones maybe faced due to rubbing against one another. The y is light and friable.

Almost all gall stones occur due to a result of Cholecystitis. The dead cells or bacteria may form the nuclei around which are deposited cholesterol, bile pigments and bile salts. Sand particles and food materials than may reach the gall bladder through the bile duct from the duodenum due to reverse peristalsis and form the nuclei of stones. Cholesterol is normally held in solution by loose combination with bile salts. This combination may be easily broken up. In Cholecystitis the bile salts are rapidly absorbed leaving the cholesterol which is precipitated.

Most of the stones in gall bladders are silent. In human beings these cause excruciating pain and as well jaundice is common when obstructions to bile ducts are there. Rupture of gall bladder also occurs in sometimes. In horses obstruction due to choleliths cause acute colic continuous pain and jaundice as that in humans. Larger stones cause ulceration mucosa.

Pancreas

The pancreas is tucked away with the duodenum in the upper abdomen where it is relatively well protected against trauma. The pancreas which lies parallel to and beneath the stomach is a very large compound gland with a structure almost identical to that of salivary glands. Digestive enzymes are secreted by the acini, and large volumes of sodium bicarbonate solution are secreted by the small ductules leading from the acini. The combined product then flows through a long

pancreatic duct that usually joints the hepatic duct immediately before it empties into the duodenum through the sphincter which protects the regurgitation of food from duodenum into the pancreatic duct. Pancreatic juice is secreted mainly in response to the presence of chime (digested food) in the upper portion of the small intestine, and the characteristics for the pancreatic juice are determined to a great extent by the types of food in the chime.

Pancreatic juice contains enzymes for digesting all three major types for food viz., proteins, carbohydrates and fats. It also contains large quantities of bicarbonate ions which play an important to in neutralizing the acid chime emptied by the stomach into the duodenum. The proteolytic enzymes are trypsin, chymotrypsin carboxypeptidases, ribonuclease and deoxyribonuclease. By far the most abundant of these is trypsin. The first three split whole and partially digested proteins into small peptides or amino acids, while the nuclease split the two types of nucleic acids RNA and DNA. The digestive enzyme for carbohydrates is pancreatic amylase. This hydrolyses starches, glycogen and other carbohydrates except cellulose to form disaccharides.

The main enzyme for fat digesting is pancreatic lipase, which is capable of hydrolyzing netural fat into glycerol and fatty acids and cholesterol esterase, which causes hydrolysis of cholesterol ester. The proteolytic enzymes when synthesized by the pancreatic cells are in the inactive form trypsinogen, Chymotrypsinogen and procarboxypolypeptidase, which are all enzymatically inactive. These become activated only after they are secreted into the intestinal tract.Trypsinogen is activated by an enzyme called enterokinase which is secreted by the intestinal mucosa when chime comes in contact with the mucosa. Also trypsinogen be activated to trypsin that has been already been formed. Chymotrypsinogen is also activated by trypsin to form chymotrypsin, and procarboxypeptidase is activated in a similar manner. The pancreas in addition to its digestive functions secretes two important hormones insulin and glucagons.

The enzymes of the pancreatic juice are secreted entirely by the acini of the pancreatic glands. On the other hand two other important components of pancreatic juice, water and bicarbonate ion are secreted mainly by epithelial cells of the small ductules leading from the acini.

Pancreatic secretion like gastric secretion is regulated by both nervous and hormonal mechanism. When the cephalic and gastric phase of stomach secretion occur, parasympathetic impulses are simultaneously transmitted along the vagus nerves to the pancreas, resulting in acetyl choline release followed by secretion of moderate amounts of enzymes into the pancreatic acini. However, little secretion flows through the pancreatic ducts to the intestine because only small amounts of water and electrolytes are secreted along with the enzymes. Therefore most of the enzymes are temporarily stored in the acini.

After chime enters the small intestine, pancreatic secretion becomes copious, mainly in response to the hormones secretion. In addition a second hormone cholecystokinin causes greatly increased secretion of enzymes.

The pancreas develops from two primordial out pouching, dorsal and ventral from the endodermal lining of that portion of the embryonic gut destined to become the duodenum. The ventral diverticulum's arises in relation to or from the primitive hepatic diverticulum. As a result of unequal growth of duodenal wall the hepatic and ventral pancreatic stem cells are rotated so that the ventral and dorsal stem cells are brought into apposition and fuse. As the ventral stem cells of origin grows in the surrounding mesenchyme, a duct forms and arborises under the inductive influence of the mesenchyme, and acinar cells differentiate from this ductal epithelium very early in organogenesis. The ventral stem cells are destined to become the right lobe of the definitive pancreas, and the dorsal analge, to become the left lobe. The duct system of the two pancreatic anlagen also fuses to produce an anastomotic network. There are differences between and within species as to which of the embryonic ducts is predominant in the developed pancreas. The accessory pancreatic duct, derived from the dorsal analgen, does not persist in small ruminants and in the majority of the cats; it is the major duct in the dog, the lesser duct in the horse, and the only duct in the pig and ox. The pancreatic duct, derived from the ventral analge, is the only duct in small ruminants and most cats; it is the main duct in horse, and is the lesser duct, and occasionally absent in the dog.

The islet cells are also derived from larger ducts. The relative contribution of dorsal and ventral duct stem cell to the distribution of islets in the organ is not known. The differentiation of islet cells begins even earlier than that of acinar cells in the developing embryo. Different functional types of islet cells may have different origin.

Islet cells of human pancreas can be classified as A, B, D, F and G. A(Alfa- cell) secretes glucagons; β (beta- cell) secretes insulin; δ (delta-cell) secretes somatostatin; F-cell secretes pancreatic polypeptide, G-cell secretes gastrin. The alpha cells, which produce glucagons, are typically located at the periphery of islets and constitute about 15% of cells in the islets in which they are present; they are not however uniformly distributed. The beta cells, which produce insulin, are present in all islets; they are distributed throughout the islet, composing about 70% of the cell population.

The delta (α) cells are also present in all islets in low numbers, there are two subtypes, one of which produces somatostatin, and the other produces vasoactive intestinal polypeptide. Gamma (γ) cells, which produce pancreatic polypeptide, and the enterochromaffin cells, which produce serotonin, are sparsely and variably distributed. The four main types of cells are β, δ, γ and PP (pancreatic polypeptide). The % of cells in the pancreas is 68%, 20%, 10% and 2 % respectively. The pancreatic

polypeptides that exerts a number of gastrointestinal effects, namely, stimulation of secretion of gastric and intestinal enzymes and inhibition of intestinal motility.

Anomalies of the pancreas: Variation of the disposition of ducts are common in dogs. Accessory or ectopic portion of the pancreas is observed in dogs. In cats, pancreatic bladders which resemble gall bladders and which are formed by dilatation of ducts are recorded. Cystic pancreatic ducts may occur with polycystic kidneys and cystic bile ducts in various species.

Hypoplasia of pancreas is seen in dogs and claves: It is in the development of acinar tissue, the islet cells are qualitatively and quantitatively are normal. Clinically steatorrhea and diarrhea reobserved. These become emaciated. At postmortem these dogs are pot bellied and intestinal veins are congested and the intestinal lumen contains bulky fatty food. Aplasia of islets causing diabetes had been reported in dogs.

Pancreatic lithiasis: The calculi consisting mainly of calcium carbonate and calcium phospahtes.The calculi are associated with inflammation such as by flukes. The calculi are never large, but they may be numerous like sand grains.

Inflammation of the pancreas

Pancreatitis; acute hemorrhagic pancreatitis is characterized by centrilobular and peri ductal necrosis. This is humans is due to Biliary calculi or alcohol abuse. Acute interstitial pancreatitis is common in systemic toxoplasmosis, especially in cats. In cattle in foot and mouth disease infections and in poultry in variety of diseases like avian encephalomyelitis, in Marek's disease and infectious hepatitis infections.

Chronic interstitial pancreatitis is seen consequent parasitic invasion and bacterial inflammation, larvae of strongylus in equines. In chronic interstitial pancreatitis the organ may be reduced in size or enlarged. In horses it is enlarged and replaced by fibrous tissue. In cats the pancreas is usually reduced in size, firm, gray and irregular. Clear retention cysts are visible. Histologically the ducts contain catarrhal exudates and are surrounded by a fibrous tissue.

Ascarid may invade the pancreatic duct from the intestine in swine and dogs. A variety of trematodes including Dicrocoelium dendriticum, Opisthoorchis felines, Opisthoorchis sinesis occur in pancreatic ducts. Eurytrema pancreatiucm of ruminants is probably the most importantspecies as it is common in parts of Asia.

The essential lesions are necrosis of pancreas by its own enzymes. The proteolytic enzymes liberated by the pancreas are involved in the pathogenesis of lesions. The enzymes escaping out of the pancreatic tissue digest the surrounding peripancreatic fat and the pancreatic parenchyma subsequently. The fats are hydrolyzed with liberation of fatty acids, which form calcium soaps in the tissues round about the pancreas. Entering lymph channels the lipase may produce fat necrosis in different and distant organs, even as far as anterior mediastinal region.

Grossly in fatal cases there is small quantity of fluid in the abdominal cavity. Heaemorrhages may be present in the omentum. In the mesentery and around the pancreas, whitish areas or nodules of fat necrosis with inflammatory zones surrounding them are found. The pancreas is swollen and soft, yellowish or slightly hemorrhagic. The lesions may be wide spread or localised. Encapsulation occurs for limited lesions. On section yellowsh soft pus like areas of necrosis may be visible.

Histologically necrosis of the parenchymatous cells and fat, edematous swelling, infiltration of inflammatory cells, heaemorrhages and thrombosis of vessels are observed.

Death in acute cases with severe abdominal pain and cardiovascular collapse in shock. Chronic inflammation may result if episodes are repeated and chronic fibro sign pancreatitis results with atrophy of organ. Steatorrhea occurs due to loss of pancreatic juice. In this condition the faeces is fatty and foul smelling.

Neoplasia of pancreas: Nodular hyperplasia of pancreas is common finding in older dogs, cats and cattle. The cells may appear as enlarged counter parts of normal exocrine cells with bulky, brightly acidophilic cytoplasm or they may of indifferent character, producing a low cuboidal lining for glandular spaces or they may form small indifferent clusters without a lumen.

Adenomas of acinar and ductules origin, when distinguished from nodular hyperpalstic lesions are extremely rare. Adenocaricnomas occur with some frequency in dogs and less often in cats.

Endocrine disorders

Necrosis of the islets occurs in acute pancreatic necrosis. Their progressive destruction, along with the acinar tissue, is a common cause of diabetes mellitus in dogs. Atrophy of islets occurs as a result of fibrosis in chronic interstitial pancreatitis, but because the islet tissue is more resistant to atrophy of this cause then is the acinar tissue, diabetes mellitus is seldom a complication of pancreatitis. Amyloidosis of the islets is regularly associated with diabetes in cats. Number of viruses is known to replicate in the pancreas but with the exception of the diabetes mellitus, which may be seen in chronic foot and mouth disease of a cattle.

Diabetes mellitus is due to inadequate insulin action. The inadequacy of action may be due to deficient production of insulin, or to failure of insulin as effectors hormone in peripheral tissue or to antagonism other tissues. Diabetes mellitus is therefore not to a single disease but a syndrome in which all cases sharing some common metabolic, clinical and pathologic features.

Diabetes mellitus

Diabetes mellitus is a chronic disorder of carbohydrate, fat and protein metabolism. A defective or deficient insulin excretory response, which translates

into impaired carbohydrate (glucose) use, is a characteristic feature of diabetes mellitus, as is the resultant hyperglycemia. About 3% of world population and approximately 100 million people suffer from diabetes. It may occasionally arise secondarily from any disease causing extensive destruction of pancreatic islets, including pancreatitis, tumors, certain drugs, and iron over load (Haemochromatosis), and certain chemical like alloxan administration, certain acquired or genetic endocrinopathy and surgical excision.

The most common and important forms of diabetes mellitus arises form primary disorders of the islet cell insulin signaling system. These can be divided into two common variants (types I and II) thatdiffer in their patterns of inheritance, insulin response, and origins and less common specific genetic defect of β-cell function.

1) Type I diabetes called insulin dependent diabetes mellitus, juvenile onset and forms around 10% of primary diabetes. This is due to decreased output of insulin from the islets, which in turn is the result of depleted number of β-cells. Alloxan and streptozotocin intoxication destroys β- cell. Immune mediated destruction is common in human beings. Presumably susceptible individuals are exposed to a foreign antigen structurally similar to a component of β- cell cytoplasm and which provokes a cell mediated immune response. Auto-antibody is also produced, but it is doubtful whether they contribute to the cellular injury. Virus infections of pancreas are also contributory. Interleukin-I inhibits release of insulin from islet cells.

2) Type II diabetes – non-insulin dependent diabetes mellitus, adult onset diabetes. Genetic influences are important. Other constitutional factors such as obesity, exercise, and diet are important. Here the levels of insulin in the pancreas are about normal, but release of insulin from β- cells in response to glucose load is impaired, or the released insulin may not be consumed in peripheral tissues. Peripheral insulin resistance may be due to deficient insulin receptors or intracellular mediators of insulin action. The hyperglycemia and glucose intolerance may be in these cases be accompanied by levels of plasma insulin which are above normal. Abnormal control of islet secretion appears to be central to the development of non-insulin dependent diabetes in desert rodents. It is possible that the observed degranulation and degeneration of β- cells represents exhaustion atrophy.

3) type III- maturity onset diabetes of young, genetic defects of β-cell function (less than 5%) is manifested by hyperglycemia and transmitted as an autosomal dominant trait.

Diabetes results in long term complications in blood vessels, kidneys, eyes and nerves.

Pituitary tumors as a source of unregulated production of growth hormone cause diabetes in dog's, cats and horses. The adenomas in dogs and cats are of acidophil cells. In horses diabetes has been associated with the acidophil cell tumors of the

anterior lobe and with adenomas of pars intermedia. Insulin-resistant diabetes is the most consistent expression of hyperadrenocorticism in cats and is common also in dogs, in which it may be consequence of exogenous gluco-cortiocids administration.

Gross lesions in dogs: The lesions of diabetes mellitus in dogs and cats are comparable. Apart from emaciation, and possibly dehydration, the principle lesions at autopsy are yellow fatty liver. The pancreas may appear normal or reveal the lesions of fibrosis. Lipemia is evident as milkiness of the serum.

Cataract formation is early common complications of diabetes in the dog and it may the presenting signs. Cataracts do not occur in cats. Suggesting that the lens metabolism differs from that in dogs. Glucose readily enters the lens form aqueous humor. Persistence elevation of glucose saturates the normal anaerobic glycolytic pathway the excess glucose then being converted by the activity of aldolase reductase to sorbitol and fructose. The latter to sacchrides, cannot diffuse freely through the lens capsule. They act osmotically, causing influx of water which leads to swelling and degeneration of the lens fibers.

The biochemical mechanisms leading to cataract may also operate in peripheral nerves. Peripheral and autonomic nerve neuropathies are common and important in diabetic humans, but they are rarely reported in animals. The changes are a mixture of degeneration and regeneration distally affecting motor and sensory nerves. The neuropathy is reversible if blood sugar levels are controlled.

Action of insulin

Insulin is an anabolic hormone with direct effects on carbohydrate, protein and fat metabolism. This is produced by the β-cells of islets of Langerhans. It is a protein having a molecular weight of 6000. It has 51 amino acids arranged in two chains and these contain 17 different amino acids.

Glucose is the primary stimulus for insulin release from islet cells in humans. It promotes the uptake of cells of glucose to form intracellular glycogen; uptake and utilization by peripheral tissues; it directs amino acids to protein synthesis instead of to gluconenogenesis; and it promotes the uptake of fatty acids by adipose tissue to form storage triglycerides. Inadequate insulin action therefore leads to a general catabolic state. There is increased liponeogenesis from glycogen and protein leading to hyperglycemia; protein synthesis is reduced leading to wasting of tissues; and hyperlipedemia results for increased lioplysis and is diminished uptake of free fatty acids in adipose tissue. Hyperglycemia increases the filtered load of glucose in primary urine to levels in excess of the tubular transport mechanism, leading in turn to Glycosuria, osmotic diuresis, and thirst. The excess of fatty acids presented to the liver is metabolized via acetyl co-A, in the absence of glucose, to form the ketosis. The ketoacids, acetoaceic and β-hydroxy butyric acid and acetone dissociate to produce ketoacids.

Thus insulin has the following actions. Helps in storage of glycogen in the liver, facilitates the entry of hexose's across the cell membrane into the cells especially muscle cells; stimulates hexokinase for formation of hexose-6-phophate, and inhibition of activity of hepatic glucose-6-phohpatase and thus preventing over-production of glucose.

The complex of metabolic disturbances if uncontrolled by therapy or unless partially suppressed by residual insulin action, leads to hyerposmolarity, profound dehydration, acidosis, and other electrolyte disturbances, which results neuralgic derangements and coma.

Diabetes mellitus is not a disease of sudden onset or of all none expression. The normal pancreas contains a substantial reserve of β -cells and insulin producing capacity, which may have to be reduced to 20% of normal before the catabolic processes to become dominant. The anabolic effects of insulin are exerted on many tissues and through numerous metabolic steps, totally all of which are deranged equally or simultaneously as insulin effect declines. Reduced glucose tolerance is a feature that is early and common to all types of diabetes mellitus.

The immune destruction of cells in human's proceeds slowly and years may lapse between the triggering event and the onset of clinical diabetes. During the progress, some islets will have lost all beta (α) cells, some will have infiltrate of lymphocytes with a few monocytes, and some will be normal. Ultimately all beta (β) cells are lost. The inflammatory infiltrates disappear.

Thus to summaries, diabetes mellitus occur in the following conditions.

Insulin may not be adequately secreted due to necrosis of pancreas. The causes for this necrosis have already been described.

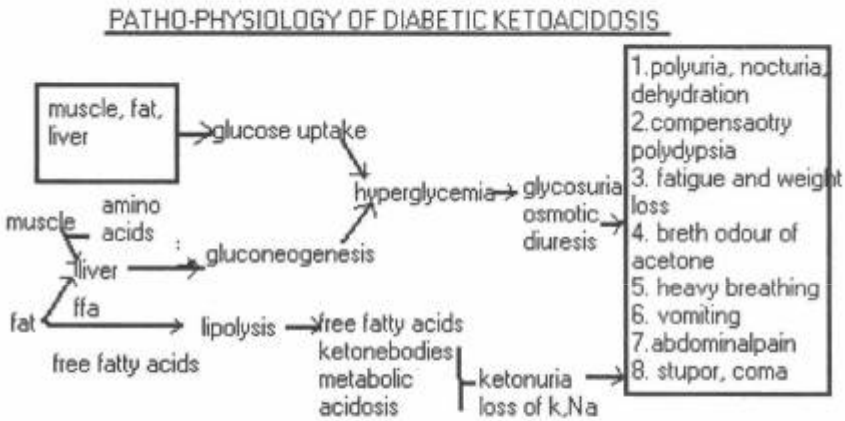
Insulin may not be liberated into the circulating though synthesized by the β cells. Cause is unknown and it has already been discussed.

Diminished production of insulin due to work exhaustion. This occurs when insulin antagonists act for a long time. Under this category most causes like insulinase a proteolytic enzyme which destroys insulin; glucagons and epinephrine production which are anti-insulin by virtue of their capacity to stimulate hepatic phosphorylases and produce glycogenolysis and hyperglycemia; increased liberation of growth hormone. Growth hormone antagonizes the effect of insulin on hexokinase, the ability of insulin to transport glucose across the cell membrane, by stimulating insulinase, by probably stimulating the release of glucagons; thyroxin release creates diabetic condition due to increase in the metabolic rate and liponeogenesis; excess adrenal cortical hormone increase also creates diabetes mellitus due to antagonistic action of gluconenogenesis and thus supporting the action of growth hormone. These antagnaonistic acts first by stimulating islets to secrete insulin as a result these become hyperplasic and release excess of insulin to arrest the hyperglycemia and in times the cells are exhausted and atrophied

leading to chronic diabetes on set. Unless a cure or some preventive measures are found for diabetes, this number will continue to increase in human population for the following reasons.

1. The population grows and becomes older
2. The life expectancy of the treated diabetetic is steadily increasing
3. Since more diabetics live on enough to have children an increasing number of children with inherit the diabetic genes and
4. Obesity which appears to precipitate diabetes among those predisposed to it is also on the rise thus allowing more potential diabetics to emerge.

Pathophysiology of Diabetic ketoacids



The following changes in the metabolism of carbohydrates take place in insulin deficiency. Though carbohydrates transported in the form of glucose it should be first converted into glycogen in the muscle cells before it can be metabolized to CO_2 and water. For this therefore glucose has to be transported across the cell membrane, to enter into the ells.

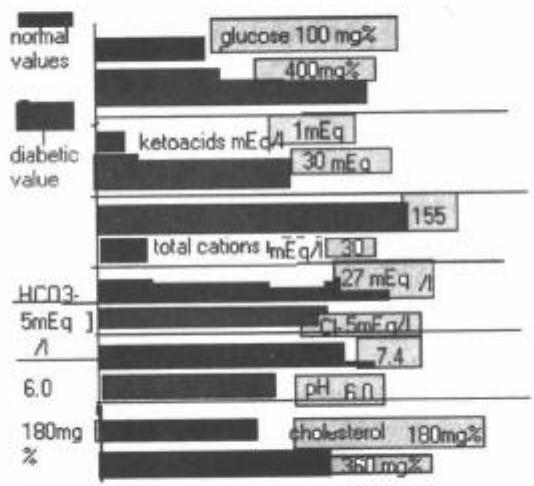
In the absence of insulin, normal quantities of glucose molecule are unable to move across the cell membrane and so it is not utilized and hence blood glucose level rises results in hyperglycemia. When this is above the renal threshed hold is 160 to 180 mg/1oo ml of blood, renal tubules is unable to completely reabsorb the glucose from the glomeruli filtrate and so glycosuria results. Now because of glucose is there in urine its osmotic pressure rises and this prevents the reabsorption of the water by the tubules and so polyuria and also results giving rise to increase thirst, polydypsia and dehydration. Glycogen stores of the liver are depleted due to glycolysis. So sufficient amounts of pyruvic acid and oxaloacetic acids are not formed to combine with active acetate formed from the fats. So this active acetate accumulates, condenses and forms Ketone bodies, which in excess

produce ketonuria and ketonuria. Being acidic the Ketone bodies neutralize the alkali reserve resulting in acidosis which terminates in air hunger and coma.

Since tissue are unable to utilize glucose except nerve cells and RBCs which do not require insulin for glucose utilization, catabolism of proteins and fats take places as source of energy. Since fat of fat depot has to move into liver for phosphorylation without which it cannot be utilized in the tissue fatty infiltration of liver occurs. Ketone bodies are therefore formed in excess due to catabolism excess fat and so ketonemia occurs. Normally small quantities of Ketone bodies are produced but these are metabolized in the body. So ketonuria gives rise to ketonuria. The breath and urine have the characteristic sweet odor. The ketoacids interact with sodium and potassium with resultant loss of these bases and also these bases are lost in the urine and acidosis develops. Acidosis, dehydration and ketonuria give rise to coma.

Proteins catalyzed to amino acid form glucose that is gluconenogenesis and fatty acids are formed. Glucose cannot be utilized and so is lost in the urine. Hence body weight decreases. Excess of amino acids are diminished in the liver and so there is elevation in blood and urine. Blood glucose levels as high as 400 to 1200mg/ 100 ml of blood are observed. Blood non-proteinnitrogen rises. With the depletion of carbohydrates, fats and proteins, body loses weight in spite of consuming considerable quantities of food.

Ketone bodies could be detected by Rothera's test where in urine is saturated with ammonium sulfate. For this urine sodium nitroprusside 1% solution and few drops of ammonia are added. Result is permanganate color to he urine. The level of aceto-acetic acid and β-hydroxy butyric acid are from 1 mEQ/litre to mEQ/litre.



chnages in blood constituterits in diabetic coma, showing normal values ■ and diabetetic ■

Hyperinsulinism: This can occur in dogs with excess of insulin injections or increased production of insulin by tumor of beta cells. In this condition, glucose is removed from the blood by glucose oxidation by insulin sensitive tissues, deposition of glycogen in the liver and by lipogenesis resulting in hypoglycemia. The nervous system which depends primarily on the glucose for energy suffers and its dysfunction is manifested by inco-ordination, dizziness, muscular weakness, tremors, loss of consciousness and convulsions.

Moderate hypoglycemia activates the sympathetic nervous system and so epinephrine is released. This brings about glycogenolysis in liver. Similarly glucagons is released which also causes glycogenolysis in the liver. Hypoglycemia also stimulates the release of adrenocorticotrophic hormone which in turn gluconenogenesis and suppressing the peripheral utilization of glucose.

Glucagon: this is polypeptide hormone secreted by α-cells of the islets and contains 29 amino acids in a single chain. Its function is quite opposite of insulin, namely to produce glycogenolysis of liver glycogen. The release of glucagon is brought about by hypoglycemia.

Glucagon action is to increase the activity of liver dephosphorylase kinase which activates phosphorylases and this causes glycogenolysis leading to elevation of blood sugar level. This activity is similar to that of epinephrine. But Glucagon does not cause glycogenolysis of muscle glycogen since it has no effect on muscle phosphorylases, while epinephrine acts both on liver and muscle phosphorylases.

Diseases of peritoneum

Ascites or hydro peritoneum is oedema of the peritoneum and is common in dogs and cats but may also be encountered in sheep and cattle.

Causes: Portal obstruction, due to hepatic lesions, cirrhosis, hydatidiosis, fasciolosis, neoplasms and secondary metastatic growths and pressure upon the vein by neoplasms abscesses and enlarged lymphnodes. General chronic venous congestion with resultant cardiac valvular disease or pulmonary lesions. Urinary obstruction male cattle and sheep with or without rupture of bladder. Hypoproteinemia consequent to gastrointestinal trichstrongyloid and Johne's disease in sheep and cattle brings about protein loss and consequent ascites. Variety of wasting disease like anemia and starvation in which general oedema is seen. Increased capillary permeability due to histamine released in shock or due to toxins released in oedema disease of pigs. Lymphatic obstruction as seen in neoplasms. Mesothelioma of peritoneum, pearls disease of tuberculosis or secondary implantations due to neoplasms contributes ascites condition in animals.

Heaemorrhages into peritoneum are common in all animals and may be due to trauma of organs or sweet clover disease. Small focal heaemorrhages are common in acute toxemia including enterotoxaemia and infectious diseases like anthrax, hemorrhagic septicemia and infectious canine hepatitis. The heaemorrhages are

found on the serosa of diaphragm stomach and intestines. Heaemorrhages in the peritoneum are also in the course certain parasitic diseases such as liver fluke infestation and strongylus edentates infection.

Peritonitis is a very common condition in most of the domestic animals and may be localised or generalised. Thecommon pathogenic bacteria that cause peritonitis are *Escherichia coli* streptococci, *staphylococci, Corynebacterium* infections, *clostridial organisms*, pasteurella organisms. Viruses of bovine cephalitis, helminths, chemical and endogenous substances like bile and pancreatic juice.

The peritonitis maybe set in through external entry like surgical wounds or trauma or by blood stream, by rupture of abdominal organs, as in acute appendicitis and peritonitis in human beings by extension through walls of stomach, intestine, uterus when their mucosa is infected, through osteum abdominal of an infected oviducts or from an infected umbilicus or by way of lymphatics from scrotal infections and infections of abdominal wall or direct extension from an infected kidney.

The irritant first produces a serous inflammation which later becomes fibrinous or fibrino-purulent. The fibrin is helpfulin localizing the inflammation by forming adhesions. Being a very large absorptive surface of the body, toxins are speedily absorbed from the peritoneum and damage the other parenchymatous organs. In visceral gout of birds, uric acid peritonitis occur characterized by the deposit of urates on the serous membranes which constantly shows inflammation; tuberculosis of peritoneum is very frequent in cattle, less frequent in dogs and are also met within other animals. Fibrin that occur consequent to inflammation not recovered within 6 to 10 days will be organised and inhibits movement of the intestine and uterus leading to digestive and reproductive processes as well induce colic in animals and human beings. In fact, this is complication in most of other septic operations.

Parasitic diseases of the peritoneum: Most of the parasites found in the peritoneal cavity are there in the normal course of migrations. *Cysticercus (Cysticercus tenuicollis)* in ruminants and *Cysticercus pisiformis* in rabbits are common. These cysts do not evince any inflammatory reaction except presence of a thin band of a fibrous capsule. Rarely, cysticerci have been encountered in the abdomen of carnivores. Spargana, elongated larval form of *Spirometra* spp. may encyst in abdominal cavity of carnivores and swine. *Tetrathyridia*, the larvae of the tape worm of Mesocestoides, may proliferate extensively in the abdominal cavity of carnivores. Where they cause characteristic pyogranulomatous peritonitis or parasitic ascites.

Fasciola hepatica larvae can cause acute and chronic peritonitis in cattle and sheep, the inflammation involves the parietal peritoneum and sometimes visceral peritoneum especially that of liver, spleen and omentum. *Dioctophyma renale* or its eggs in canines produce chronic perihepatitis. Stephanurus dentatus in the course

of its migration is through the liver and peritoneal cavity to the kidneys in pigs may cause local hemorrhage, peritonitis and perihepatitis. *Strongylus edentatus, Strongylus equines* pass through the liver and the ligaments and lumen of the peritoneal cavity in their migration. Fibrous tags on the liver particularly the diaphragmatic aspect are Sequleae of *strongylus edentatus.* Ascarids of all species occasionally may cause obstruction and rupture of the small intestine or bile duct, so that they may be found in the abdomen as a terminal event. Setaria spp (Onchoerca worms - filaroid species) are inhabitat of the peritoneal cavity of many domestic and wild ungulates such as horses, cattle, buffaloes, camels, sheep, goats, swine, and deer. Adult *setaria* usually do not cause significance peritoneal lesions in their normal host. There are reports of occlusion of the uterine tube by setaria labipapillosa in cattle and *S. labiatopapillosa* are also present in the peritoneal cavity or in the vaginal or testis and induce granulomatous peritonitis or peri-orchitis if they die. The larval form of *S. digitata* can produce mild adhesive peritonitis and grnaulomas in the retro peritoneum and bladder of cattle. Setaria digitata is normally found as an adult in the peritoneal cavity of cattle and buffaloes. The migrating larvae in the brain and spinal cord of aberrant hosts, such as horses, camels, sheep and goats, cause a neurological diseased, called lumbar paralysis or Kumri. These may produce characteristic neurological lesions such as ataxia, weakness or paralysis. *Setaria digitata* larvae may invade the eye of horses, via the optic nerve as do the microfilaria of Setaria equine. Here they produce endopthalmitis. Hydatid cysts that of cysticerci of *Echinococcus granulosus* is common in the peritoneal cavity of many domestic animals.

Neoplasms: frequently primary tumors of mesothelioma of muticentric origin are seen and are common in the bullocks. They are sessile or pedunculated nodules from few millimeters to 6 to 10 cm in diameter or as villous projections, on a thickened mesentery or serosa surface. Fibrous or sclerosing forms which is more plaque like have also been reported. Ascites as a result of blocked lymphatics usually is present with peritoneal tumors. The tumor is made of single layers of dark, plump, cuboidal, columnar or rounded epitheloid neoplastic meosthelial cells with a distinct boarder and abundant think cyt0plasm over a proliferating firbocellular stroma. Mitotic figures are typically not numerous. The meosthelial cells forms loops and festoons in papillary pattern, or line cystic spaces and tubular structures. Secondary tumors observed are metastases from the liver or uterus. Transcoelomic implantation of ovarian tumors are found with transmissible venereal tumors of dogs and as well certain ovarian tumors in women.

Lipomas are the most frequent tumors of the peritoneal cavity. They may reach enormous size but their significance is that they tend to become pedunculated and may cause acute strangulation obstruction when pedicle winds about the loop of the intestine.

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Chapter 5

Urinary System

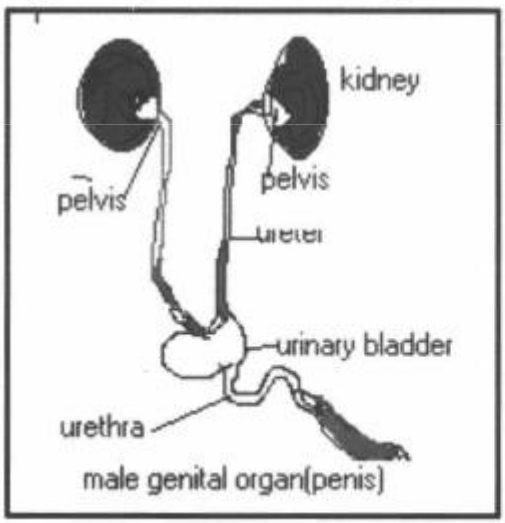
Summary

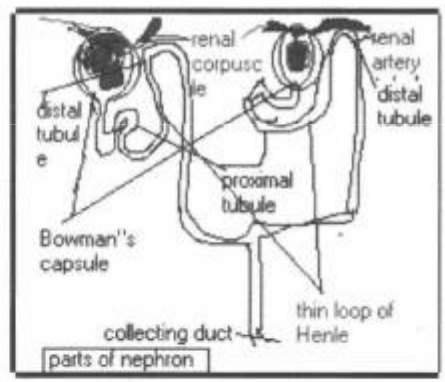
The renal collecting system – urethral bud – metanephric duct – Wolffian duct – ureters, pelvis, calyces and collecting ducts – Nephrons and collecting tubules - renal calyces- functional unit of kidney - Nephrons- renal corpuscles, proximal tubules, loops of Henley and distal tubules. Functions of kidneys – extra renal factors – Embryology of kidney- Mesonpehros – Physiologic anatomy of kidney – description of kidneys of different species of animals – Physiology of kidney – – oxygen – hypoplasia – Renal Dysplasia – Renal cysts – polycystic kidney – Disease conditions of kidneys – Degenerative processes in the kidney – Hydronephrosis – Toxic nephrosis – Ochratoxin nephropathies – Lower nephron nephrosis – Pigmentary changes in kidneys of animals-Calcium casts – Metastatic calcifications. Inflammation of kidneys (Nephritis) – Pyaemic nephritis or embolic nephritis – Pyelonephritis – Histological-findings-Glomerulonephritis-acuteGlomerulonephritis, Gross, Histological – Sub-acute – Glomerulonephritis-gross and Histological and clinical findings – *glomerular sclerosis – extra capillary lesions* – Membranous Glomerulonephritis – extra capillary lesion – Interstitial nephritis – Classification of Interstitial nephritis – histologicalDifferences between chronic Glomerulonephritis and interstitial nephritis – Diseases of urinary bladder,- renal function tests – urine volume in different species of domestic animals – oliguria, Pyuria, Haematuria, acid-alkaline reaction (pH), colour reaction, Ketone bodies, Blood – dye excretion tests – Sodium suphanilate clearance test-BUN tests (Blood urea nitrogen)-*Urinary casts* – Urolithiasis – Type of calculi – Uric acid and urate calculi-cystine calculi - Cystine stones.

Urinary system

Anatomically the urinary system consists of two kidneys on either side of the body, left and right, two ureters, the bladder in most of the mammals, lacking in poultry, followed by a urethra opening into the respective genital organs. The renal collecting system is derived from the urethral bud, metanephric duct, a diverticulum of the mesonephric, Wolffian duct, and consists of the ureters, pelvis, calyces and collecting ducts. Nephrons develop from the metanephric blastema and attach to the growing ends, ampullla of the collecting system. The uriniferous tubule consists of Nephrons and collecting tubules the renal calyces are the cup shaped recesses of the pelvis, which enclose conical masses of medullary pyramids.

The apex of a pyramid is referred to a papilla and its tip fenestrated by collecting ducts. The functional unit of kidney each is Nephrons and consists of renal corpuscles, proximal tubules, loops of Henley and distal tubules.



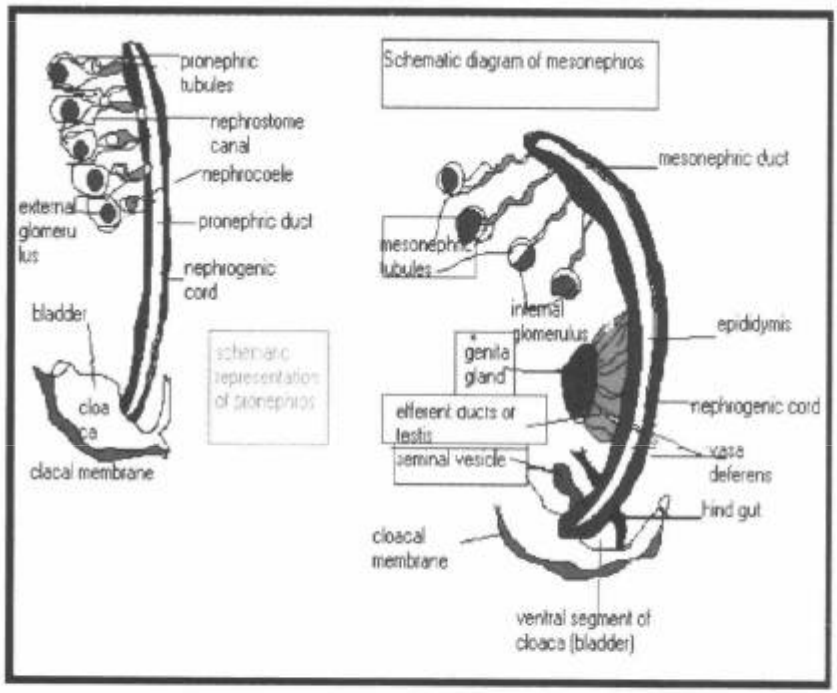


Functions of kidneys: The functional unit of the kidney is nephron which consists of two functionally distinct units, the glomerulus, a bed that serves a filtration unit and the tubule, which is lined by epithelial cells. The tortuous route through which the blood must pass the kidney has important bearing functional considerations. The greatest bulk of the bloodthat supplies the tubules first passes through the glomeruli. Any interference in blood flow through the glomeruli will affect total renal function and is followed by degenerative changes in the tubules.

In passing through the glomeruli the blood loses an essentially protein free plasma filtrate. As this filtrate passes through the tubules, it is modified by excretion, reabsorption and other activities of the tubular epithelial cells. The end product of this complex of activities is urine.

The kidneys perform two major functions: first, they excrete most of the end products of bodily metabolism and second they control the concentration of most of the constituents of the body fluids. The excretion of metabolic end products of nitrogen metabolism namely urea, creatine, creatinine, ammonia etc. by kidney is as to maintain a standard chemical composition of the blood. Kidney also functions in regulation of maintenance of acid base balance of the extracellular fluids. Further functions of kidney are selective reabsorption and thereby conservation of substances useful to the body namely sodium chloride and glucose. Maintains standard extracellular body fluid volume by excretion of water or its reabsorption whenever is indicated.

The following extra renal factors interfere with the functions of the kidney namely haemoconcentration, low blood pressure, and obstruction to the outflow of the urine. Injury to the glomerular filter, injury to the tubules and alteration in the circulation of kidney also interfere with the function of the kidneys. Failure of the urinary mechanism occurs if there is inadequate perfusion, prerenal failure, inadequate processing, renal failure, or inadequate discharges that are post renal failure.



The functional capabilities of the kidney are dependent upon the manner in which blood flows through it. After entering the kidney the renal artery divides successfully into interlobar, acurate and interlobular arteries. The interlobular branches become the afferent glomerular arterioles, which become a set of capillary loops. Each loop is closely enveloped and bound to the external layer of Bowman's capsule. The attached walls of the capillaries of the glomerulus and Bowman's capsule form a semi permeable membrane across which substances pass from the blood plasma to the lumen of the tubule by means of simple filtration.

Embryology of kidney: The kidneys develop from the nephrotome (nephrogenic cords). This is short segment of unsplit mesoderm that connects the somite with the splanchnic and somatic mesoderm. Three sets of kidneys are formed during embryologic development. Two sets are temporary structures and the third set becomes the kidney found the adult. The embryology of mammalian kidney

involves the sequential development of three successive but over lapping structures, the Pronephros, Mesonpehros and Metanephros. The first two becomes vestigial, but act as inducers of definitive kidney, the Metanephros.

Pronephros: The nephrotome first forms a duct that extends caudally and empties into the cloaca. At each segment, this duct communicates with the coelome via pronephric tubules and not functional. In mammalian embryos, the utilization of their duct by the mesonephric tubules gives them potential significance in the genesis of renal anomalies.

Mesonpehros: It develops from segmentally arrange tubules that empty into pronephric duct. Mesonephric tubules develop from thoracic mesoderm caudad to the Pronephros. The other end these newly formed tubules surrounds tufts of blood vessels (called glomeruli) that arise from the branches of aorta. No loop of Henle is present. Material is removed from the blood of foetal circulation, transported to mesonephric ducts and finally carried to urogenital portion of cloacae. Selected mesonephric tubules and mesonephric ducts form the Wolffian duct and the masculisation of urogenital sinus. 7 to 12 mesonephric tubules in the area of developing testis are preserved and become efferent ductules. The part of the mesonephric duct adjacent to testis undergoes extensive coiling and forms the epidididymis. The caudal part of the duct becomes the ductus deferens. The urogenital sinus into which the mesonephric duct empties in the embryo, is from the prostatic membrane and spongy (cavernous) parts of the male urethra. In female, bulk of mesonephric tubules and mesonephric ducts are Gartner's ducts and are opening into the vestibule adjacent to the vaginal opening. The mesonpehros is well developed in the pig. The mesonpehros is functional in mammalian embryos but degenerates before birth.

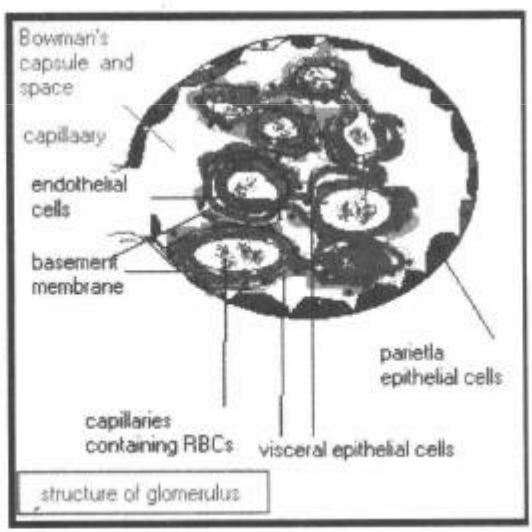
Metanephros: Metanephros or adult mammalian kidney is formed by small outgrowths from each of the mesonephric ducts near the point where the ducts enter the cloaca. These outgrowths are the metanephric ureteric buds. The metanephric buds induce the surrounding mesoderm to form a mass called metanephrogenic blastema. The parts of the ureteric buds nearest to its origin become ureters. The parts surrounded by metanephrogenic mesoderm dilate and branch to form pelvis, collecting ducts and tubules of kidneys. The metanephric blastema forms the nephrotome units. The tubules become S-shaped and lumen develops at one end of the tubule and is funnel like and surrounds tuft of capillaries. The other end connects the terminal branches of the collecting system.

The cavitated cell masses develop into Nephrons. Connection of the lumens of the Nephrons and the collecting tubules occur very soon after the cell mass cavitates. Glomerular development involves the formation of lateral invagination in the S-shaped mass by mesenchymal cells, which differentiate into endothelial and mesangial cells and become linked with the renal-vasculature.

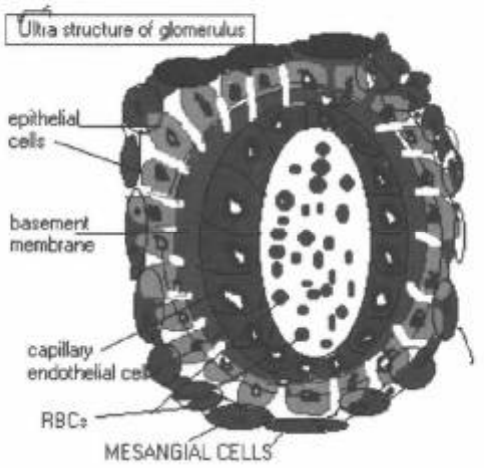
Nitrogenous waste and multitude of other organic compounds and inorganic substances impose a substantial load on the renal mechanism. Mammals excrete urea which is highly soluble, diffusible, and osmotically active; excretion of wastes and conservation of water in mammals require concentration mechanisms capable of raising osmotic pressure of urine above that of blood.

The kidneys of domestic animals can be classified as unipyramidal (unilobar) or multipyramidal (multilobar). Cats, dogs, sheep and goats and horses have unipyramidal kidneys. In cats one lobe is present and papillary duct is open into a calyx on a single renal papilla. In dogs and sheep and goat and horse there is complete or partial fusion of several lobes and a single crest like papilla and renal crest is present. Pigs have multipyramidal kidneys in which there are several distinct renal lobes, pyramids and their respective papillae. The kidneys of cattle are also multipyramidal but have distinct external lobation, pseudolobulation with each pole presenting a pyramid.

On saggital section of kidney subdivisionof cortex and medulla are distinguished. The cortex has a dark outer zone and a pale inner zone.

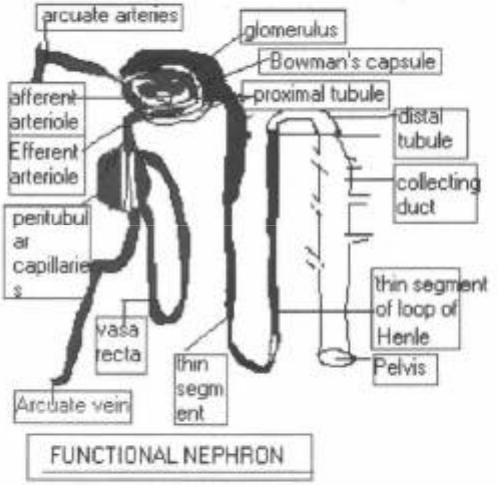


The glomerulus is a vascular-epithelial structure designed for the filtration plasma. It develops embryo logically by the invagination of capillary rich mesenchyme mass into Bowman's capsule, an epithelium lined sac. The visceral epithelium covers the glomerular capillaries to become an essential part of the filtration membrane and the parietal epithelium which lines the Bowman's capsule lines the urinary space which receives glomerular filtrate.



The glomerular capillaries are supported on a basement membrane and are held together by the Mesangium. Mesangium is a glycoprotein matrix which is positive to periodic acid Schiff stain and contains positive mesangial cells. The glomerulus is covered by the visceral epithelial cells and in-between cementing membrane known as basement membrane lies. Thus the capillary endothelium lies on the basement membrane and is covered by epithelial cells. The visceral epithelial cells are structurally complex cells and possess interdigitating processes embedded in the basement membrane processes known as foot processes or pedicles.

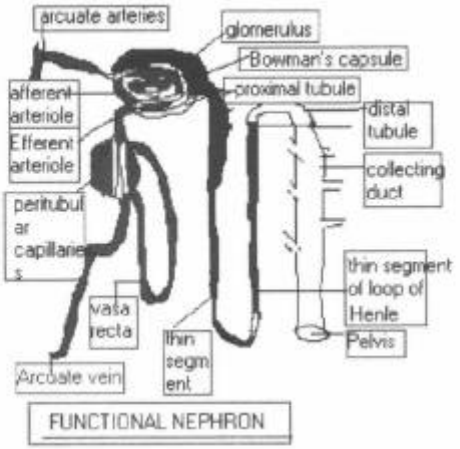
The arterioles enter and leave the glomerulus at the vascular pole and urine enters the proximal tubule at the urinary pole of the glomerulus. The glomerular filtration membrane consists of three layers. Capillary endothelium containing holes or



fenestrae of 50 to 100 nm diameter and glomerular basement membrane which is 100-300 nm thick and consists of central electron dense lamina dens and peripheral electron lucent layers namely the lamina rare interna and externa and visceral epithelial cells (podocytes). The podocytes have complex interdigitating trabaculae whose foot process or pedicles are embedded in the lamina externa of the globular basement membrane. The foot processes are separated by 25 to 30 nm wide infiltrating slits, which are bridged by thin slit diaphragm white pores of 6-9 nm diameter. Glomerular basement membrane is produced continuosously by podocytes and is continuous below these cells but does not completely encircle the glomerular capillaries and endothelial cells and mesangial are in direct contact.

Physiologic anatomy of kidney: The two kidneys together contain about 24 million Nephrons at least in an adult human being and each Nephron is capable of forming urine by itself. The Nephrons is composed basically of glomerulus from which fluid is filled and along tubule in which the filtered fluid is converted into urine on its way to the pelvis of the kidney. Blood enters the glomerulus (tuft of capillaries) through the afferent arteriole and then leaves through the efferent arteriole. The glomerulus is a network of up to 50 small capillaries covered by epithelial cells and encased in Bowman's capsule.

1/4th of blood always goes to the renal artery from the heart pump. Human kidneys convert over 1700 liters of blood per day into about 1 litre of urine.



A large volume of glomerular filtrate is formed as a product of high hydrostatic pressure of arteriolar blood, and the selective permeability of the filtration membrane. The entire plasma volume is filtered about 1000 times per day. The glomerulus is highly permeable to water and small solutes, but virtually excludes albumin whose molecular weight greater than 70,000 and having radius 3.6 nm and higher molecular weight plasma proteins from the filtrate. The glomerular basement membrane is a size-dependent barrier to filtration, prohibiting passage

of particles with radius greater than 3.5 nm. The filtration membrane also excludes particles from filtration on the basis of charge. A small amount of albumin normally passes through the filter but is rapidly reabsorbed in the proximal tubules. The glomeruli of neonates are permeable to colostral proteins for a few days.

The mesangial is the central region of the glomerulus, which forms supporting frame work about which the glomerular capillaries ramify. The mesangial matrix is basement membrane like periodic acid Schiff positive glycoproteins, and the mesangial cells are phagoyctic and contractile cells. These cells function in phagoyctic removal deposited macromolecules removal of glomerular basement membrane and many modulate intraglomerular blood flow; mesangial cells both respond to and produce a variety of cytokines. Mesangial cell hyperplasia and increased mesangial matrix are common changes in glomerular disease.

The primitive kidney possess a duai vascular arrangement, somewhat comparable to the mammalian liver and it is retained in reptile and birds; the glomeruli are perfused with arterial blood and tubules are supplied with venous blood in the renal portal system derived from the venous system in the caudal part of the body. Mammals have discarded the portal system and the tubules are supported with blood that was first passed through their respective glomeruli.

The renal calyces of cattle join directly to form the ureters without forming a pelvis. Mucous glands are common in the pelvis of horses. In normal human around 10 lakhs of Nephrons, in dogs 4 lakhs, in cat 2 lakhs. Normally the kidney measures around three vertebrae long. The cortex and medullary ratio varies form1:2 or 1: 3.

Whereas in birds, the ureters of metanephric kidneys open directly into the cloaca, those of the adult mammal open into a bladder which has a separate exit from the body. The bladder derives largely from the proximal part of the allantois and part of the cloaca itself provides much of the neck of the bladder. The ultimate fate of mesonephric ducts is determined by the sex of the embryo; in the female they degenerate but in the male they contribute to the ductus deferens.

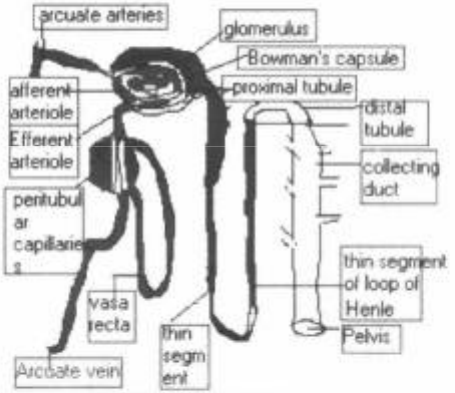
Dog kidneys are smooth; bean shaped and is reddish brown in colour. They are having a dorsal and ventral surface, a convex lateral border and a concave medial border, containing the hillus. The hillus is where the renal artery, vein, ureters, nerve and lymph vessels enter or leave the kidney. Dog kidneys are in the lumbar region. Left kidney varies with the stomach contents. Horse kidneys are smooth, left being longer and more beans shaped and right is heart shaped. In ox these are grooved, exhibiting clear lobation into 18 to 20 lobes. Right kidney is irregularly flattened in the dorso ventral plane and rough. Avian kidneys are divided into cranial, middle and caudal divisions by large blood vessels and nerves crossing their ventral surfaces and passing into the left.

Sheep. The kidneys are smooth and bean shaped with the left kidney laterally flattened by the rumen. In pig kidneys are smooth and bean shaped somewhat

flattened dorsoventrally. In cat kidneys are smooth large capsular veins are characteristic of cat kidney and are visible under the capsule. Marine birds which consume large quantities of salt than non marine birds possess a salt gland in the head which discharges concentrated salt solution in the nasal cavity. Birds with functional salt gland have relatively larger kidneys than which do not have salt gland. Renal portal system is present in birds and absent in mammal.

Physiology of kidney: Kidney elaborates rennin, prostaglandins and 1, 25 dihyxoy cholecalciferol. Within 1 minute 2.5 liters of blood is pumped in the mammalian kidney. Around 800 liters of blood is pumped through the kidney and is being filtered through giving the filtrate of 80 liters per day and 120 ml per minute. The portion of the total cardiac output that passes through the kidneys is called renal function. Thus normally 12 to 30% of the blood flows in the normal resting portion.

The vasa recta are a special portion of the peritubular capillary system is the vasa recta, which are a network of capillaries that descend around the lower portions of the loops of Henle. These capillaries form loops in the medulla of the kidney and then return to the cortex before emptying into the veins.The vasa recta play a special role in the formation of concentrated urine. Pressure of the blood in the glomerulus causes fluid to filter into Bowman's capsule, from which it flows first into the proximal tubule that lies in the cortex of the kidney along with the glomerulus. From there the fluid passes into the loop of Henle. Those Nephrons that have glomeruli lying close to the renal medulla are called juxtamedullary Nephrons. From the loop of Henle the fluid flows back to the renal cortex through the distal tubule. Finally it flows into the collecting duct, which collects fluid from several Nephrons. The collecting duct passes from the cortex back downward through the medulla, paralleling the loops of Henle. Then it empties into the pelvis of the kidney. As the glomerular filtrate flows through the tubules, most of its water and varying amounts of the solutes are reabsorbed into the peri tubular capillaries and small amounts of other solutes are secreted into the tubules.



FUNCTIONAL NEPHRON

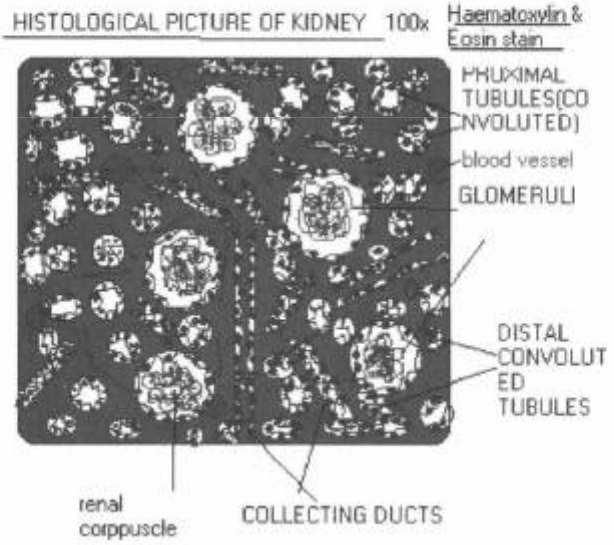
The remaining tubular water and solutes become urine.

There are 7 zones in the mammalian tubule to concentrate urine above the toxicity of plasma. This function is provided by the loop of Henle. Those animals with a preponderance of long loops have greater concentration ability. The volume of medulla is determined by the number of long loops and a simple index of concentration ability is the ratio of cortical volume to medullary volume. When the ratio is wide that is 7:1 and part of the medulla is destroyed in disease, there is high level of susceptibility to serious imbalance of fluid and electrolytes.

In acute disease, only 30% of Nephrons are functional. The kidney functions by producing a large volume of protein free glomerular filtrate from which are resorbed the constituents that the body needs. Thus about 995 of sodium chloride and water filtered are resorbed. The cells of proximal convoluted tubules have a well developed brush border and numerous mitochondria. Energy for the sodium pump in this actively resorptive area is provided by mitochondrial oxidative phosphorylation. About 90% of the hydrogen excretion by the kidney occurs in the proximal tubule. The proximal tubule actively resorbs large quantities of sodium and chloride, and water passively follows, hence 60 to 80% of the glomerular filtrate which enters the proximal tubule is resorbed isotonically. Sodium is co-transported with glucose and amino acids. Hydrogen ions are accompanied by sodium bicarbonate as counter ion. In addition to salt and water, proximal tubules reabsorb glucose, amino acids, calcium, phosphate, uric acid, proteins and potassium. Overloading of the resorptive capacity of the proximal tubules in conditions such as diabetes mellitus also overwhelms the resorptive capacity of distal tubules and leads to osmotic Diuresis. Interference with the production, release or action of ant diuretic hormone on the distal Nephrons and collecting ducts, as occurs in pituitary or renal diabetes insipidus, results in obligatory water Diuresis and excretion of hypo-osmotic urine and hence polyuria. Proximal tubule secretes hydrogen ions, organic acid, paraminohippurate, penicillin and some iodinated radio-opaque materials.

The long loops of Henle of the juxtamedullary Nephrons penetrate deep into the medulla and assist in making the renal medulla the only hypertonic tissue in the body. Urine concentrating ability is directly proportional to the length of the loop of Henle; baby pigs have short loops and thus cannot concentrate slats and are very susceptible to dehydration. The source of the solute gradient that becomes greater toward the tip at the papilla is the loop of Henle. The gradient is preserved by the vasa recta countercurrent exchanger. Sodium chloride is pumped from the ascending limb in this chloride is actively resorbed, sodium in passive way from the ascending limbs of the loop of Henle into the interstitium, in turn drawing water from the descending limb and progressively increasing the solute concentration in the descending limb. The ascending limb is impermeable to water, thus the tubular fluid becomes dilute and may be hypotonic. More salt may be resorbed from the collecting ducts, further diluting the fluid. Water Diuresis

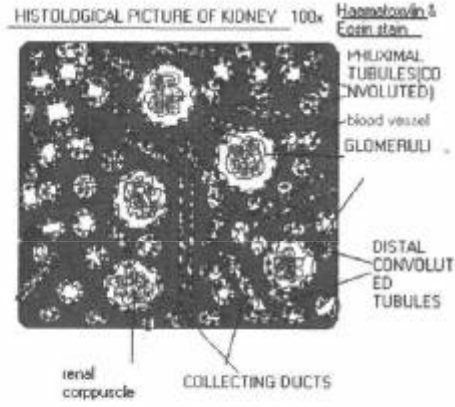
occurs when a state of water excess exists and Antidiuretic hormone is not to be released from the neurohypophysis. If Antidiuresis is required, ADH is released and renders the epithelium of the collecting tubules highly permeable to water, reducing the volume of tubular fluid entering the hypertonic medulla. The remaining fluid is then concentrated to three to four time the blood osmolarility during passage to that of the papilla. The water resorbed in the medulla is passively transported in the ascending vasa recta and removed. Antidiuresis hormone increases the permeability of the medullary portions of the collecting ducts to urea and water and urea then diffuses from collecting tubules to interstitium and luminal urine and interstitial concentrations are equal. The quantities of urea and sodium chloride resorbed are decreased due to decreased tubular fluid transit time; hence the medullary solute gradient decreases as does urine concentrating ability. Kidneys correct metabolic alkalosis by excreting the alkaline urine containing the excess bicarbonate. The kidney correct metabolic acidosis by increasing resorption filtered bicarbonate, excreting titratable acids and secrete hydrogen ions and by producing ammonia.

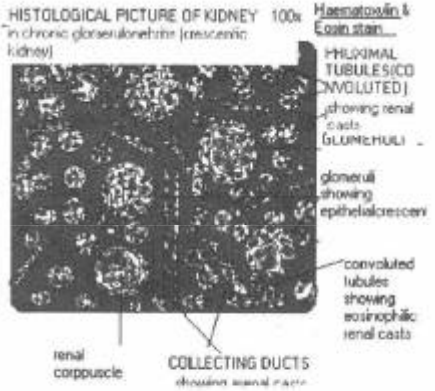


In addition to the usual haematoxylin and eosin staining of paraffin sections several other techniques are useful in study of histological sections of kidney. The PAS stain and PAS-silver metheneamine stains and Phosphotungsitic acid Haematoxyin stains are useful in studying the morphology of the mesangial, basement membrane and as well tubules and interstitium of kidney sections.

Water and salt are quantitatively and in an evolutionary sense, the most important constituents of body fluids. To maintain homoeothermic and terrestrial existence, a need for control of peripheral circulation and structural modifications to the

integuments are required. CO_2 is very soluble in water, and highly diffusible, and responsibility for its excretion has been transferred from the integument of aquatic and amphibian ancestors to the respiratory system of mammals. Nitrogen wastes are excreted in the form of urea which is highly soluble, diffusible and osmotically active through the kidnyes. The extracellular fluid and plasma of the body are dialyzed through the kidney may any times in a day, producing copious amount of primary urine of which almost reabsorbed. Although this system effectively rid the body of wastes, it requires a large expenditure of energy and a dependable renal blood supply. Kidneys are always perfused withhold and blood supply is diminished only in the event of crisis, in order to preseverve circulation to the prime priorities of cardiac output the heart and the brain. Renal oxygen consumption is relatively small in relation renal blood flow.





Nomalies of development:

Agenesis is the absence of one or both kidneys. In hypoplasia wherein affected kidney is smaller. In such animals other kidney shows compensatory hypertrophy. Persistent lobulation may be seen in dogs, sheep and swine. In this ones should remain all foetal kidneys are lobulated and pseudo-lobulation is seen in bovine kidneys. Horse shoe kidney is seen in all species and these results from fusion of the kidneys at the posterior poles. Duplication of one kidney is seen in pigs and in some animals three kidneys may be noticed. Malpositions of the kidneys (ectopic kidneys) observed more frequently in swine than in dogs or cats is usually caudal with the kidney in the pelvic or inguinal position. One or both kidneys may be displaced. Renal Dysplasia is disorganized development of renal parenchyma due to anomalous differentiation. One oar both kidneys may be affected. Viral etiology for the Dysplasia has been considered.

Renal cysts

These are either solitary or single or multiple in nature. One or both kidneys are involved. These are common in all species of animals. Cysts can arise during organogenesis and may be associated with histological criteria of renal Dysplasia. Cysts can develop in any part of nephron, including the glomerular space or in the collecting system. In glomerulocystic diseases the cysts develop in Bowman's space. The author observed these cysts in kidneys of cattle and buffaloes. These cysts are the dilated Nephrons. Three mechanisms have been postulated for origin of cysts. The first category cysts are due to obstruction of nephron due to inflammation occurring in the kidney. These types of cysts are seen in chronic renal diseases. The second type of cysts is due to change in the tubular basement membrane and resulting in formation of saccular or fusiform dilatation of the tubules. The third type of cysts is due to discarded growth of tubular epithelial cells. The author has opined that the congenital renal cysts are due to the failure of metanephric blastema in differentiation and to unite with renal corpuscle.

Steroid induced cysts in various species and atypical cysts in patients undergoing long term haemodialysis. The fundamental change that allows cyst development probably occurs in the tubular basement membrane and results in the formation of saccular or fusiform dilatation of the tubules. Renal cysts are common in pigs and calves. Cysts can arise in Nephrons and collecting tubules after the end of nephrogenic. Three mechanisms which are mutually exclusive may lead to formation of renal cysts. Renal cysts may be caused by obstructive lesions as seen with acquired retention cysts of chronic renal disease and possibly those of glomerulocystic disease. A fundamental change may occur in the tubular basement membrane and result in formation of saccular of fusiform dilatation of the tubules and disordered growth of tubular epithelial cells may lead to focal hyperpalstic lesions and cyst formation. Cystic kidneys are very common in bovines.

Renal cysts are caused by many chemicals like corticosteroids, diphenylamine, polychlorinated biphenyls, - 5, 6, 7, 8-tetrahydrocarbazole-3-acetic acid, alloxan, biphenyl-thiazole and nor-dihydroguiaiaretic acid in experimental animals.

Renal cysts vary in size from the barely visible to structures which exceed that of the organ itself. They lie in cortex as well in medulla. Histologically cysts are lined by flattened or cuboidal epithelium, which grossly is smooth and shiny. A few cysts are more or less divided by thin trabaculae and most of them are unilocular. Cystic renal disease could be inherited in pigs and calves as autosomal dominant trait. When number of cysts is there it is called as polycystic kidney disease. Simultaneously cysts are seen as cystic bile ducts and pancreatic ducts in calves, puppies, kittens and foals.

Disease conditions of kidneys

Degenerative processes in the kidney: Degenerative renal lesions are known as

nephrosis. This term is applied to necrotic lesions of the kidney also. The degenerative processes affecting the tubules mainly include cloudy swelling, fatty degeneration and even necrosis. It is highly functional and specialized epithelium of the proximal convoluted tubules that is greatly susceptible to the irritants. Next order is the Henle's loops and distal convoluted tubules.

Cloudy swelling: The causes are various like inorganic, organic and bacterial toxic substances. These toxic substances reach the kidney through the blood strema. They injure the glomeruli and convoluted tubules first and collecting tubules next. The proximal convoluted tubules are often the only tubules affected due to their suceptibility to injury.

Grossly the kidneys are swollen has a bulging surface and have a cooked appearance. Histologically the change in cells appear as cloudy, their cytoplasm is granular and these granule stain intensely with eosin. Postmortem changes that sets in kidney after the death should not be mistaken for the cloudy swelling.

Hydropic degeneration: This is characterised by formation of clear cytoplasmic vacuoles which do not contain glycogen, fat or mucin and are presumed to be tissue fluid. The cause include over dosage of ether, chloroform, and circulating toxins.

Fatty change: The disturbances in the fat metabolism lead to fatty changes in the renal epithelium. In most of the cases the results is of toxic injury. Histologically the tubular cells particularly the lining cells of convoluted tubules contain distinct vacuoles of variable size. Nuclei may be dark and pyknotic. Fatty changes can be confirmed by staining sections with a fat stain.

Hydronephrosis: Hydronephrosis is dilation of the renal pelvis and calyces associated with progressive atrophy and cystic enlargement of kidney. The cause is due to urinary obstruction which may be complete or incomplete, existing at any level from the urethra to the renal pelvis. The obstruction may be caused by anomalous development of the lower urinary passages, or it may be acquired. Acquired causes include urinary calculi in any location, Prostatic enlargement in dogs and humans, cystitis especially if it is hemorrhagic, compression of the ureters by surrounding inflammatory or neoplastic tissue, displacement of the bladder in peri renal hernias, and acquired urethral strictures. Depending on the site of obstruction, hydronephrosis may be unilateral or bilateral, and there may be some degree of hydroureter and dilation of the bladder.

Pathogenesis of hydronephrosis is based on the persistence of glomerular filtration in the presence of urinary obstruction, plus the development of urinary obstruction, and added development of ischemic lesions. Even with sudden complete obstruction, glomerular filtration continues, since filtrate diffuses into the renal interstitium and prerenal spaces, where it is drained by lymphatics and veins. Continued filtration creates increased pressure throughout Nephrons, collecting

ducts and calyces and pelvis and shearing force develop between the compressible parenchyma and their resistant connective tissues of the trabaculae. Pressure atrophy of tubular epithelium occurs with resultant tubular function and concentrating ability diminishes. As well blood vessels are compressed, particularly hilar veins and inner medullary vessels, leading to papillary ischemia and necrosis. Glomerular filtration progressively decreases due to intrarenal vasoconstriction and Nephrons atrophy and are replaced by scar tissue.

The degree of development of hydronephrosis depends on whether or not it is bilateral, the completeness of the obstruction, and on other complications of obstruction. The development of an extensive degree of hydronephrosis requires that it be unilateral. Bilateral obstruction, which includes obstruction, localised to be bladder or urethra results in early death from the uremia. Unilateral obstruction produces greatest degree of hydronephrosis and such kidneys are massively enlarged, if an obstruction is removed within about a week, renal function returns. After about 3 weeks of complete obstruction or several months of incomplete obstruction, irreversible renal damage occurs. If hydronephrosis is unilateral the remaining kidney if normal compensates adequately. Urinary stasis predisposes to infection; hence pyelonephritis maybe superimposed on hydronephrosis or vice versa.

Early gross changes consist of progressive dilation of the pelvis and calyces with blunting of the apices of the pyramids. Eventually these may become excavated to form multilocular cysts communicating with the pelvis and separated by an intricate series of ridges which represent original septa. In advanced cases, the kidney may be transformed into a thin walled sac with only a thin shell of atrophic cortical parenchyma.

Histological changes begin with dilation of the proximal convoluted tubules, and shortly there is dilation also of the distal and straight segments. The straight segments persist with atrophy of the epithelium, but the dilation of the proximal tubules subsides; these portions then atrophy, become separated and are replaced by light diffuse cortical fibrosis. Glomeruli persist for a long time, flattened and spread apart. There is progressive destruction of the pyramids by liquefaction necrosis, which spares the pelvic epithelium and tissue in narrow zone immediately beneath. The necrotic tissue, to which is no reaction, is liquefied and removed and the pyramids are gradually destroyed.

Sometimes, the fluid in the kidney may be filled pus due to supervening pyelonephritis, when the condition is known as pyonephrosis. If infection supervenes Pyonephrosis ends with pyelonephritis.

Toxic nephrosis. Acute tubular nephrosis results due to the toxins conveyed to the kidneys by circulation. These could be due to chemicals, either of inorganic or organic, or due to ischemic or anoxic nephrosis, lower Nephrons nephrosis as seen with a hemoglobinuric nephrosis.

The exogenous chemicals are antimicrobial substances like amino glycosides like neomycin, kanamycin, streptomycin, cephalosporin's, polymixin, tetracycline's, sulfonamides, amphotericin B, metals like arsenic, bismuth, cadmium, lead, mercury, thallium, anticoocidial substances like monensin, antineoplastic agents like doxorubicin, methotrexate, ethylene glycol, chlorinated hydrocarbons, contrast media, methoxyflurane, sodium fluoride, oxalates from various plants, mycotoxins like aflatoxin, ochratoxin A, citrinin, tannins from various feed materials, lantana poisoning, animal venoms like cobra venom, scorpion venoms, vitamin K3, menadione derivatives, and derivatives of cantharidin. The endogenous substances that often produce toxic nephrosis are bile derivatives, haemoglobin derivatives, and myoglobin accumulation.

Organo mercurials were commonly used as fungicides on seed grains, which were occasionally fed inadvertently to animals and humans with disastrous results. Highly chlorinated naphthalene's which cause hyperkeratosis and nephrosis in cattle if Sulfonamides are not alkalinized, precipitate in tubules and produce toxic nephrosis. Amino glycosides and numerous additional antibiotics like penicillin, semi synthetic pencillins and polymixin may also prove to be toxic to domestic animals. The toxicity of many of the exogenous agents is exacerbated by various systemic states, such as dehydration or shock, which concomitantly impair renal function the affected animal.

Nephropathy due to antibiotics (aminoglycosides): In cats aminoglycosides are ototoxic as well nephrotoxic. Aminoglycosides are not metabolized but are eliminated from the body primarily by glomerular filtration; they selectively accumulate in and cause damage to proximal tubules. The toxicity is due to overloading of lysosomes with phospho lipids. Lysosomal dysfunction and leakage may lead to tubular cell necrosis. Toxicity is manifested clinically by inability to concentrate urine, polyuria, enzymuria, proteinuria, haematuria, cylindruria and Azotemia.

Tetracycline's especially but using outdated tetracycline containing degradation products cause nephrogenic diabetes insipidus. An overdose of ox tetracycline cans produce acute tubular necrosis and renal failure in dogs. Tetracycline administration has been reported to cause acute nephrosis and death in claves due the presence of tetracycline degradation products. Doxyycline is not reported to be nephrotoxic.

Sulfonamide nephropathy: Severe nephropathy may follow the ingestion of excessive doses of sulfonamides, especially if treated animals are dehydrated. Toxicity was much more common previously when only less soluble forms of the drugs like sulfa pyridine, sulfathiazole and sulfadiazine are available. Crystalline nephropathy results with these drugs use. Affected kidneys are slightly enlarged and congested, and the sulfonamide crystals are grossly visible in the medulla, pelvis and in some cases even in heavy deposits in the bladder. The deposits are

yellow and form pale radial lines in the medulla. Crystals are not observed in sections as they are dissolved during processing.

Amphotericin: This is an antifungal agent, a polyene antibiotic. It causes decreased renal blood flow and glomerular filtration due to renal vasoconstriction. Necrosis of proximal and distal tubules occurs, and there is mineralisation of intra tubular casts.

Ethylene glycol: Dogs and cats are commonly poisoned by ingestion of ethylene glycol. Ethylene glycol forms as antifreeze solutions in engine. It is having a sweet taste and is usually voluntarily ingested especially by young male dogs. Cats are more susceptible but less commonly affected than dogs. The minimal lethal dose is 1.5 ml/ kg for cats and 6.6 ml/kg for dogs. This is being excreted as unchanged in the urine. A small percentage is oxidized by alcohol dehydrogenase in the liver to glyceraldehydes, which is in turn oxidized to glycolic acid, glyoxylate, and finally oxalate. Other end products of metabolism are lactic acid, hipppuric acid and CO_2. Depression, ataxia, and osmotic Diuresis develop within a few hours after ingestion of ethylene glycol. If the animal survives for 1-3 days after ingestion, acute renal failure develops, primarily due to renal tubular damage caused by glyceraldehydes, glycolic acid, glycoxylic acid and oxalate. Severe renal oedema impairs and intrarenal blood flow and contributes to nephrosis and renal failure.

Oxalate nephropathy: Plants are the usual source of oxalate poisoning in sheep and cattle. Young plants may contain the equivalence of 7% or more of potassium oxalate; the amount decreases with maturity and drying of the plant. The fungi of *Aspergillus Niger* and *Aspergillus flavus* can produce large quantities of oxalates on feed stuffs. Large dose of ascorbic acid have caused oxalate nephrotoxicosis in humans and in goats. Pyridoxine deficiency and methoxyflurane anesthesia can also cause renal oxalosis. Calcium oxalate may crystallize in vessel lumens or walls, causing vascular necrosis and hemorrhage or in renal tubules causing tubular obstruction and acute renal failure.

Oxalates are produced endogenously in the degradation of glycine, an important constituent of amino acid of collagen and elastin.

Mycotoxins

Ochratoxin nephropathies

Ochratoxins were reported during the course of an investigation into the toxicity of moulds due to cereal and legume crops in South Africa. Ochratoxins are produced by several species of genus Aspergillus and punctilio. In the cluster of ochratoxin, the ochratoxins A, B and C are gaining importance. Ochratoxin is a potent toxin, having multiple toxic properties, like-nephrotoxic, and heapatotoxic, teratogenic, immunosuppressive and carcinogenic properties. Now Ochratoxin A is frequently detected in human blood sera (56.6% are positive out of 306 Germans tested). Ochratoxin a residues are detected in food of animal or plant origin

continuously. Hence the ochratoxin is getting attention due to its potential threat to animal and human origin.

Several species of genus *Aspergillus and pencillium namely Aspergillus ochraceus, Aspergillus alliaceus, Aspergillus mellens, Aspergillus ostianus, Aspergillus pertakii, Aspergillus sclerotiorum, Aspergillus sulphrueus, Pencillium viridicatum, Pencillium verrucosum* produce ochratoxins. *Aspergillus ochraceus* is supposed to be the principal producer of ochratoxin in grains particularly in the United Kingdom.

Ochratoxin A, which is more toxic than other ochratoxins, is a colorless crystalline compound, moderately soluble in organic solvents, with a molecular formulá of $C_{20}H_{18}CINO_6$ and the chemical structure is, 7-carboxy-1-5-chloro-8,hydroxy,1,3-dihydro – 3R,methyl isocoumarin linked to 1 α-phenyl alanine.

Ochratoxin A is a stable compound and can be preservedin ethanol at refrigerator temperature for more than a year. Ochratoxin affected bean will lose around 47% activity by blanching salting and heat processing in tomato sauce and large proportion of survived autoclaving in cereals for up to 3 hours. The dried whole coffee beans subjected to heat treatment at 200°C for 10 to 20 minutes reduced the levels of ochratoxin-A by 0 to 12% only.

Ochratoxin A competitively inhibits mitochondrial transport carrier protein and resulted in lowered energy for cholesterol synthesis. Ochratoxin is 3 times more toxic than aflatoxin in broiler chicken. Ochratoxin A inhibits protein and RNA synthesis in bacteria. Body weight decrease was observed in broiler birds. That ochratoxin; levels of 0.8 mg to 1 mg/kg body weight lowered the body weigh levels.

The main symptoms are mortality, nephrtoxicity that is pale swollen kidneys and decreased consumption of feed. Ochratoxin induced severe leucopenia and in layers decreased egg production and stained egg shells are observed. At lest in mice ochratoxin A fed to pregnant mice produced malformations and feototoxic effects.

Breaking strength of tibia decreased at the growth inhibitory levels of 2 ppm of dietary ochratoxin, but bone diameter was reduced only at ochratoxin a levels of 4 ppm or higher in broilers. Bone becomes brittle after feeding dietary ochratoxin. Higher levels if fed produce nephrtooxicity and air sacculitis with enlargement of kidney liver, regression of thymus, bursa and spleen.

Ochratoxin A is the only member of the group that produces proximal tubular degeneration and atrophy, cortical interstitial fibrosis and glomerular hyalinosis in pigs. Citrinin also contributes to renal nephrosis. Ochratoxin has been suggested as the cause of endemic nephropathy (Balkan) in humans.

Glycogen nephrosis: In diabetes mellitus in dogs and cats, glycogen is deposited in the tubular epithelium producing marked vacuolation of the epithelium in the

outer medulla and inner most cortexes. The deposition occurs in the ascending, disappears following insulin administration and has no effect on renal functions.

Hypokalaemic nephropathy: Chronic potassium depletion in humans, caused by diarhoea, adrenal over activity can result in impaired urine concentration and polyuria. Coarse vacuolation of the proximal convoluted tubules is due to reversible dilation of intercellular spaces. Corticosteroids produce hypokalaemia and reversible vacuolar degeneration of tubular cells. Cholemic nephrosis is seen in jaundiced animals. The nephrosis is believed to be due to the action of the substances retained in the bile on the tubules. This condition therefore is more pronounced in obstructive jaundice. In this condition, the kidneys are swollen, pale and opaque and brown in colour due to the deposition of pigments in the renal tubules. The pigment is found intracellular.

Lower nephron nephrosis: crush syndrome, or hemoglobinuric nephrosis: When large quantities of haemoglobin are excreted through the kidneys, lesions are found in the lower portions of the Nephrons namely the ascending loop of Henle and the distal convoluted tubules. The condition, therefore, occurs whenever there is haemolgobinemia is seen in excessive hameolysis, and severe burns, equine azoturia and incompatible blood transfusions and severe burns and in crush injuries as occurring in automobile accidents and in air raids. In acidic urine the pigment is precipitated which blocks the tubules resulting in haemoglobinuria and anuria. Selective damage seems to be caused in the lower nephron with haemoglobin casts in these places. Tubular epithelium contains fine particle of haemoglobin and may show hyaline drops formation. Grossly the kidney is swollen and pale with reddish streaks in the medulla.

Pigmentary changes in kidneys of animals

Following acute haemolytic crisis haemoglobin deposition is seen in clusters of Nephrons and there is discoloration of kidney. Histologically the haemoglobin appears as fine red granules in the epithelial cells of the tubules as red casts in the lower reaches of the nephron, especially Henle's loops and collecting ducts. Haemosiderosis occurs in the course of chronic haemolytic anemia and as residue from acute hemoglobinuric episodes. The pigment is found in epithelial cells of proximal tubules, where it is produced by degradation of resorbed haemoglobin, and it may be sufficient to produce a distinctive brown coloration of the cortex.

Lipofuscinosis of the kidneys of adult cattle also referred to as Haemochromatosis and xanthomatosis, consists of deposition of brown iron free pigments with staining characteristic of Lipofuscinosis. The pigmentation also affects striated muscles, giving them a dark brown appearnace. On the cut surface of kidney, the pigmentation occurs as radial dark line in the cortex but spares the medulla. Histologically it is present as fine brown granules in the epithelial cells of the convoluted tubules.

In congenital porphyria of cattle, swine and cats, brown pigmentation affects the cortex. Histologically, the pigment is present in the tubular epithelium and the interstitial tissue. The pigment is excreted in the urine, which if allowed to stand in the light, develops a port wine colour due to photo activation of porphyrin.

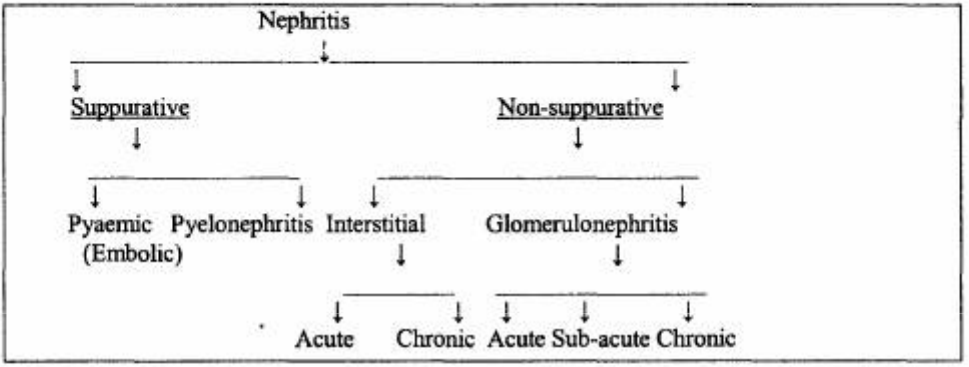
Nephrocalcinosis: Three types of disturbances in calcium metabolism are met with. Dystrophic calcification or a primary epitheilial calcification is where epithelial cells of the tubules are affected. This is seen in poisoning with mercurial salts, where in tubular epithelial cells are degenerated and necrosed and calcium salts are deposited on them.

Calcium casts are seen in the urine and urine is concentrated and inspissataed in the distal convoluted tubules, the ascending loops of Henle and at the proximal part of the collecting tubules. The calcium in the urine is precipitated as albumin casts. These calcium casts may destroy the epithelium of tubules with resultant inflammatory reaction.

Metastatic calcifications are seen when the urine's saturated with calcium salts and in hypervitaminosis D, here glomeruli and renal arteries and distal convoluted tubules and collecting ducts are deposited with calcium salts. This is due to consequent hypercalcemia reaction and due to the presence of supersaturate calcium in the blood.

Inflammation of kidneys (Nephritis)

Nephritis in domestic animals could be classified as follows



Pyaemic nephritis or embolic nephritis

It is a focal suppurative nephritis consequent to the deposition of pyogenic organisms from haematogenous route. The pyogenic organisms in different species are as follows *Escherichia coli* in calves, *Corynebacterium pyogens* and streptococci and*Corynebacterium pyogenes* infection in cattle, Shigella and streptococci and Actinobacillus equuli infections in foals. The most common cause of embolic

nephritis in swine is due infections with streptococci and staphylococci and *Erysipelothrix rhusiopathiae* and in sheep and goat renal abscessation with *Corynebacterium pseudotuberculosis or renale* is common.

This Pyaemic nephritis is of descending in origin, because the bacteria are there in the blood vessels, stay in the glomeruli migrates to the interstitium and in tubules. Infection may occur as a secondary to suppurative processes elsewhere like umbilical veins, mammary gland, uterus, pericardium or the lung. In calves and foals the infections acquired in utero also responsible for bringing about embolic nephritis in young ones. Consequent to bacteremia clumps of bacteria form emboli circulate in the blood and are arrested in the valves of the heart resulting in vegetations as well in the glomeruli and in inter-tubular capillaries resulting in formation of abscesses.

Grossly there are numerous tiny abscesses studded throughout the kidney. These may be visible on the cortex through the capsule. Abscesses are also seen in the cortex as circular areas while those in the medulla as elongated ones. All abscesses are of the same size, being of the same age. In foals which survive for several days, typical microabscessation is seen in the kidneys and other organs, and polyarthritis is present.

Histologically, abscesses with Leukocytic infiltration are found. Bacterial emboli are found in the glomerular loops and capillaries between the tubules.

Sequel: terminates death of the animal.

Pyelonephritis

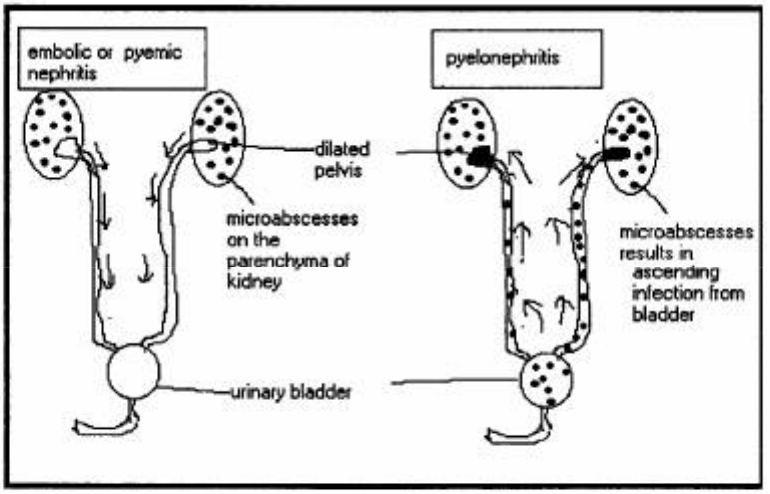
Pyelonephritis is inflammation of the pelvis and renal parenchyma, usually resulting from infections ascending from the lower urinary tract. It is pelvis infections and from there it ascends on to the tubules and to the glomeruli. Strictly speaking this is of ascending in origin. As such pelvis of kidney is discernable in human beings and in non- ruminants. Whereas ruminants have no definite pelvis, but calyces acts as harbouring agents. All parts of kidney involving the pelvis and parenchyma of kidney are affected. Usually this condition is met with cows, but it may also find in sheep and swine. Infection in most cases is though to be ascending ones from lower region of urinary tract for such an infection occurs stasis of urine is essential predisposing factor. When stasis occurs, the bacteria especially the motile one ascend to the pelvis. In human beings, stress in pregnancy brings about the infection in pelvis. The urinary bacteria ascend from bladder to pelvis. Invariably most of the women suffer with stress at one or more time during pregnancy with urinary infection and pyelitis occurs.

It is characterized by inflammation, necrosis and eventually deformity of the calyces, in association with the areas of tubules, pelvis and necrosis. Pyonephrosis is the term applied to severe suppuration of the kidney in the presence of complete or nearly complete ureteral obstruction; the infected hydronephrosis kidney is

converted to a sac of pus. Suppuration may extend through the renal capsule during the course of pyelonephritis to produce a perinephric abscess.

Pathogenesis: The pathogenesis of pyelonephritis begins with establishment of infection in the lower urinary tract. Organisms involved in urinary tract infection are usually endogenous bacteria of the bowel and skin such as *Escherichia coli*, staphylococci, streptococci, enterobacter proteus and *Pseudomonas* and more specific pathogens like *Corynebacterium renale, cystitidis and pilosum in cattle.* The infectious procedure is enhanced due to the pH of the urine. *Escherichia coli* are another culprit involved in urinary tract infections.

One of the urinary tract defenses against bacterial infection and colonisation is shedding of mature epithelial cells with attached bacteria.



Normal voiding of urine, plus immune mechanisms maintain sterility of the bladder, but once bacteria enter the bladder due to cystitis that is either by catheterization or incomplete bladder evacuation, these bacteria grow well in urine of low osmolality or alkaline pH. Stasis of urine is an important predisposing factor in the pathogenesis of cystitis and pyelonephritis. Urinary obstruction may be caused by ureteral anomalies in young animals, kinked ureters in pigs, pregnancy, urolithiasis and Prostatic hypertrophy. Females are predisposed to urinary tract infections because of their short urethra, urethral trauma and possibly hormonal effects. Especially in cows and buffaloes, the short urethra and dung soils the hind quarters and chances of bacterial infection is more. Especially in abortion cases when the cow lies on the floor with abundant discharges, the entry of soiled contaminated mud with bacterial load has easy accessibility into the bladder. Clinically infection is indicated by bloody or cloudy urine, with Pyuria and bacteriruria.

Once infection is established in the bladder, probably the most significant mechanism in causing renal infection is vesicoureteral reflex. The retrograde flow of urine up the ureters during micturition may carry bacteria as far as the urinary space of glomeruli. Reflux may occur during micturition, especially if there is urinary obstruction, or as a result of external compression of the bladder, as occurs during manual compression of the bladder in dogs and cats for collecting of urine samples. Vesicoureteral reflex is very common in puppies, and is a function of the short intravesical length of ureters and hence an easily overcome vesicoureteral valve; reflux decreases with age and the development of greater intravesical length of the ureters and is more oblique entry through the bladder wall. Vesicoureteral reflux of sterile urine does not encourage renal damage; maximum the ureteral muscular layers may hypertrophy. Cystitis with bacterial infections alters and causes reverse peristalsis thus animal with chronic bladder infections contribute to chronic active pyelonephritis. Progression of pyelonephritis is probably depends on persistence of bacterial infections.

Gross lesions: Acute disease characteristically begins with necrosis and inflammation of papilla or renal crests in irregular pattern. Bacteria may be abundant in collecting tubules. Associated wedge shaped areas of parenchyma are swollen, dark red and firm.

Histological findings: Tubules are obliterated by the inflammation, tubular obstruction and dilation occur, and glomeruli although initially resistant may be obliterated. Leukocytic casts are present in the tubules. As the process becomes chronic, mononuclear cells replace neutrophils and fibrosis proceeds and eventually predominate. Contraction of the scars results deep cortical depressions. The pelvis often contains exudates and debris.

Glomerulonephritis

In Glomerulonephritis the glomeruli are chiefly affected. This condition has not been studied much in animals. This has been recorded in all the species of animals, but the clinical significance has not been studied.

The causes of Glomerulonephritis in man are many. It is believed to be an antigen-antibody reaction for foreign proteins.

Reaction to tissue antigens: type II antigen-antibody reaction: The antigens may be expressed on intracellular structural proteins or on the surface of cells. Autoantibody is produced to glomerulus's basement membrane in Good pasture's syndrome. Auto antibodies to the pancreas in diabetes mellitus are an example for this type of reaction.

Reaction to tissue antigens: type III antigen-antibody reaction: Immune complex injury is characterized by acute necrotizing vasculitis, microthrombi and ischemic necrosis accompanied by acute inflammation of the affected organs. The necrotic vessel wall takes on an eosinophilic appearance and is called fibrinoid necrosis.

Kidneys as filtering organs are invariably affected. The immune complexes, are deposited on the basement membrane, mesangial cells are also active in removing these complexes. Proliferation of the mesangial cells are seen and thickening of basement membrane of glomeruli results in disease condition. Protein is lost. Filtration mechanism is disturbed. Acute Glomerulonephritis or chronic glomerulonephritis results in depending on the destruction of the kidney tissue.

Glomerulonephritis could be classified depending on the a) duration of disease as acute, sub acute and chronic Glomerulonephritis b) Glomerulonephritis could also be classified histologically as per the histological component involved.

Classification of Glomerulonephritis as per duration of disease:

Acute Glomerulonephritis Grossly; both the kidneys are enlarged and pale. On the cortex flea bitten red dots are seen indicating congested glomeruli. Small heaemorrhages are also observed on the cortex. On section the kidney slightly bulges on the edges. Capsule could be easily peeled off.

Histologically there is hyperemia of the glomerular capillaries, followed by mesangial cell proliferation, as the visceral and parietal epithelial cells of glomeruli. The proliferation blacks the capillary lumina and so glomerular ischemia results. Infiltration buy inflammatory cells aggravate the ischemic condition. Consequently nutrients are diminished to the tubules. There is increased cellularity of glomeruli. The capsular space is filled with swollen glomerular tuft, leukocytes (neutrophils), precipitating protein and RBCs. The sub epithelial basement membrane is thickened and deposition of electron dense material between the membrane and endothelium, within the membrane and between the membrane and epithelial cells. The membrane becomes leaky. Fibrin thrombi forming in glomerular capillaries may cause heaemorrhages. Casts of protein, leukocytes and RBCs are seen in the lumina of tubules.

This may heal or progress to sub acute and chronic phases.

Clinical findings: Oliguria, this is due to ischemia of glomeruli and intense pain in lumbar region. Animals evince colic. The specific gravity of urine is high. Pus cells are frequent in the urine. Proteinuria is common. Urine contains apart from pus cells casts, RBCs and renal cells. Blood urea nitrogen is elevated more than 40 mg%.

Sub-acute Glomerulonephritis: Histologically this is called as large white kidney. This is sub-acute form.

Grossly the kidney is enlarged, pale and smooth with non-adherent capsule. Cortex may reveal few haemorrhages.There capsule is tense. The cortex is wider than normal and is yellowish in colour and so there is distinct colour contrast between it and the medulla.

Histologically proliferation of visceral and parietal epithelial cells is pronounced. The proliferation of the parietal layer of epithelial cells of Bowman's capsule results in crescent shaped tissue and is known as epithelial crescents. Due to deposition of fibrinous like material between the crescents and the tufts, adhesions develop.

The tubular epithelium undergoes fatty degeneration, which progresses to hyaline droplet degeneration and necrosis. The tubules reveal casts of proteins, leukocytes and necrotic epithelial cells. The interstitial tissue is oedematous and contains infiltrated inflammatory cells.

Clinical findings: Early stages there are oliguria, due to ischemia of glomeruli and intense pain in lumbar region. Animals evince colic. The specific gravity of urine is high. Pus cells are frequent in the urine. Proteinuria is common. Urine contains apart from pus cells casts, RBCs and renal cells. Blood urea nitrogen is elevated more than 40 mg%. Later stages polyuria and lower specific gravity urine is excreted. Inflammatory cells are few in urine.

Chronic Glomerulonephritis: The sub acute Glomerulonephritis may imperceptibly merge with chronic phase.

Grossly the kidney is shrunken and contracted. Surface is finely granular. The capsule is adherent and when removed some of the cortex is peeled off. On section the cortex is found to be narrower and markings are obscure. Small retention cysts, due to obstruction of the tubules are seen.

Histologically almost all the glomeruli are found to be affected and most of them are fibrosed. Some show hyaline changes while quite a few are atrophied and may disappear altogether. Still others may show adhesions between the tufts and capsular epithelium. The interstitial changes in the inflammatory tissue are more pronounced. Lymphocytic infiltration is heavy and interstitial fibrosis is also seen. Glomerular fibrosis is marked and most of the tubules around the glomeruli are also started disappearing. Arteries showed sclerotic changes with hyperplasia media and intima. Some of the tubules which are still connected have functional glomeruli which are dilated.

Clinical findings: Polyuria and urine is having low specific gravity. Decrease in the volume of urine that is excreted out from the animal. Urine show albuminuria, presence of casts, RBCs and leukocytes (pus cells). Blood urea nitrogen is elevated; more than 40 mg/100ml. Filtration rate and renal plasma flow are reduced.

Histological-classification of gomerulonephritis (ultrastructural classification)

a) Membranous Glomerulonephritis
b) Mesangium-proliferative Glomerulonephritis
c) Membranous-proliferative Glomerulonephritis
d) Glomerular sclerosis
e) Extra capillary lesions

a) **Membranous Glomerulonephritis**: Electron-microscopically visualized sections of kidney showed thickening of capillary walls. Electron dense deposits of IgG and C_3 occur at the epithelial aspect of basement membrane. New basement membrane contains extra deposits of material which stains as black spikes with silver metheneamine methods and diffuse thickening of basement membrane. Fusion of foot process are prominent. This cause widespread nephrosis.

b) **Mesangio-proliferative Glomerulonephritis:** Mesangial cells are increased in number; Mesanagial cells accumulate immunoproteins with IgM and IgA.

c) **Membrnoproliferative gomerulonepрhtis:** The basement membranes are thickened and cellular proliferations seen. This is seen commonly in animals. In dogs immune complexes such as IgM, IgA, and C3 are found on the endothelial side of the basement membrane.

d) **Glomerular sclerosis**: Increased mesangial matrix and basement membrane that is type IV collagen is found.

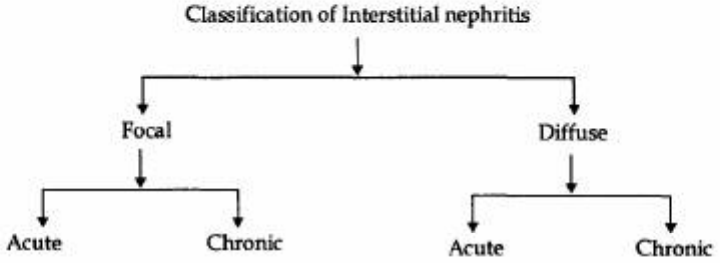
e) **Extra capillary lesion**: In Acute Glomerulonephritis gaps in the capillary walls may result in fibrinous exudation into the urinary space. This is seen commonly in swine and linked to the erysipeloid lesions. This is called extra capillary Glomerulonephritis.

(Interstitial nephritis)

Non-suppurative nephritis

Interstitial nephritis is common nephritis seen in domestic animals. Focal interstitial nephritis in calves is due to *Escherichia coli,* salmonella and brucella infections and also due to tuberculosis. In pigs this condition is a metastatic infection and the organisms responsible are organisms of *Erysipelothrix rhusiopathiae, Corynebacterium, Escherichia coli and non-haemolytic staphylococci and streptococci,* besides Leptospira. In dogs, interstitial nephritis is due to visceral larval migrans *(Toxocara canis),* leptospirosis, and viruses of infectious canine hepatitis, other causes like metritis, Pyometra, bronchopneumonia, cystitis, prostatitis, and chronic peritonitis and bronchopneumonia conditions and in horses due to *strongylus vulgaris* species larvae and due to tubular damage or from haematogenous sources infection or immunological in nature. Consequence to nephritis uremia is common in dogs.

The best example is focal interstitial nephritis in calves due *Escherichia coli* infections and is called as white spotted kidney. In all species of domestic animals Leptospira organism are involved in initiating interstitial nephritis. In most of the cases, the cause is obscure. Usually the condition is associated with retention of urine. Lesions of the lower region of the urinary tract causing hindrance to free passage of urine are conducive to the development of the condition. Possibly damage is a starting point and a factor in many cases, damage occurring while toxins are excreted by the kidney.



Diffuse interstitial nephritis: When most of the kidney is affected, this term is used. Grossly in acute type the kidney may be of normal size or slightly enlarged. The capsule strips off easily. The cortex shows a mottling of red and grey areas. The grey areas are the places of infiltration of inflammatory cells and are present in the cortex and may also occur in the outer medulla.

Gross changes: In chronic type of interstitial neprhtitis the kidney is smaller in size, pale grey in colour, is hard and cut with difficulty. The thickened capsule peels with difficulty and when stripped some portion of cortex is torn off. The cortex is shrunken and very narrow. The surface is uneven due to irregular contraction of the fibrous tissue name of the small granular contracted kidney. It is very difficult to differentiate from chronic glomerulonephritis and from chronic interstitial nephritis. These following differences could be brought about. But in most of these nephritides these lesions are admixed.

Histological Differences between chronic Glomerulonephritisand interstitial nephritis

Chronic Glomerulonephritis	Chronic interstitial nephritis
Surface finely granular	Surface coarsely granular
Inflammatory process begins in the glomeruli	Inflammatory process begins in the interstitial tissue
Involvement of interstitial tissue secondary	Involvement of glomeruli is secondary
Diffuse involvement of glomeruli	Glomeruli not involved or only few affected.

Similarly difficulty in differentiating between the kidney with interstitial neprhtitis and pyelonephritis may be met. In pyelonephritis the lesions are more irregular and asymmetric and histologically the lesions are found in the pelvis and inflammatory cells are in the lumina of tubules. Retention cysts of varying numbers and sizes are present. Sometimes they may be some many as to resemble the polycystic kidney.

Histologically the acute diffuse interstitial neprhtitis presents a picture that is essentially a true inflammatory reaction consisting of exudates of inflammatory cells and proliferating fibrous tissue. The infiltration consists of mainly of lymphocytes and plasma cells, with little number of neutrophils. The infiltration of the leukocyte is found mostly in the cortex and outer medulla and in diffuse

interstitial nephritis the cells are widely dispersed and form nodules. Early in the lesions, fibroblastic proliferation is evident, especially in case of Leukocytic, if irritation continues. Glomeruli however aren't involved normally. The epithelium of tubules show generative changes and are so severe extensive. These are more pronounced in proximal tubules.

In chronic diffuse interdigital nephritis, the tubules show atrophy and disappearance of tubular epithelium as well as the tubules. Some of the tubules may show cystic dilatation in the proximal to constriction by the fibrous tissue. Granular and hyaline casts are found in such dilated tubules. As the fibrous tissue increases, the leukocyte diminish in number and completely disappear denoting thereby the inflammatory reaction exists. Peri-glomerular fibrosis is common. Collagen that forms may contract producing the granularity of the surface. In some cases the glomeruli are completely displaced by eosinophilic mass of collagenised substances.

In the cortex may be found hyperpalstic and hypertrophic changes which in histological picture gives adenomatous appearnace as the tubular lining epithelium show hypertrophic changes. Dystrophic calcification of tubules is seen in the medulla. The walls of the blood vessels become thickened and the lumina narrowed.

Extensive fibrosis of the medulla and cortex occurs due to the continuous stimuli that occurs due to the leaked constituents of urine from damaged tubules; the degenerative changes seen in the tubules is due to encircling fibrous tissue and alteration of blood vessels also due to encircling fibrosis.

Neoplasms: Primary tumors like embryonal nephromas are common in animals. Secondary tumors are more often common than primary. The author observed secondary of melanosarcomas in bovines and lymphosarcomas in cattle.

Diseases of urinary bladder: Persistent urachus is seen in foals but rarely in other animals. Urachus is the tube that connects the bladder to the umbilicus in foetus. Just before death, this is severed from the umbilical cord and becomes obliterated. But income instances, it is still patent after birth and is said to be pervious.

Diverticula of bladder may occur due to trauma seen at automobile accidents; gunt shot wounds and faulty catheterization. Obstruction to the urethra consequent to calculi, enlargement of prostate pressing the urethra, neoplasm urethra and inflammatory debris occluding urethra area responsible in causing rupture of bladder.

Prolapse of the bladder is seen especially in cows, mares, sows after parturition due to straining. The short broad urethra facilitates this condition.

Perineal herniation of the bladder may occur in male dogs during straining in Prostatic enlargement.

Bladder calculi are common in male and less in females.

Bovine enzootic haematuria or chronic bovine haematuria:

This is chronic disease of cattle that is observed in all parts of the world, in India especially in Northern part. it occurs in an enzootic proportions, various agents have been incriminated like coccidia, liver fluke infestation, piroplasms, schisotsomes, the fern plant Aspergillus kamala, high oxalic acid content food, deficiency of minerals in the soil especially phosphours, feeding on bracken fen etc. Braken fern (*Pteridium aquiline*) is toxic and damages to the liver. The urinary bladder is also affected. Transition cell papillomas of urinary bladder are seen with brken fern poisoning when fed at the rate of 300g/day for a period of 180 days.

Sun drying and drying at 80°C for 2 hours and hand pounding did not detoxify the toxins present in the braken fern. Serum minerals namely calcium, phosphorus, copper, zinc and iron levels are lowered in cattle affected with haematuria.

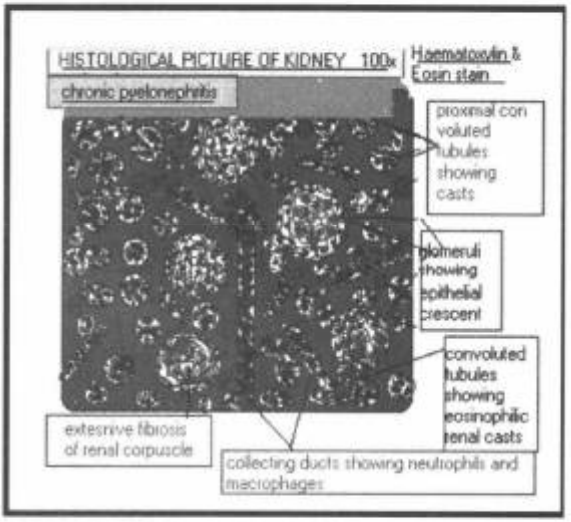
The course of the disease is chronic and may last for months or one or two years. The early symptoms are the presence of blood in the last few drops of urine. As the disease progresses the blood content increases and at later stages, pure blood may be passed. Secondary anemia supervenes with degenerative changes in various organs of the body. Animal becomes emaciated and finally dies.

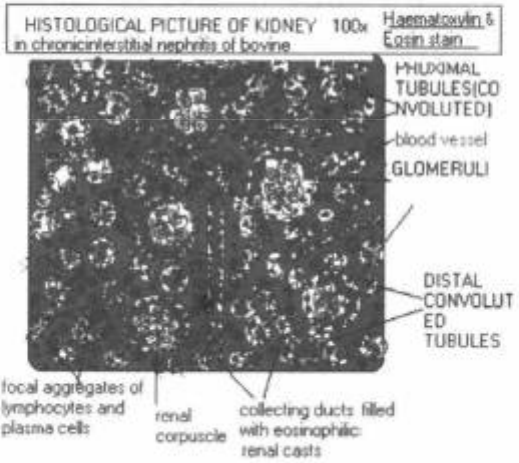
Grossly the lesions may be found on the mucosa of the bladder. In the early stages peticheal or ecchymosed may be found, which enlarge and become confluent as the condition progresses. The mucous membranes become thickened and red cauliflower like tumor masses develop on the walls. During excretion the irritant produce inflammation of kidneys which therefore manifest heaemorrhages.

Histologically in the early stages may be seen heaemorrhages on the bladder followed by hyperpalstic proliferation of the epithelium. Metaplasia to squamous or columnar epithelium is frequent. The hyperplasia may be of neoplastic dimensions and may be precursor to carcinoma that is precancerous stage.

The capillaries are also proliferating and growths similar to haemangiomas are observed. These are of two varieties. One is arranged as cavernous haemangiomas with thin walled, large dilated blood spaces. The secondary is capillary haemangiomas in which masses of endothelial cells invade the surrounding structures, even into the muscular coat.

Membranoproliferative glomerulonephritis.Dog. Note histological section showing thickening of capsallry basement membrane and extensive mesangial cell proliferation. Observe periglomerular fibrosis





Renal function tests

A basic understanding of the mechanism of kidney function is essential to an appreciation of the significance of urinary findings and renal function tests.

Analysis of this end product of kidneys function will often reveal alterations atypical of diseases of that organ but in addition may provide in formation concerning alterations in other physiologic processes in the body.

The kidneys are the chief organs regulating the internal environment of the body. Urine is a byproduct of these regulatory activities. To maintain a reasonable constancy of composition of the extracellular and to a lesser extent the intercellular fluids, kidneys become involved 1) in the body in excess of their amount required

for normal metabolic processes; 2) Elemination of inorganic elements according to the needs of the body; 3) Elemination of nonvolatile end products of metabolic activity; 4) Retention within body of substances required for the maintaining of normal functions. Included in this group are amino acids, hormones, vitamins, plasma proteins, glucose and so forth. 5) Elemination of certain foreign toxic substance. 6) Formation and excretion of substances such as hydrogen ions and ammonia.

The kidneys therefore lay an important role in regulation of water balance, electrolyte balance and acid and base balance. They also play an important role in the maintenance of osmotic pressures of body fluids and in removal of metabolic waste products as well as certain toxic substances.

Collection and preservation of urine specimens: Voided urine (mid stream samples) are to be collected, the vulva or prepuce should be cleaned of all contamination. Containers used for urine specimens must be clean. Catheterisation is employed in many species as a method of collecting urine specimens for analysis. The first portion of the urine should be discarded, as it is often contaminated with debris accumulated during catheterization. In the smaller domestic animals dogs, and cats urine can be obtained by cystocentesis. Urine specimens can sometime be obtained by manual compression of the urinary bladder.

The following observations are made in the collected urine.

1) Urine volume is noted
2) Colour
3) Transparency
4) Odour
5) foam
6) Specific gravity
7) pH
8) protein
9) glucose
10) Ketone bodies
11) blood
12) urinary sediments
13) casts
14) epithelial cells
15) microorganism
16) blood chemistry
17) renal clearance tests
18) renal biopsy

Table 8. Urine volume in different species of domestic animals

Species	Urine–volume/ml/lb.Body weight/24hours
Dog	12-30 ml
Cat	4.5-9.0 ml
Cattle	8-20 ml
Horse	2-8 ml
Swine	2-14 ml
Sheep and goat	4.5-18 ml

Urine volume: Increase in volume that is **polyuria** is seen transiently owing to diuretic therapy or increased fluid intake and following parenteral treatment of fluids or administration of ACTH or corticosteroids. Pathologic increases in urine volume occurs with chronic generalised nephritis, acute generalised nephritis, diabetes mellitus, diabetes insipidus, toxic nephrosis, primary renal Glycosuria, Pyometra, advanced renal Amyloidosis, hyperadrenocorticism, generalised pyelonephritis, compulsive polydypsia and some liver diseases, in hypercalcemia and hypomagnesemia.

Decrease in the volume output is known as **oliguria.** Seen with decreased fluid intake, high environmental temperature and hyperventilation. Oliguria is commonly associated with dehydration resulting from loss of body water as in diarhoea and excessive vomiting, with markedly decreased blood pressure, in acute nephritis, prolonged fever and circulatory dysfunction, and renal oedema hypovolemic shock, loss of fluids.

Anuria: complete failure of urination. This is seen in obstruction to the urethra, last stages of failure of kidneys. Anuria or oliguria is seen in animals suffering with glomerulonephritis. In Glomerulonephritis the swelling of the capillary endothelium, infiltration of inflammatory cells, the capillaries of the glomeruli are compressed and so blood flow through them is blocked, so urine is not filtered; Cloudy swelling and fatty degeneration of the tubular epithelium wherein the pressure within the kidney is raised so much by swollen cells than it obliterates the blood vessels. The tough inelastic capsule of the kidney does not permit any expansion of kidney and so the pressure of organism passed onto the vessels, compressing them; stagnation of the secreted urine; if the urine formed is not evacuated from the kidney due to obstruction, the back pressure thus exerted will oppose the filtration pressure thereby preventing the formation of urine; extensive destruction of tubular epithelium where in this condition there is diffusion of therein filtered by the glomerulus into the lymphatics and veins; extreme dehydration where in sufficient fluids are not present to be excreted out by the kidney.

Pyuria: Pus in the urine literally says presence of neutrophils consequent to the suppurative inflammation of kidney. **Haematuria:** Presence of blood in the urine.

Therefore the urine's coloured red. On centrifugation or standing of urine, the RBCs settle down leaving a clear supernatant fluid. This conditions due to hemorrhage from any part of the urinary apparatus. It maybe due disease of the urinary organs like acute neprhitis, pyelonephritis, cystitis, chronic bovine haematuria, urethritis, renal infarctions, truamtism, chemical irritant when administered like cantharides, turpentine, carbolic acid; calcui; acute septicaemic conditions like hemorrhagic septicemia, anthrax; presence of neoplasms like carcinomas of bladder or kidney; seen with parasites like Diactyohyma renale.

The colour of urine specimen should be noted and recorded.

Colour of urine	Disease condition
Yellow	Dehydration, fever, decreased blood pressure, reduce fluid intake, circulatory dysfunction with oedema,
Pale urine	Diabetes mellitus, diabetes insipidus, increased water intake, Pyometra, toxic nephrosis, Amyloidosis, Glycosuria, hyperadrenocorticism, pyelonephritis
Yellow-brown urine	Presence of bile pigments
Dark brown urine	Theilerosis, babesiosis, hemoglobinuric syndromes
Red colour	After administration of drugs like phenothiazine, phenolphthalein, azosulfanimide
Greenish blue colour	Methylene blue and dithazanine iodide administration
Red to violet colour	Phenolsulfonpthalein and sulfobrompthalein

Transparency: The transparency of urine is described as clear, flocculent or cloudy. Normally in most species of animals, although clear on being voided, may become cloudy as it rolls and precipitation of crystals occurs. Cloudy urine's observed when there is increase in cells in the urine like leukocytes, RBCs, epithelial cells bacteria, mucous, fat and crystals.

Odors: Normally ammonia Odour to certain extent could be perceivable. Ketone bodies impart a characteristic sweetish, fruity Odour and may be detected in urine in association with pregnancy disease, acetonemia and diabetes mellitus.

Foam: When shaken after collection, normal urine produces white foam that is limited in quantity. If there is proteinuria, the amount of foam produced is in excess and slow to disappear. If bile or bile pigments are present, the foam may be green, yellow or yellow brown, if haemoglobin present the foam is red to brown.

Specific gravity: The specific gravity of urineranges from 1.015 to 1.045. Increases in specific gravity of urine occurs due to increase in concentrations of urinary solids as seen in dehydration due to diarhoea or vomiting, hypovolemic shock, oedema associated with circulatory failure, burns with considerable loss of extracellular fluid and high fevers. Decreased specific gravity occurs following administrations of corticosteroids, diabetic insipidus, diabetes mellitus, primary renal Glycosuria and disorders of liver.

Acid-alkaline reaction (pH): The normal pH of urine varies with the type of diet the animal takes. Animals with vegetable diet have alkaline urine, where acid urine is normal in animals that are consuming either a cereal diet with high protein content or diet derived from animal protein.

Normal values for pH: Bovine: 7.4-8.4; Ovine: 7.4-8.4; Caprine: 7.4-8.4; Porcine: 6-7; Canine: 6-7; Feline: 6-7.

Protein: The amount of protein is estimated by the degree of turbidity and the best method is shaking, boiling. Others test's like Robert's test, adding concentrated nitric acid 1 part and saturated magnesium sulfate 5 parts (2 ml of reagent) to 2 ml of urine and found out the white precipitate in between the junctions.

Physiologic transient albuminuria is common in excessive muscular exertion, emotional stress, excessive ingestion of protein and convulsions. Certain drugs and chemicals may produce severe renal damage characterized by nephrosis, wherein the proteinuria is common. Amyloidosis also causes proteinuria, the Renal infraction, neoplasms, trauma and acidosis may also result in nephrosis and accompanying proteinuria. Hemorrhages in the urinary tract may be accompanied by high concentrations of protein in urine. Haemoglobin and myoglobin at traces are also give positive tests for protein.

Glucose: Reducing sugars in urine react with copper sulfate to reduce the cupric ions to cuprous oxide resulting in colour changes that is dependent upon the most of reducing substances present. These tests employed in Benedict's qualitative reagent wherein 2 to 3 ml of Benedict's copper reagent which is blue in colour is taken and boiled. Blue colour should stay. To this equal quantity of urine is added and boiled and cooled for couple of minutes. Persistence of blue or light green colour indicates absence of glucose in urine. Starting from dark green to brown to red colour indicates the presence of sugar. Usually dark green as: 5%, brown: 25%, dark brown: 50% and red: 100% of sugar indication in the test sample.

The development of colorimetric strip tests has simplified the detection of Glycosuria and provides an accurate method for estimation of glucose. These tests strip containing glucose oxidase, peroxidase and ortho- toludine. These appear strips produce a colour reaction when moistened with urine containing glucose.

Canine urine may contain high concentrations of ascorbic acid, which interferes with development of the colour reaction.

An emotional Glycosuria occurs as a result of fear, excitement and restraint. The administration of glucose solutions or general anesthetic may be followed by Glycosuria. Glucose in the urine is seen in diabetes mellitus, acute or chronic pancreatitis accompanied by hyperglycemia, chronic liver disease, and

hyperpituitarism with hyperglycemia, increased intracranial pressure, and enterotoxaemia in sheep due to *Clostridium perfringens* type D toxin.

False positive tests occur consequent administration of antibiotics like streptomycin, chlortetracycline, pencillins and chloramphenical, reducing sugars such as lactose, pentose, maltose or others, ascorbic acid, morphine, chloral hydrate, formalin, glucoronic acid, glucoronate, uric acid and salicylates.

Ketone bodies: These are acetone, acetoaceetic acid and β-hydroxy butyric acid. If Ketone bodies are present in the urine, there is a concomitant accumulation of these substances in the blood. The Rothera's test is used. The reagent consists of a powdered mixture of one part of sodium nitroprusside and 100 parts of ammonium sulfate. About one half inch of the powered reagent is placed in dry test tube, 5 ml of urine is added, and the mixture is agitated. 1 to 2ml of concentrated ammonium hydroxide is added to form layer about the mixture. If Ketone bodies are present a purple to black colour will appear, the depth of colour being dependent upon amount of Ketone bodies present in the specimen.

In cats and dogs the principal cause of ketosis is diabetes mellitus. However high fever, starvation may result in ketonuria in puppies and kittens. Ketosis in high producing milk cows that are improperly fed or that develop anorexia. Ketosis associated with hypoglycemia occurs, particularly in ewes carrying twin lambs.

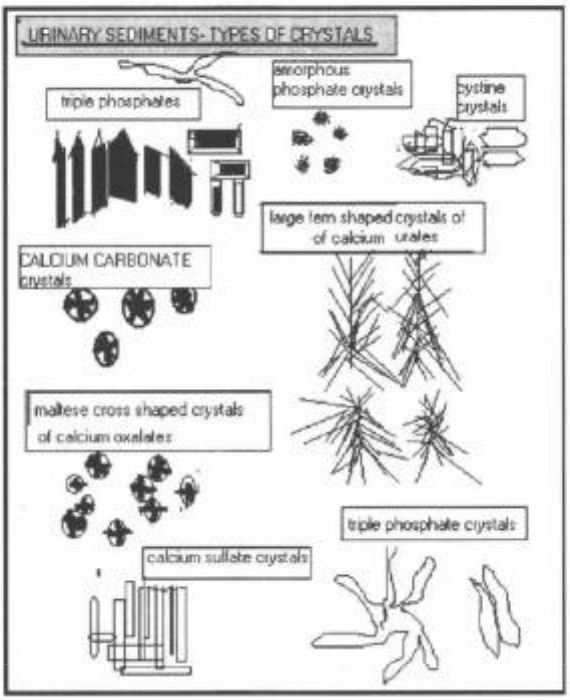
Blood is present in the urine. The simple test is Benzidine test. Haemoglobin contains a peroxidase which can liberate oxygen from hydrogen peroxide. This oxygen gives a blue colour in the presence of benzidine. In a test tube dissolve a small quantity of benzidine glacial acetic acid. Added 2ml. of urine to this. To this one ml. of fresh H_2O_2 and mix. If blood is present a blue or green colour develops.

Differentiation between haematuria and haemoglobinuria is important. Haemoglobinuria occurs as a result of an excessive hameolysis of RBCs as seen in leptospirosis, piroplasmosis, babesiosis, photosensitisation, chemical hameolytic agents such as copper and mercury, consumption of certain plants, severe burns, an incompatible blood transfusions and haemolytic disease of new born, *clostridium hameolyticum* causes bacillary haemoglobinuria and haemoglobinuria which occurs postparturiently.

Dye excretion tests:

Phenolsulfonphthalein (PSP) clearance test- a dose of 5 mg/kg is used. 3ml of blood samples are withdrawn. Normal values for dog are 18 to 24 minutes.

Empty the bladder by catheterization or permit the dog to micturate to remove the majority of accumulated urine. Inject 6mg of PSP (phenol sulfonphthalein) dye intravenously noting the exact time of injection. Contents of the bladder are gently aspirated with a syringe, and all urine is collected in flask. The procedure should be complete exactly 20 mts following dye injection. Calculate the amount



of dye that has been excreted according to the following technique; place all urine and dye collected in a 1 litre graduated cylinder and dilute with water to 400 ml. Add 10 ml of 105 sodium hydroxide and mix well. A pink colour will develop following addition of the sodium hydroxide. If the colour is deep pink add enough water to bring the total volume to 1000 ml. if the alkalinized urine is light pink, add sufficient water to bring the total volume to 500 ml and divide the final result by 2. The quantity of dye excreted can be found in by measurement in a spectrophotometer set at a wave length of 560 ml. Normal dogs excrete 33 to 55% of the dye in 20 minutes.

Sodium suphanilate clearance test:-

Suphanilate is removed from the blood by glomerular filtration. Measurement of sulanilate clearance should therefore be a method for evaluating glomerular filtration. The sulfanilaate clearance test is completed as follows. Inject sodium sulfanilaate i/vly in a 10% solution at a dosage of 20 mg/kg of body weight. After injection draw blood samples of 2 to 3 ml at 30, 60, and 90 minutes. Determine sulfanilate concentration of whole blood. Plot results on semi log co-ordinate and calculated T 1/2 Normal half value for dogs is 66+11 minutes.

Inulin and paraminohippuric acid clearance test: 100 mg of Insulin/kg body weight is used. 10, 20, 30 and 60 minutes time issued as a clearance test.

BUN tests (Blood urea nitrogen): Non-protein nitrogen substances include urea, creatinine, creatine, uric acid, ammonia and amino acids. Among this urea is the predominant nitrogenous substance present in mammals in blood. The anticoagulant of choice for collecting of blood is the EDTA (Ethylene diamino tetracetic acid). A variety of laboratory techniques like chromatographic technique, mercury combining power with nitrogen and dipstick methods are used. In laboratories where spectrophotometer is not available mercury combing power for nonprotein nitrogenous substances is the choice.

For this

10% TCA: Add 10 gm of TCA to 50 ml of distilled water. Dissolve and dilute to 100ml; 5% mercuric chloride: dissolve 5 gm of mercuric chloride in 50 ml of distilled water and dilute to 100 ml ; saturated solution of sodium carbonate.

Procedure; 1.Add equal quantities of whole blood and TCA of 5 ml each. Add the blood drop by drop to the acid, mixing thoroughly. 2.Centrifuge for 5 mts or filter. 3. Pour off the clear supernatant or filtrate into a clean tube. 4. Place 5ml of the supernatant or filtrate into a small, 50 ml beaker. 5. Add 1.5 ml of 5% mercuric chloride to the filtrate and mix completely. 6.Add additional mercuric chloride a few drops at a time. Test a small quantity of the mixture by placing a drop of the mixture on spot palate and adding one drop of the saturated sodium carbonate. This should be continued until a drop of the mixture and a drop of sodium carbonate result in dark brown precipate 7.Calculate the blood urea level by recording to the total quantity of mercuric chloride required to result in a brown precipate. Each 0.1 ml of mercuric chloride is equal to a blood urea value of 4 mg/ dl.

Urinary casts: Casts are organic pertinacious substances originating from renal tubules and are excreted into the urine. Presence of casts in the urine known as cylindruria. Casts may also contain tubular epithelial cells. Presence of casts in urine is indicative of some type of nephritis and is of diagnostic value. Hyaline casts are pale, often colorless homogenous and cylindrical in shape. They have straight parallel sides and rounded ends. These casts dissolve in acetic acid. Hyaline casts are found in congestion and in inflammation of kidney.

Granular casts are either coarsely granular or finely granular. They may be curved or straight with rounded or broken ends. The granular materials composed of albumin, fat, epithelial cells or disintegrated RBCs.

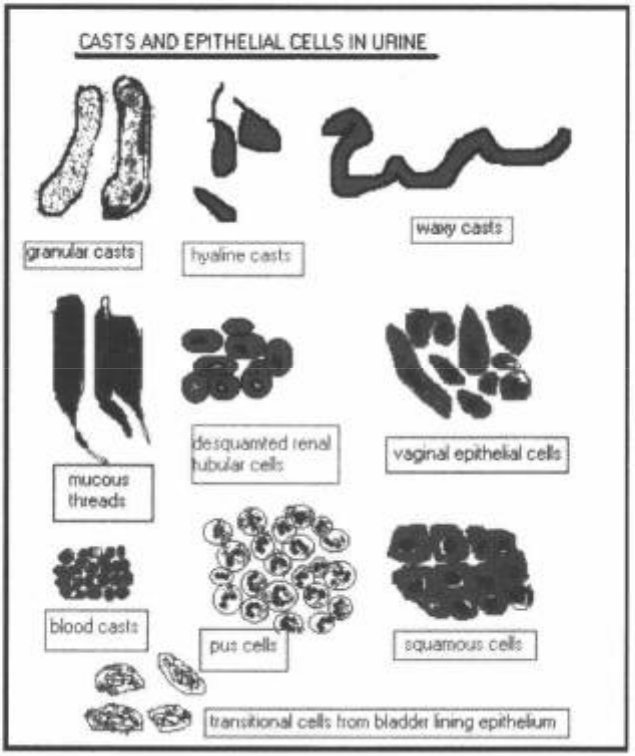
Epithelial casts contain epithelial cells of the tubules and indicate acute neprhtitis. They may be yellowish due to imbibition of blood pigment. When the condition changes to sub acute or chronic, these casts may become fatty or waxy.

Waxy casts are more opaque than hyaline casts and are yellowish in colour. They are found in chronic nephritis. They are found in the amyloid degeneration of the kidney.]

Blood casts are found in acute nephritis, renal heaemorrhages and in acute congestion of the kidneys. They are formed of RBCs so they are coloured red.

Fibrin casts are found in cases where there are heaemorrhages. They maybe yellowish due to altered blood p pigment.

Pseudocasts have no connection with renal disease but occur duet conglomeration of various substances on mucous threads. Urates and phosphates may aggregate together to resemble casts. Fatty casts, pus casts, cylindroids bacterial casts are pseudocasts. Cylindroids contain mucous and some fat globules.



Urolithiasis

Urolithiasis is a disease condition due to presence of stones or calcui in any part of the urinary tract. Nephroliths are the presence of calculi in kidneys. Cystoliths presence of calculi in urinary bladder. Uroliths presence of calculi in anywhere in the urinary tract. Microconcretions or Nephrocalcinosis is the first step in the formation of Calculogenesis.

The uroliths may be micrconcretions or macroconcretions. Small concretions (microconcretions) formed in these places may be carried by the urine into the ureters and urethra.

The disease caused by uroliths is among the most important urinary tract problems of domesticated animals. Several factors are important in predisposing to calculus formation, and several are important in precipitating disease. Calculogenesis is governed by certain factors like urinary pH, reduced water intake, in relation to the degree of urine concentration, deficiency of vitamin A and presence of infections in urinary tract.

In these conditions, urine is often supersaturated with respect to the components of stone forming salts, and this super saturation leads to uroliths formation (nucleation).

The disease caused by uroliths is among the most important urinary tract problems of domesticated animals. Several factors are important in predisposing to calculus formation, and several are important in precipitating disease. Calculogenesis is governed by certain factors like urinary pH, reduced water intake, in relation to the degree of urine concentration, deficiency of vitamin A and presence of infections in urinary tract.

In these conditions, urine is often supersaturated with respect to the components of stone forming salts, and this super saturation favors uroliths formation (nucleation). Saturation may be in the unstable region, where spontaneous precipitation occurs, or in the metastable region where precipitation occurs by epistaxis or heterogeneous nucleation. Thus a foreign body such as suture or a grass awn can act as a nidus for uroliths formation. Though horses suffer with crystalluria with supersaturated calcium carbonate solutions, low prevalence of calculi is seen in these species. Deficiency of inhibitors of crystallization may be important in calcium oxalate and calcium phosphate carcinogenesis.

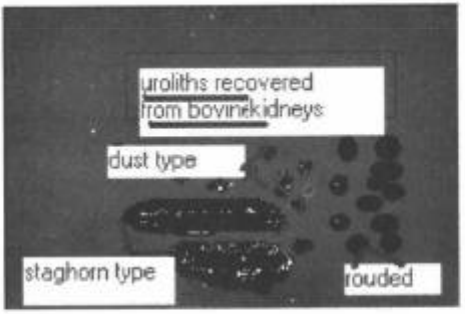
In general calculi are important in cattle, sheep, dogs and cats and less important in horses and unimportant in pigs. In dogs, several breeds are predisposed to formation of calculi, namely Dachshunds, Dalmatians, Cocker spaniels, Pekingese, Basset hounds, Poodles, and Small terriers.

Type of calculi: Silica calculi, struvite calculi, oxalate calculi, uric acid and urates calculi, cystine calculi, clover stones, xanthine calculi, tetracycline and barium stones.

Urolithiasis has been associated with the use of hormones or their analogs for stimulating growth in feed lot lambs. Lambs which are fed diethyl-stilboestrol or have had implantation of this compound; may develop urinary obstructions in several days. In man renal calculi has been observed with parathyroid hyperactivity.

The size and shape of urinary calculi vary with the species of animal, place at which they are formed, and their composition. Urinary calculi are variable in size and shape. These may be lodged either in the cortex, medulla or in the pelvis of the kidney.

These calculi may be round to irregular in shape, white or brown or metalloid with luster. The author's observation in the bovines was that (stag horn) the calculi were single large size to that of multiple smaller ones. The larger ones were weighing around 8 gm and smaller ones to 0.117 gm. multiple calculi were innumerable in number that is in hundreds. They are lodged either in the calyces, or in the renal pelvic fat or in the cystic cavities of the pelvic region.



The more common calculi in the horse containing calcium carbonate and phosphate and magnesium carbonate. In ruminants, calcium, magnesium, and aluminum salts of phosphoric acid compose the calculi. The present author observed that the chemical composition of renal calculi from Karnataka region of India was predominantly of calcium carbonate type. Reports from North America and Western Australia revealed that the stones found in beef cattle were made up of ammonium magnesium phosphate and in range herds where that of silica type.

The silica calculi of ruminants are hard, white to dark brown, radio-opaque and often laminated as much as 1 cm across. The bladder stones of silica calculi of ruminants are spherical, ovoid or mulberry shaped and has smooth surfaces, but in the kidney they are angular and irregular.

Pure silica stones contain about 75% silica as silica dioxide. Mixed calculi contain some calcium oxalate or carbonates. Silica calculi contain about 20% organic matter. Most have a friable core, which is high in amorphous silica and low in organic matter; which separates it from the outer concentric lamination; which is high in silicon. Silica calculi are present in more than 50% of steers on cattle of Western Canada; fewer than 5% develop urethral obstruction.

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polymerized silica acid. Rumen fluid is saturated with respect to silica acid. After absorption, some is returned to the gut and digestive secretions contain less than1% of dietary silicic acid and are excreted in the urine, and as much as 60% is reabsorbed from the filtrate. However when urine production is very low either because of the nature of the diet or because of the high insensible fluid losses in hot climate the concentration of silicic acid in urine may reach five times the saturation level. Even so, precipitation from solution requires other substances, probably proteins of renal or serum origin, in the urine. It has been tried that calculus formation could be reduced to sub clinical level by adding salt to the ration, there by ensuing high water consumption.

Struvite calculi that are magnesium ammonium phosphate calculi (triple phosphate calculi) are important in dogs, cats and ruminants. In female dogs, these are more common perhaps the reproductive infections are common. Bacterial ureases from staphylococci and proteins induce super saturation of urine with triple phosphates by increasing urine pH and ammonium ions.

In cats, addition of 0.15 to 1.0% dry weight of magnesium induces struvite calculi formation in urinary bladder. In ruminants, struvite calculus develops in adult cattle when they have been fed with high grain rations. Calculi are gritty with high proportion of matrix. Inhibition of urethral growth but early castration predisposes to obstruction and increased water consumption, tends to prevent obstruction.

Diets high in phosphates can cause a very high incidence of calculi in sheep; calcium and phosphorous ratio of 1: 2 or wider appears to be the critical factor. Additional potassium tends to promote phosphate urolithiasis. Genetic tendency is also involved. Urolithiasis is more likely to occur in sheep that excrete phosphates in urine than that of faces.

Uric acid and urate calculi: These calculi are usually multiple, hard, concentrically laminated, yellow to brown and moderately radio dense. In the bladder, they are frequently spherical and less than 5mm across. Most contain ammonium urate with some uric acid and phosphate, in others sodium urate is the predominant salt.

Urate stones are common in Dalmatian dogs, but also occur in pigs and rarely in cats. Dalmatian excretes high levels of uric acid in their urine. Normally in all animals uric acid is converted to allantoin by the liver enzymes. In the Dalmatian, these enzymes are absent; hence uric acid is excreted in the urine.

Cystine calculi are small and irregular. Soft and friable, these are also waxy and yellow in colour. And on exposure to air and light it turns as green. Many cystine calculi consists of pure cystine, others may contain calcium oxalate, triple phosphates, brushite (calcium hydrogen phosphate dehydrate) and complex urates.

Cystines stones occur in dog especially Dachshunds and rarely in cats. Cystine

calculi occur in male dogs, but cytinuria is recorded in females. Blood cystine levels are normal.

Cystine precipitates in acid urine, but factors other than urinary pH probably are important in the genesis of cystine stones. Genetic factor have been attributed.

Xanthine calculi: Xanthine stone are yellow to brown red, often concentrically laminated, friable and irregularly shaped. They are radiolucent. Xanthine is a metabolite of purine and seldom appears in urine because normally it is degraded by xanthine oxidase to uric acid. Xanthine calculi appear in sheep and calves and occasionally in dogs. A high incidence in sheep was circumstantially related to deficiency of molybdenum. And these are fed on these pastures. Molybdenum is a component of xanthine oxidase. Xanthine precipitates in acid urine. Calculi usually form in the collecting ducts and may cause hydronephrosis.

Other types of calculi: The tetracycline and barium stones are common in animals. Stones with high carbonate content are associated with alkaline urines and are seen in ruminants consuming high oxalate plants or clover dominated pastures.

Clover stones: These are present in sheep grazing estrogenic pasture, particularly sub-terranean clover or injected or implanted with oestrogens. Three factors are operating for the formation of these calculi. One is the urethral obstruction by desquamated cells, and secretions of accessory glands originating in the urethral udder the influence of oestrogen.

The second type is so called clover stone, is usually found in the renal pelvis as a yellow, soft material, which leads eventually to fibrosis and shrinkage of kidney.

Thirdly sudden and serious mortalities occur in male grazing on subterranean clover during the period of rapid maturation. Urethral process becomes impacted with soft paste consisting of mainly calcium carbonate.

Oxalate Calculi: Oxalate calculi are hard, heavy, white or yellow, and typically covered with jagged spines, though some are smooth. They tend to be large and solitary in the bladder. Oxalate calculi occur as calcium oxalates. Hypercalciuria are involved in the development of calculi.

Oxalic acid is synthesized from glyoxylic acids and ascorbic acids and may be ingested in certain foods. Hyperuricosuria maybe involved in oxalate precipitation. Oxalate containing plants ingestion is not important, since oxalate is metabolized in the rumen.

Feeding a low calcium diet that is as low as 0.3% produced oxalate urolithiasis in steers; this is due to bone resumption that is hydroxyl praline liberation and oxalate synthesis.

Summary of Calculogenesis: However urinary calculi form is not very clear. The following factors singly or in combination maybe the cause;

1. Vitamin A deficiency: In vitamin A deficiency, the transitional epithelium of the urinary tract undergoes metaplasia into keratinized stratified squamous epithelium. The keratinized cells get exfoliated and may form the nidus of calculi.
2. Infection of urinary tract by streptococci, *Escherichia coli* and micrococcus may occur when formation of calculi maybe facilitated because the exudates and bacteria may not form the nidus but the reaction the medium may be suitably altered for deposition slats.
3. **Concentration of salts:** The organic and inorganic salt content of the food and water has an influence on formation of calculi. If the feed consists of concentrates with inadequate water, then calculi may be formed. Also if drinking water contains a high percenretage of minerals formation of calculus is facilitated, because in these circumstances the mineral concentration of urine is increased. Hypervitminosis D may cause hypercalcemia and so Hypercalciuria. Curtailment of water, excessive sweating and ingestion of plants with high oxalic acid content increase the salt concentration of urine.
4. **Deficient green feed:** It was found that when animals were maintained on dry concentrates without Alfa or green forage, incidence of urinary calculi was greater. This was due to the excretion of mucoprotein in the urine in the absence of green fodder. These immunoproteins act as nuclei for the calculi.
5. **Hormones:** Diethyl stilboestrol when given to fattening lambs; this has metaplasia action on the urinary epithelium, which is transformed to keratinized epithelium. The desquamating cells for nuclei for the deposition mineral salts. The calculi that form in the bladder may cause obstruction of the urethra. In man tumors of parathyroid wherein hypercalcemia and associated urolithiasis is seen.
6. Prolonged confinement as seen in man with recumbence and confined to bed for long periods with inability to move their limbs, the bones are decalcified and phosphatic calcui are formed in the bladder.

Sequleae of calculosis: Calculi are harmful as they irritate the urinary passage and cause inflammation. They obstruct to the passages and the results depend upon the place of obstruction. If the obstruction is in the urethra, there is retention of urine with attendant uremia and dilatation the bladder. In some extreme cases there is rupture of the urinary bladder with fatal results. If the obstruction is in the ureters, atrophy of the corresponding kidney and hydronephrosis results, if there is partial obstruction.

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Chapter 6

Pathology of Female Reproductive System

Summary

Embryology of reproductive organs; Ovaries, Tertiary follicle, Oestrous cycle, White heifer's disease; Cystic disorders of ovary, Cystic follicles; Cystic rete ovarii; Cysts round the ovary; Para-ovarian cysts; Neoplastic diseases of ovary; Granulosa cell tumor; diseases of salpinx, diseases of uterus; Abortions in animals; Bang's disease.; Brucella suis infections; Slamonellosis in animals; Weil's disease, circling disease; Symptoms: Nervous form Viruses that cause abortions in animals; Pathogenesis; Blue tongue during pregnancy Mycotic abortions; Trichomonas foetus; Causes of sterility in uterine diseases; Miscellaneous disease conditions of uterus; Diseases of cervix and vagina.

Pathology of female reproductive system

Embryology: 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. The gonads originate as thickenings and known as gonadal ridges on the medial side of the mesonpehros. The gonadal ridge is the mesenchymal thickening covered by mesothelium. The mature male and female germ cells are direct descendants of the primordial germ cells, which in human embryos appear in the wall of the yolk sac at the end of the third week of development. These are endodermal derivative. These migrate to the gonadal ridge through mesentery, and the overlying cuboidal epithelium which is superficial, invades the under lying mesenchyme. Thus at this stage, germ cells, which arises from the endoderm of the yolk sac of the embryo, have migrated to bilateral swellings of pelvis mesoderm (genital ridges) and overlying the mesonpehros (primitive kidney) to form paired bipotential gonads. At about the same time, small mesonephric tubules form the mesonpehros also grow caudally and fuse to form a pair of ducts, the para-mesonephric ducts (Wolffian ducts). At about the same time a second pair of ducts, para-mesonephric ducts (Mullerian ducts) forms on the ventral aspect of each mesonpehros. The caudal most portion of para-mesonephric duct fuse with each other on the midline, and form Y-shaped-configuration.

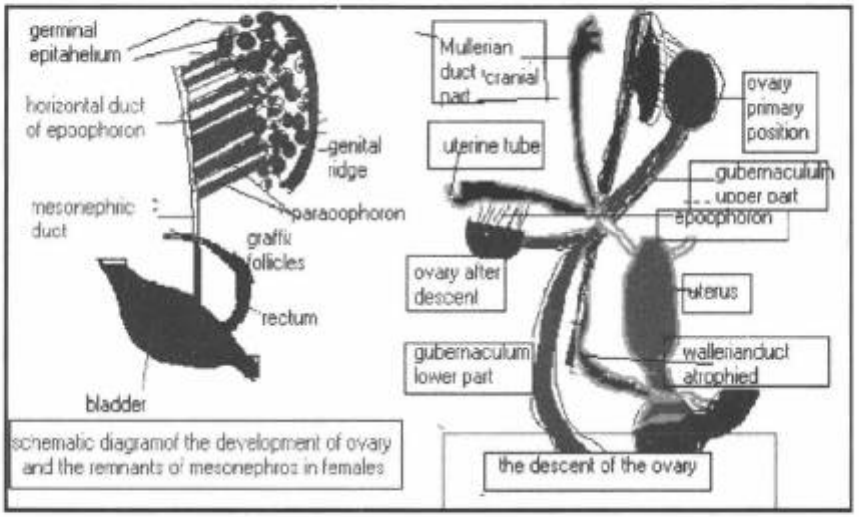


Fig.6.1.Embryological changes in the female reproductive organs of mammals

The cranial most portion of the duct becomes convoluted and forms the oviduct. Unfused portion as uterine horns and fused portion as body of uterus, cervix and cranial parts of the vagina. The various adult uterine shapes found in different species are based upon the extent of fusion of the para-mesonephric duct, greatest amount in the horses and least amount in the pigs. The greater is the fusion, the greater part of the uterus that comprises the body.

The critical stage of genital development involves differentiation of the bipotential gonads into the testis and ovaries. Upon entering the genital ridges, after migrating from the yolk sac, the primitive germ cells increase in number by mitosis in the superficial mesenchyme of the bipotential gonads. During this period of active proliferation, the germ cells loose their mobility and become somewhat smaller and thus are transformed into oogonia or spermatogonia.

Gonadal differentiation is determined genetically and involves the expression, or lack, there of a gene normally found on the Y-chromosome of the male. This gene is referred to as the SRY gene or sex determining region of the Y-chromosome and codes for a protein referred to as testicular determining factor (TDF).

Thus the determination of genetic sex is fixed at the time of fertilization. Y-chromosome is strongly male determining. The bipotential gonads of embryo not having the SRY gene (XX-genotype) automatically differentiate into ovaries. Ovarian differentiation occurs somewhat later in gestation than that of the testicles and in histologically less striking.

In the developing embryo, the genital tract of both sexes consists of Wolffian and Mullerian ducts. The Wolffian ducts, the primordial for male accessory organs,

originate from the excretory canals of the primitive kidney, the mesonpehros. The female counterparts, the Mullerian or paarmesonephric ducts sprout from longitudinal invasions of coelome epithelium adjacent to urogenital ridges. The ducts arise and parallel to Wolffian ducts but unlike the Wolffian ducts opens directly into the coelome cavity. The Wolffian ducts remain connected to the mesonephric tissue by a series of tubules. Female differentiation occurs in the absence of gonadal hormone. Masculine differentiation is imposed on the system at an early age, and thus differentiation prevents further female development. All sexual development would be feminine if not prevented from being so by testicular hormones. In the presence of Y-chromosome as already told a protein H-Y antigen, a product is synthesized and embryonic gonad becomes testis. Male differentiates very early and female very late. The foetal testis produces two hormones critical for normal male differentiation. The Sertoli cell of developing testis secretes a Mullerian duct inhibitory factor, the anti-Mullerian hormone that brings about Mullerian duct regression. At the same time the Leydig cells of testis secrete testosterone, which prevents Wolffian duct regression and brings about its differentiation, into vasa differentia, seminal vesicles and epididymides. The testosterone is also converted into dihydrotestosterone, and this hormone induces development of penis and scrotum from the bipotential external genital primordial.

Most evidence suggests that the onset of secreting of hormones by early testicles and ovaries is an autonomous event, whereas inter embryonic development gonadal hormone, a production of gonadotropin dependent that is chorionic gonadotropin in primates, pregnant mare serum in horses, and leutenising hormone or interstitial cell stimulating hormone in other species.

It should be noted that carnivores and certain non-human primate's species onto develop seminal vesicles and dogs lack bubo urethral glands.

With the onset of sexual maturity, the internal and external gnitalia of both sexes undergo further growth and development leading reproductively competent genital tracts. These final stages of development are largely sex hormone dependent.

It has already been stated that the fusion of para-mesonephric duct creates different uterine shapes in different species. Duplex uterus is found in rabbits, whereas cervix and body of uterus is divided into two portions and there are two uterine horns. There is infact no uterine body. Uterus bicornis is present in the pig and cow. Here there is only one cervix, uterine body is small and there are uterine horns. Uterine bicornis with a large body of uterus is present in the mare. This is also called as bipartite uterus. There is one cervix, uterine body is present and there are two uterine horns. Uterus simplex is an example for the woman. Here there is one cervix, uterine body is prominent and uterine horns are absent.

The shape of ovary varies greatly with the species and depends largely on whether the female is polytocus or monotocus. In the monotocus the ovary is ovoid. The ovary of the cow is approximately 10 to 15 mm long and is almond shaped. Right ovary is usually larger than the left, since it is physiologically more active. Ovarian weight varies from 5 to 15 g per ovary, with both ovaries weighing around 19.5 Gms. The pocket formed by the utero- ovarian ligament and the mesovarium is called the ovarian bursa or ventricle. The ovarian follicle measures 1 to 2cm, whereas corpus leutea measures 2 to 3cm. The corps leutea weighs around 3 to 9 Gms. Its consistency is liver like. The corpus albicans replacing the corpus leutea of pregnancy persists indefinitely.

The weight of the sow ovary is around 20 g and is 30 to l60 mm long. It is mulberry shaped and the follicles and corpora leutea bulge from its surface. Mature follicles in the sow are around 8 to 10 mm in diameter. The sow's ovaries are almost completely covered in the bursa ovariii but the mesosalpinx.

The ovary of the bitch is oblong and is approximately around 20 to 30 mm long and is completely enclosed within ovarian bursa. The width is 7 to 12 mm and 5 to 8 mm in when rolled between the fingers.

The ovary of the mare is kidney or bean shaped with a notch like depression known as ovulation fossa. The diameter of adult ovary is around 51 mm long 28 mm wide and 32 mm high. C.L. of mare is cauliflower shaped about¾ to 1 inch in diameter, within the substance of the ovary. It cannot be palpated except for several days after ovulation in the region of ovulation fossa. It does not project above the surface of the ovary, because of the dense, thick tunica albuginea investing the ovary of the mare. The free border or concave portion of the ovary in the mare is spoken of as the ovulation fossa.

The ovary consists of stroma of network of connective tissue and blood vessels surrounded by a covering of peritoneum except at the attached border or hillus where the vessels and nerves enter. Within the ovary are interstitial cells, primitive ova, developing or secondary ova or follicles, atretic or degenerating follicles and developing mature or degenerating corpora leutea. The ovary is supported and attached but the portion of the broad ligament called mesovarium dorsally and laterally and but the utero-ovarian ligament medially. The blood supply to the ovary is from ovarian artery and a branch of utero-ovarian artery. The nerve supply is the autonomic nerves from the ovarian plexus that arises from the renal and aortic plexuses. Ovaries increase in size as the animal becomes older.

The uterine tube is divided into four anatomic segments, namely infundibulum, ampullla, isthmus and uterotubal junction. The infundibulum is 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 ampullla form the proximal 2/3rd 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 mean length of the uterine tube in cows is 20 to 35 cm long. The uterine tube of the sow is 15 to 30 cm long. The uterine tube of the mare is 20 to 30 cm long. The uterine tube of the Beagle bitch is around 6 cm long. The uterine tube of the queen (female cat) is 5 to 6 cm long.

The uterus of domestic animals consists of a cervix, a uterine body and two uterine horns. The uterus is a muscular membranous structure designed for the reception of fertilized ovum. The form of uterus in animals varies with the degree of fusion of the paarmesonephric ducts; the endometrium of uterus in domestic animals is the only structure that can form sufficient placental attachment to result in the normal development of embryo and foetus. In uniparous animals the placenta lies against the cervix, while in multiuparous animals the placenta does not touch the cervix.

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 measures from 20 to 45 cm long. The two uterine horns leaving the body of uterus at an acute angle and lying nearly parallel to each other. The uterus is located on the floor of the pelvis or on the pelvic brim.

In mare the uterine body is much larger than any other species and is the same length of the uterine horns. The uterine horns measure 14 to 15 cm in length and 3 to 4 cm width. The non-pregnant uterus is a cruciform or T-shaped with horns perpendicular to body of uterus. The uterusis suspended in pelvic and abdominal cavities. Unless gravid the uterus usually does not lie on the floor of the pelvic or abdominal cavities.

In the sow the body of the uterus is 3 to 5 cm long and the uterine horns are extremely long and tortuous. These are freely movable because of long broad ligaments. In pregnant animals the horns may be 1, 2 to 1.8 meters long.

In ewe and doe (female goat) have big uterine horns.

In the bitch the uterine body is short and the uterine horns are very long and of uniform in diameter. In the nulliparous medium sized bitch the uterus has a short body of 2.5 cm. long with straight horns of 12 to 165 cm. long and 0.5 to 1 cm. in diameter. These horns diverge at an acute angle toward the pole of each kidney. In cats the uterine horns is similar to that of bitch.

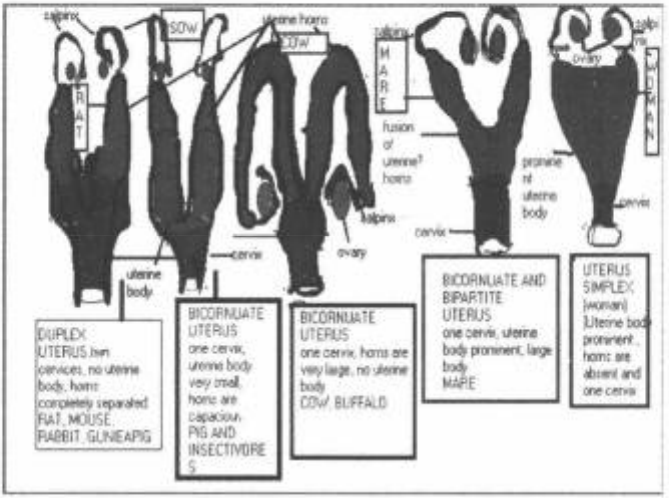
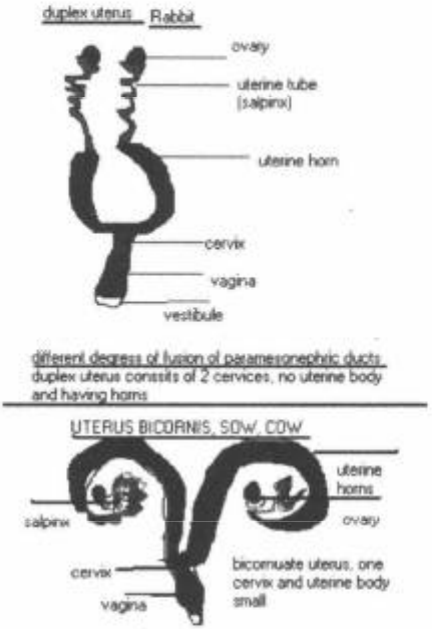
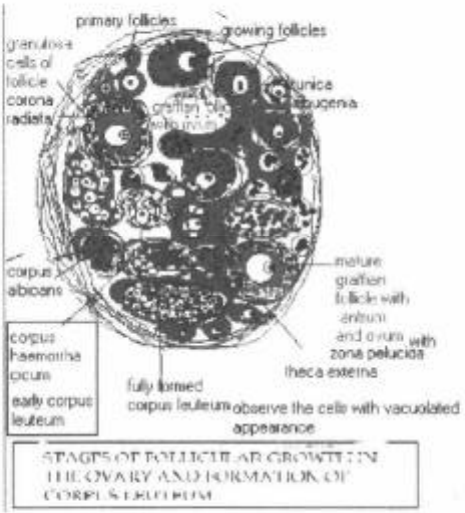


Fig.6.2. Different-types-of-fusion-of-paramesonephric-ducts



The cervix is a powerful tubular sphincter muscle between the vagina and more rigid than are the walls of either uterus or vagina. Cervix in the cow is about 5 to 10 cm in length and 1.5 cm to 7 cm in diameter. Cervix is usually located either into the pelvic cavity oar in the pelvic brim or in the abdominal

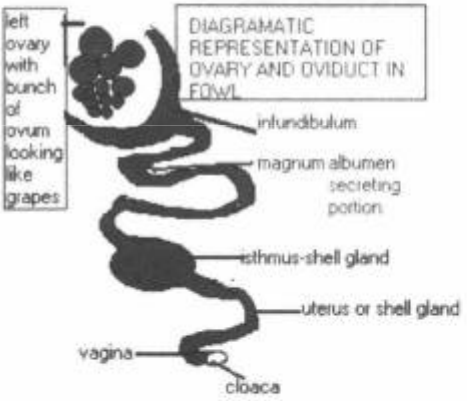


cavity. The cervix of them is 5 to 7.5 cm long and 2.5 to 5 cms in diameter. It is suspended in the pelvic cavity. Cervix of ewe is about 2.5 to 5 cm long and is similar to that of cow.

Vagina is muscular membranous structure lying in the pelvic cavity dorsal to the bladder that acts as a copulatory organ and passage of foetus at the time of parturition.Vagina of cow is about 25 to 30 cm long. Vagina of mare is about 18 to 23 cm long. Vagina of ewe is 7.5 to 10 cm long and vagina of sow is 7.5 to 11 cm long .Vagina of bitch is 10 to 14 cm long and 1.5 cm narrow.

Vulva is comprised of two labia the dorsal and ventral commisures and the clitoris and the vestibule located between the vulva and vagina. Vestibule in cow is about 10 to 12.5 cm long.

Reproductive tract of birds



In aves left ovary and oviduct are only functional. The avian follicle has not antrum and follicular fluid, the ovum filling follicular sac completely. No structure comparable to the mammalian corpus leutea is formed in birds ovulated follicle persists for a long time. Avian oviduct is divided five major portions namely infundibulum, magnum, isthmus, shell gland (uterus) and vagina.

Ovaries

The ovaries except those of the mare are subdivided into cortex or zona parenchymatous and medulla or zona vacuoles. At the hillus, where the mesovarium is attached, the medullary substance extends through the cortex and the tunica albuginea to the surface. The connective tissue frame work or stroma of the cortex condenses on the surface of the ovary to form the tunica albuginea, which is covered by germinal epithelium.

In young animals, the germinal epithelium consists of a single layer of cuboidal or columnar cells, which are flattened in the adult and become interrupted by scar tissue. It is continuous with the epithelium of the oviduct and with the peritoneal mesothelium.

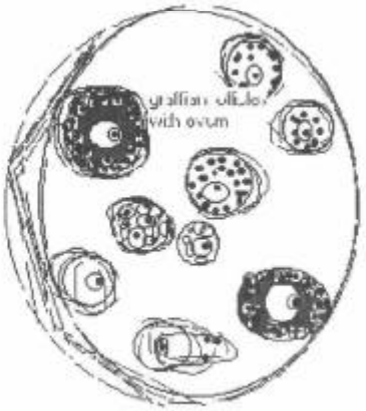
The tunica albuginea may be up to 100μ in thickness. It is richer in collagenous fibers and somewhat poor in cells than the cortical stroma, into which it blends. Usually the fibers are irregularly interwoven, but occasionally they are arranged, in lamellar as in man. The albuginea lacks elastic and reticular fibers.

The cortical stroma is very rich in cells but is free from elastic tissue. The cellular structure is reinforced by reticular fibers, which cannot be demonstrated by usual stains. The aggregated connective tissue cells have elongated nuclei and occur in dense strands. Their direction is parallel to the surface of the ovary or the follicles and blood vessels which hey enclose.

The stroma of fibroblasts is capable of further differentiation, dye storage and proliferation. In response to certain stimuli they may leave their cellular associations and differentiate into wandering macrophages. They may round up, store lipids and assume an epitheloid character, performing nutritive and secretory functions in the follicles and occurring single or in clusters in the stroma as the interstitial cells (of bitch and cat). These various functional forms may revert to stromal fibroblasts at any time. In the mare pigmented cells are present. These decrease in number with age.

The cortical stroma contains the ovarian follicles, the various stages of development and regression. The follicles are very numerous (in swine about 60, 00 n each ovary) and are of varying size, usually becoming larger from the periphery in ward. They occur in two main layers. Immediately below the tunica albuginea, the small primary follicles are evenly distributed (in ruminants) or clustered in groups (in carnivores). In the deep layers, which are more favorable to their development lie the larger graffian follicles.

In the embryo the germinal epithelium covering the genital ridge contains the primordial sex cells. It forms cord like proliferations which invade the underlying mesenchyme to form the inner epithelium mass of the developing ovary. This epithelium, which contains primitive oogonia surrounded by smaller cells, degenerate early and is replaced by the connective tissue in medulla. The cortex is formed by a new proliferating germinal epithelium in which there are large mitotically active sex cells, the oogonia. These finally stop dividing and begin to grow into primary oocytes. The mesenchyme growing toward the periphery breaks up the epithelium into primary follicles that consisting of an oocytes surrounded by smaller cells. These are more numerous in young animals. The mesenchyme continues to proliferate and forms the cortical stroma and the tunica albuginea, the latter of which separate the germinal epithelium from the cortex. It has been claimed that no new primary follicles are formed after the consolidation of tunica albuginea but there is evidence that new follicle may be formed throughout life at least in some species like bitch by in growth of epithelial cords through tunica albuginea. The mature male and female germ cells are direct descendants of the primordial germ cells which in human embryos appear in the wall of the yolk sac at the end of the 3rd week of development. These cells migrate by amoeboid movement from the yolk sac towards the developing gonads where they arrive at the end of 4th or 5th week.



Oogenesis: once the primordial germ cells have arrived the gonad of genetic female, they differentiate into oogonia. These cells undergo number of mitotic divisions, and by the end of 3rd moth, they become arranged in clusters which are surrounded by a layer of flat epitheloid cells. While all the oogonia in one cluster are probably derived from a single primordial germ cell, the flat epithelial cells are believed to have originated from the surface of epithelium covering the ovary. The majority of oogonia to continue to divide by mitosis, some of them differentiate into much larger primary oocytes. Immediately after formation they replicate their DNA and enter the prophase of the first meiotic division. During next few days' oogonia increase in number by 7 millions. At this time cell degeneration

begins and many oogonia as well primary oocytes become atretic. By 7th month majority of oogonia degenerated. All surviving primary oocytes entered in the 1st meiotic division and are surrounded by individual epithelial cells. Primary oocytes together with its surrounding flat epithelial cells are known as primordial follicle.

Postnatal maturation: All primary oocytes have finished the prophase of 1st meiotic division, but instead of proceeding to metaphase, they enter the dictyotene stage (a resting stage of prophase). Primary oocytes do not finish their first meiotic division until they reach the maturity. Oocytes maturation inhibitor, a substance secreted by follicular cells stops the mitotic activity of oocytes at this stage. The oocytes will be atretic, by the time puberty is reached only around 40,000 oocytes may be present at maturity. Chromosomal abnormalities increase with maternal age, and then extended meiotic division makes the primary oocytes vulnerable to damage.

With each ovarian cycle number of primordial follicles begins to mature. Primary oocytes beings to increase in size, the follicular cells change from flat to cuboidal. The follicle is known as primary follicle. Initially follicular cells are in contact with the oocytes but soon layer of acelleular matrix consisting of mcuopolysaccharides is deposited on the surface oocytes. This material produced by follicular cells, as the oocytes gradually increase in thickness, thus forming a zona pellucida. Small finger like processes of follicular cells extend across the zona pellucida and inter-digitate with the microvillus plasma membrane of the oocytes. From these processes materials are transported form follicular cells to oocytes.

Primary follicle: Ova are surrounded by many layers of follicular cells; which form the granulosa layer of more mature follicle. The microscopic primary follicles measures 30-50ì, consist of an oocytes, an enveloping single layer of follicular cells and a basement membrane. The follicle cells are flat at first, later becoming cuboidal to columnar. In some what older follicles one can find several layers of follicular cells. Such follicles are called growing or secondary follicles. The oocytes have also grown and assume an eccentric position.

Secondary follicle: When an ovum acquires a membrane (zona pellucida) and is called secondary follicle. The membrane appears between the oocytes and the surrounding follicular cells. The basement membrane between the follicular cell layer and the stroma becomes more distinct. In older usually macroscopic follicles, the follicular cells separate to form clefts, which later become confluent. Secondary follicle moves from the cortex to the medulla. A clear fluid filled space (antrum) forms around the ovum and the granulosa layer surrounding it. The fluid is called follicular fluid. The cavity thus formed is surrounded by several layers of follicular cells collectively called membrana granulosa. The appearance of the cavity the follicle is called vesicular or graffian follicle. The liquor folliculi, which fills the cavity, is rich in protein and oestrogen.

Under influence of gonadotrophins, antrum is forming in oocytes and the oocytes are attached by cumulus oophorus. The larger vesicular follicles are surrounded by an envelope of stroma cells of 60-250μ in thickens. The theca folliculi is composed of two layers. An inner a cellular layer, theca interna which is rich in blood vessels and outer fibrous layers, theca externa which gradually merges with ovarian stroma. The theca interna is well supplied with capillaries, and its stroma cells become modified into epitheloid, lipid containing spheroid or polymorphic cells located in the meshed of delicate fiber net. There is physiological evidence that the cells of theca interna are the chief source of ovarian oestrogens, which enter the blood stream through the walls of abundant thecal capillaries. Some of the hormones also pass through membrane granulosa into the liquor folliculi. The theca externa consists of fusiform stromal cells, which are arranged concentrically around the follicle. The division between the two laminae is not distinct nor is a sharp line of demarcation between the theca and the surrounding stroma. The theca externa is loose on the side toward the surface of the ovary.

Adjoining the theca interna centrally the membrana granulosa which is composed of layers of columnar cells next to the thin basement membrane and of several layers of spheroid to polyhedral cells. These surround the oocytes, forming a mound of cells, the cumulus oophorus which projects into the follicular cavity. The cells of the membrane granulosa which immediately surround the oocytes are columnar and raidially arranged and are called collectively the corona radiata. They are separated from the oocytes by a hyaline membrane of about 10ì in thickness, the oolemma or zona pellucida. In carnivores, the sow, and the ewe some follicles contain 2 to 6 oocytes. The deepest portions of the largest follicles reach the vicinity of the medulla. When they are ripe, they extend to the surface of the ovary and often project beyond it. Follicle has a diameter varying form 6 to 12 mm.

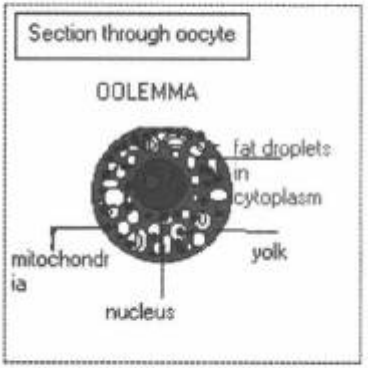
Tertiary follicle: Follicle fluid with antra is called tertiary follicles. Granulosa cells form cumulus oophorus and the corona radiate immediately around the egg. The granulosa cell is separated from theca follicluli (which consists of theca interna an externa) by the basement membrane and connective tissue cells. The granulosa cells and theca cells play an important part in the formation of corpus leutea.

The number of follicles that ripen in one oestral cyclae is more or less fixed for each species that is the uniparous animals usually produce only one. Large but immature follicles are founding larger numbers. In ruminants and sow there is about 40 in one ovary.

The diameter of ripe follicles in the various species is as follows; woman, 9 to 12 mm; mare up to 70mm; cow up to 20 mm; ewe, goat, sow 5-8 mm; bitch and cat about 2 mm.

Oocytes: The oocytes show progressive growth stages. These consists of a thickening of zona pellucida and an increase in cellular inclusions (yolk) which lead to an enlargement of the oocytes and make possible the first development process in the fertilized egg. At the end of their growth period the primary oocytes have a diameter of 100-150μ and are spherical in shape. The enveloping oolemma is perforated by radial pores through which the cells of the corona radiata send delicate processes to the surface of the oocyte. These are supposed by nutritional significance of the developing egg cell. The oocytes consist of the cytoplasm and large vesicular nucleus containing nucleolus. The cytoplasm consist stringy protoplasm with inclusion of fairly large yolk granules. The latter increase in quantity as the oocytes grows. Near the nucleus one can find an area of condensed cytoplasm containing one or two centrioles. The cell centre is not present in advance oocytes.

As soon as the follicle is mature, primary oocytes resumes its first meiotic division, leading to formation of two daughter cells of unequal size but with 23 chromosomes. One cell, secondary oocytes receives all the cytoplasm and the other 1st polar body receives none. First meiotic division occurs before Ovulation. Cells enter into second division, maturation, without DNA replication. At this stage ovulation occurs and division is completed, when oocytes are fertilized, otherwise ovum degenerates. In preparation of fertilization both male and female germ cells undergo a number of chromosomal and morphological changes, a process known as gametogenesis. The first human germ cells are known as primordial germ cells appear in the wall of the yolk sac at the end of 3rd week, and migrate to undifferentiated gonad in the 5th week. Formation of mature gametes in females is known as Oogenesis and in males knows as spermatogenesis.



The ovary performs both an exocrine function (Oogenesis and ovulation) and an endocrine one. Its hormones influence the development of primary and secondary sex characteristics and govern the sexual cycle. The process of the egg shell production causes a continuous rhythmic alteration in the gross and histological architecture of the ovary. The histological picture varies considerably depending on the plane of section and phase of the cycle.

The shape of the ovary varies greatly with the species and depends largely on whether the female is polytocus or monotocus. In the monotocus the ovary is ovoid. Mammalian ova are mcirolecithal unlike fowls does not contain vitelline membrane.

The details of the reproductive patterns differ in various species. Reproductive events are regulated by a complex of interlocking hormone systems, which are they locked into a neutral control system. The word sex means from the Latin word sexus, which means division and is derived from secare means to cut or to separate. All populations are dichotomous that is male and female differs each other. For a clear understanding one should; understand what is meant by genotypic or phenotypic sex.

Oestrous cycle:

The patterns of reproduction and breeding behaviour of vertebrates, in relation to season, are remarkably varied. In most domestic animals and in man, both sexes breed continuously throughout the year but sheep and goat and dogs have distinct breeding seasons. Most animals are classified as either seasonal or as continuous breeders, but some, such as the bitch, fit neither category. Seasonal breeder goes through a nonbreeding or anoestrous period during which they are sexually less active. In continuous breeders the sexual cycles are repeated more or less continuously throughout the year. All animals except the higher primates permit copulation only during a definite period within each sexual cycle. These periods of proper psychological and physiological state, during which copulation is permitted are called period of heat or oestrous. The period from the beginning of one heat to the beginning of next heat is called an oestrous cycle. When in heat, a female is in a psychological state that is distinctly different from her state during the rest of the cycle. Only when in heat does the female permits copulation. The reproductive cycle in the animal are called as an oestrous cycle and in the case of human being is called as menstrual cycle. Thus in animals mature females exhibit shedding of ovum is known as oestrous cycle, whereas in human it is exhibited by a period of commencement known as menstrual cycle.

Oestrous period is divided into four phases. Pro-oestrous is the period that begins with regression of corpus leutea and ends at the onset of oestrous. Oestrous is the time of sexual receptivity with ovulation occurring at the end of oestrous. Meteostrous is the period of early corpus leutea development. Diestrum is the period of mature leutea activity that begins four days after the ovulation and ends with regression of corpus leutea.

The terms follicular (which encompasses the classical stages of pro-estrous and oestrous) and leuteal (which includes the classical stage of meteostrous and di oestrous) phases is another way of classification of oestrous cycle.

The duration of oestrous cycle varies markedly varies between species from only few days in rodents to 6 months or a year in dogs. Moreover, some species the cycle is throughout the year while others like cat, ewe and mares do so only during certain seasons (seasonally polyestrous).

The permanent pattern of postnatal pituitary gonadotrophins secretion that determines the nature of gonadal hormone secretion is established in utero or in

some species early in postnatal life. This process involves the action of testosterone secreted by testicular interstitial cells, on the hypothalamus, a phenomenon known as masculine imprinting. In both sexes, neurons in hypothalamus secrete a polypeptide hormone known as gonadotrophins-releasing hormone (GnRH) that is responsible for release of (FSH) Follicular Stinulating Hormone and (LH) Leutenising Hormone or in males ICSH (Interstial cell stimulating hormone) from the anterior pituitary. These neurons have axons that terminate in the median eminence of hypothalamus located in stalk of pituitary gland (hypothysis), just above the anterior pituitary. GnRH is secreted from the axons directly into vessels in the stalk that supply the anterior pituitary. This vascular arrangement is known as hypothalamic-hypophyseal portal system. In males during this critical period of reproductive development, testosterone in the general circulation causes these neurons to release GnRH in a continuous, non-cyclic pattern into the portal system, thereby causing adenohypothysis to secrete FSH and LH (or ICSH) in a continuous non-cyclic pattern.

Female embryos exposed experimentally or inadvertently to testosterone during the critical period will also develop a permanent, noncyclic pattern of GnRH secretion after sexual maturity. In contrast, the absence of testosterone secretion during this period that is as occurs normally in female embryos or in males orchiectomised prior to this period; GnRH secretion at sexual maturity occurs in a cyclic pattern that is mediated through a positive and negative feedback loops by hormones from the ovary. This results in an oestrous cycle.

The duration of oestrous cycles varies markedly between species from only to a few days in rodent to six months or years in dogs or in some species, cycle is repeated round the year, while others it is seasonal. The period of ovarian inactivity between these seasons is referred to as anoestrous. In these species melatonin secreted by the pineal gland in response to change in the environmental lighting conditions regulates GnRH release thereby imposing seasonality to the reproductive cycles with the exception of higher primates, including humans most animal's cycle throughout the entire life span.

In females, follicular stimulating hormone stimulates follicle growth and development during the period of cycle known as pro-oestrous, whereas in male its noncyclic secretion induces maturation of spermatogonia through the secondarily spermatocyte stage of spermatogenesis. As they grow under the influence of FSH, ovarian follicles being later secrete a protein hormone, known as inhibin, which feeds back on the pituitary to suppress FSH secretion. L.H. induces theca cells of the ovarian follicles to convert cholesterol to androgens which inturn diffuse into the granulosa cells where they are converted into oestrogens by the enzyme aromatase. In males LH is required for completion of the latter stages of spermatogenesis (maturation to secondary spermatocyte to spermatozoa). Oestrogens from the maturing follicles stimulate the mitotic activity of endometrial glands and stroma and increase the concentration of progesterone receptors in the endometrium, an effect known as oestrogen priming. Oestrogens

also feedback on pituitary to increase LH secretion. Both oestrogens and FSH increase the number and concentration of LH receptors in the developing follicles making them more response to LH. This positive feed back mechanism ultimately leads to a surge in L.H. secretion (L.H peak) which results in maturation of the follicle and ovulation.

In most species, ovulation occurs 24-36 hours after L.H peak. In other species (cat, rabbit, ferrets, mink, and ilma) ovulation is induced by cervical stimulation during coitus or by manual manipulation. Following ovulation, granulosa and theca cells lining the follicles undergo marked hypertrophy and hyperplasia of from coarse folds that fill the blood filled lumen of the ruptured follicles (corpus hameorrhagicum). Vessels from theca layer rapidly grow into and vasuclarised the mass of proliferating cells to form Corpus leuteum (C.L.) C.L. begins to secret increasing amounts of progesterone under the influence of decreasing levels of L.H. Increasing concentration of progesterone fed back on the hypothalamus / pituitary to further decrease in L.H. levels and this phase is referred to as dioestrous or the leuteal phase of the oestrous cycle. Progesterone acting on the oestrogen primed endometrium, stimulates secretion by the endometrial glands and prepares the uterus for implantation of the blastocyts should fertilization of the ovulated oocytes occur. When pregnancy does not ensue at the end of dioestrous, the C.L undergoes lyses and progesterone levels decline. In domestic ungulates (horses, cattle, sheep, goats and pigs), prostaglandin F2 α secreted by endometrium in response to oxytocin, secreted by corpus leuteum is responsible for leuteolysis and initiation of new cycle. In these species PGF2α in the utero-ovarian veins diffuse by counter current flow into adjacent ovarian artery and induces its effect on C.L. In dogs and cats, which have long dioestrous, life span of C.L. is not regulated by PGF2α, as the mechanism of leuteolysis is not known.

Further more about oestrous cycle: Follicular development during oestrous cycle in cattle is characterized by two or more waves of follicular growth that produce 5 to 10 follicles on each ovary. Of these follicles one usually become dominant and larger than others within one to two days of start of wave and other under goes atresia. In cattle that have two follicular waves during their cycle - one may start on the day of ovulation and the second wave starts around 10^{th} of the cycle. The dominant follicle from the first wave enlarges for 5 to 6 days, become stationary for 5 to 6 days more then regresses. The dominant follicle from the second wave is the essential ovulatory follicle. Dominant follicles are usually 12 to 16 mm in diameter.

Cows that have 3 follicle waves start about 0, 9 and 16 days of the cycle. Cows with 3 waves of cycle tend to have longer leuteal phase and longer cycle of 22 to 24 days.

The last wave dominancy follicle is the ovulatory follicle. Leuteolysis is associated with increases concentration of PGF2α in the endometrium that eventually reaches

the corpus leuteum following transport in the utero ovarian artery. Regression of corpus leuteum causes reduced progesterone levels and triggers a large secretion of LH from the pituitary after the hypothalamus releases of GnRH. At the sometime that LH is peaking, oestradiol levels are increasing and with result oestrous behaviour. The dominant follicle is being acted upon both LH and FSH as follicular maturity occurs in the preovulatory period. L.H. acts on theca interna cells and increases androgen synthesis which eventually causes effect on granulosa cells whereas FSH enhances oestradiol production.

The preovulatory L.H. peak is associated with complex and poorly understands effect on the follicle, but the result is follicular rupture, ovulation and C.L. production. The oestradiol peak is associated with follicular maturation is thought to be responsible for the physical and behavioral signs of heat or estrous.

Following ovulation, C.L. forms from the theca and grnaulosa cells of the follicle under the influence of L.H. surge and begins to secrete progesterone. The early corpora hameorrhagicum, is friable crepitate or spongy and generally smaller than mature C.L.

Pregnancy:

Pregnancy interrupts the oestrous cycle. Implantation of blastocyts requires the C.L. allowing it to persist and functions as C.L. of pregnancy. In those species where PGF2 α is responsible for leuteolysis, during implantation, the embryo produces protein hormones that blocks the release of PGF2α from the endometrium or diverts its secretions into the uterine lumen, thereby allowing C.L. to persist. In dogs and cats which have long dioestrous, the C.L. normally persists for almost the length of gestation; hence rescue probably is not required. Progesterone is required in all species to maintain pregnancy. In some spp the rescued C.L stretches progesterone throughout gestation (dogs, cats, goats, swine) whereas in others (cows, mares), it is only secreted for portion of gestation. In mares and cows progesterone is secreted by the placenta is sufficient to maintain pregnancy to term. The synciotrophoblastic cells of the chorionic epithelium of the placenta secrete gonadotrophins which have leuteotropic activity that also assist in maintaining leuteal function and pregnancy.

In mares specialized Trophoblastic cells from the chorionic girdle detach from the foetal membranes and invade the endometrium to form what are termed endometrial cups. Between 40-120 days of gestation, these endometrial cups produce equine chorionic gonadotrophins (ECG), a substance formerly referred to as pregnant mare serum gonadotrophins (PMSG), that has marked L.H. like activity. Equine chorionic gondotorpin causes other follicles in the mare's ovary to ovulate and form secondary corpora leutea that assist with maintenance of pregnancy during this period. The endometrial cups degenerate after 120 days of gestation. Pregnancy terminates with parturition, during the foetus and placenta is expelled from the uterus. ACTH from the pituitary of the full term ruminant

foetus stimulates the foetal adrenal cortex to secrete burst of cortisol. This does not occur in equine fetuses. Cortisol, in turn acts on the placenta to induce enzymes that convert placental progesterone into estrogen. This lowered progesterone and elevated oestrogen causes decreased degradation and increased synthesis of PGF2α, increased myometrium tone, and contractility and relaxation of closed cervix. PGF2α also stimulates the C.L. of cow and placenta of mare to secrete another hormone, relaxin which further relaxes the cervix. The elevated levels of oestrogen also increase oxytocin receptors in the myometrium. Together the combination of PGF2α, oestrogen and increased oxytocin activity initiates uterine contraction (labor pain). As the foetus is forced against the internal of cervix, nerve impulses transmitted from this site to the pituitary (Ferguson's reflex) initiates a burst of oxytocin release that intensifies uterine contractions. Finally the presence of foetus in birth canal causes the dam (by spinal reflex), to have forced abdominal contraction that aid in the expulsion of foetus and foetal membranes.

Table 9. Average length of various parts of reproductive cycles of domestic animals

Species	Length anoestrous cycles	Length of oestrous	Time of ovulation	Type of placenta	Length Of pregnancy
Cow	21 days	18 hours	12 hrs after end of oestrous	Epithelio-chorial	280 days
Ewe	17 days	36 hours	30 hrs after end of oestrous	Syndesmo-chorial	147days
Sow	21 days	45 hours	36-40 hrs after beginning of oestrous	Epithelio-Chorial	113days
Mare	21 days	5-6 days	Last day of oestrous	Epithelio-chorial	345days
Doe	20 days	40 hours	30-36 hours after beginning of estrous	Syndesmo-chorial	147days
bitch	7-8 months interval	7-9 days	1st or 2nd day of estrous	Endothelio chorial	64 days

Table 10. Average length of estrous cycle in domestic animals

Species	oestrum	metoestrum	dioestrum	Pro-oestrum
Cow	12-24hours	3-5days	13 days	3 days
Ewe	1-2days	3-5 days	7-10 days	2 days
Sow	2-4days	3-4 days	9-13 days	3 days
mare	4-7days	3-5 days	6-10 days	3 days
Doe	1-2 days	3-5 days	7-10 days	2 days
bitch	9 days	-	-	9 days

Length of oestrous cycle in cattle is 21 days. Duration of oestrous in BosTaurus is 18 hours.

Length of oestrous cycle in sheep is 17 days. Duration of oestrous in sheep is 36 hours.

Length of oestrous cycle in pig is 21 days. The average length of oestrous is 2 days.

Length of oestrous cycle in goats is 21 days. Average duration of oestrous is 30 to 36 hours.

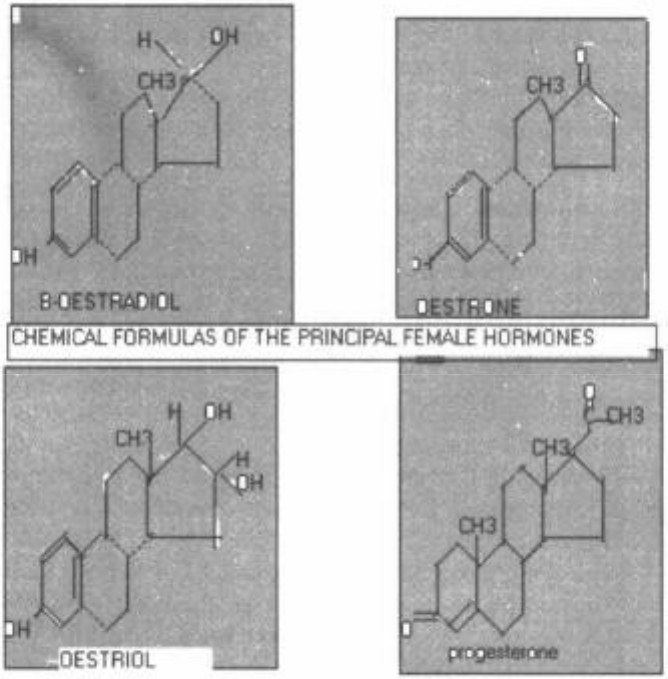
Animals may be divided into 3 classes according to their oestrous cycles. Anoestrous animals are those animals having one oestrous cycle per year; polyestrous animals such as cow, sow and mare have frequent periodic oestrous cycles, seasonally polyestrous animals are sheep.

The cat is unique among the domestic species in that ovulation is induced by coitus. If cats do not have contact with a male, they have oestrous cycle intervals of about 16 days.

Function of oestrogens: In the normal non-pregnant female, oestrogens are secreted in major quantities only by the ovaries, though minute quantities are secreted by the adrenal cortices. These are synthesized from cholesterol or acetyl Co.A. It is particularly interesting that progesterone as well as testosterone, the male sex hormone are probably synthesized first and then converted to the oestrogens. Indeed even normally about 1/15 as much testosterone is secreted by the ovaries as by the testis. In pregnancy tremendous quantities are secreted by the placenta, indeed up to 100 times the amount secreted by the ovaries during the normal monthly cycle. Both B-oestradiol, oestrone are present in large quantities in the venous blood from the ovaries and the estrogenic potency of B-oestradiol is 12 times that of oestrone and 80 times that of oestriol. Stimulates growth of endometrial glands, stimulates ductal growth, and causes secretory activity in the oviduct, initiates sexual receptivity, regulates gonadotrophins secretion, responsible for release of prostaglandins, PGF2α from both gravid and nongravid uterus. Encourages growth of long bones by initiating closure of epiphyseal growth plates, protein anabolism and is epitheliotrophic.

Progesterone: Progesterone is a steroid structure. It is synthesized principally from acetyl co. A. However it can also be formed from cholesterol. Most oestrogens and progesterone are transported in the blood loosely bound to albumen. Almost all the progesterone in the nonpregnant female is secreted by C.L during latter half of each ovarian cycle. However the adrenal glands form a minute quantity of progesterone or compounds that have progesterone activity and during pregnancy progesterone is formed in extreme quantities by the placenta, especially after fourth month of gestation.

Promotes endometrial glands growth, promotes lobulo-alveolar growth of mammary gland, promotes secretory activity of the oviduct and endometrial glands (uterine milk), promotes psychic oestrous, prevents contractility of the uterus during pregnancy and regulates secretion of gonadotrophins. Progesterone is secreted in far greater quantities than the oestrogens by the ovaries, but its potency per unit weight is much less than that of the oestrogen. Within few minutes after secretion, almost all the progesterone is degraded to other steroids that have no progesterone effect. The liver is especially important for then metabolic degradation. Progesterone is excreted in the urine in the form of pregnanediol.



Disorders of reproductive system

Developmental anomalies

Freemartin: Development of sterile female (free martin) which acts as co twin with male in bovines occur. This has been explained by various theories. The hormonal theory indicates the development of free martin to the masculisation of the female gonad due to passage of hormones from male twin through anastomose between fuse placental membranes (chorio-allantois).

Cellular theory explains this phenomenon on the basis of exchange of blood forming cells and germ cells between fetuses (during organogenesis) leading to chromosome chimerism (occurrence of identical antigen types in both foetus) in peripheral blood mononuclear leukocytes.

These following factors are also to be considered. Distribution of sex chromosomes or fragments during meiotic/mitotic cell division may cause chromosome aneuploidy in gametes.

Abnormal cortico-medullary relationships may disturb gonadal morphogenesis. Abnormal development of accessory genital structures under irregular endocrine environment or due to teratogenic factors may occur.

Secretion of medullarin from adrenal medulla and cortex in from adrenal cortex during development of gonads is also postulated. Medulla therefore persists and genes for masculinity in the Y of an XY individual prevail to develop testis. Primordial germ cells invade medulla and sex differentiation occurs (vice versa for females). A Mullerian inhibiting hormone is probably produced by foetal Sertoli cells. The XY cells from male co-twin would instruct the developing female co-twin system to masculinise. The XY cells carry H-Y antigen which may play an important role in male development.

The structural modifications of female genitalia are supposed to result from the influence of androgenic hormone produced by the male foetus.Female differentiation occurs in the absence of a functional male gonad. Masculine differentiation is imposed on the system at an early stage by testosterone produced by the Leydig cells of the developing testis and this differentiation prevents further female development. All sexual development is feminine if not prevented from being so by testicular hormones.

An important feature of gonadal differentiation as already discussed is in the chronological differences that exist between the sexes. In all mammalian species studied, males differentiate earlier than females. The foetal testis produces two hormones critical for normal male differentiation. As already discussed Sertoli cells of the developing testis secretes a Mullerian duct inhibitory factor that brings about Mullerian duct regression. At the same time Leydig cells of testis secrete testosterone which prevent the Wolffian duct regression and brings about it differentiation into vas differentia, seminal vesicles and epididymides. The testosterone is also converted to dihydrotestosterone, and this hormone induces development of penis and scrotum from the bipotential external genital primordia.

The gonads are undifferentiated. Ovaries are small. The Mullerian duct system is not differentiated fully. There are usually portions of tubular system, which do not develop and often the uterus is small and incomplete. The vulva has frequently long tufts of hair. The clitoris is quite prominent. The vagina is fairly developed and the cervix is fully absent. One feature of the reproductive tract, which is very useful in distinguishing this condition form severe cases of aplasia of Mullerian ducts is the presence of seminal vesicles. Epididymis may be present or absent. The histological appearance of the gonads is one of quite undifferentiated structure. There are small tubular structures resembling primitive seminiferous tubules with lining cells similar to the Sertoli cells. There are interstitial cells which in the new

born freemartins resemble fibroblasts. In the freemartin which is allowed to live the age of one or more layers, the interstitial cells develop and resemble leuteal cells in the ovary or Leydig cells of the testis. In the older animals these develop into multiple large masses of organ or tan colored masses which resemble both interstitial cell tumor or corpora leutea on gross examination. Most free martins do not develop ovarian follicles. Endometrial glands are present and produce fluid resulting in cystic distension of vestige remnants.

The seminal vesicles are usually small and have abundant fibrous stroma. The epithelium resembles that of seminal vesicles of a castrated bull.

Incidence: The frequency with which this condition appears is directly dependent upon prevalence of heterosexual twinning in the population. Studies showed 92% of cattle female co-sibs are sterile freemartins while the other 8% are normal and fertile. Bhagat (1966)[1] recorded a case of free martin in a 6 year old heifer in India. Narasimha Rao and Murthy (1971)[2] recorded the incidence as 0.1% among 1,058 unfertile buffaloes examined in Andhra Pradesh.

White heifer's disease

This condition is seen more commonly in short horn cows due to arrest in the Mullerian duct system and consists of a number of abnormalities. Depending on the intensity of arrest in the development it may be classified into three groups.

Group A : where is Hymenal constriction, absence of anterior vagina, cervix, and uterine body, cystic dilatation of uterine horns and presence of well marked Wolffian bodies and occasional submucous vaginal canals.

Group B : This is uterus unicornis and abnormal horn being present as a flat muscular band. The abnormal horn being present as a flat muscular band. Hymenal constriction may or may not be present.

Group C: Essential Hymenal constriction may or may not be present. Rest of the enitalia compartmentally developed. If constriction is complete gross utero vaginal distress results.

White heifer disease was also reported in a Rathi heifer (Kohli, 1967)[3], in buffaloes (Rama Rao and Rajya, 1976)[4] and cross bred Jersey heifers (Majumdar and Dey, 1985)[5], in India.

1 Bhagat. S. 1966. Artificial induction of lactation in a free martin. Indian Vet. J. 43:218

2 Narasimha Rao, A.V., and Murthy, A.K. 1971. Studies on the reproductive disorders in buffalo cows of Andhra Pradesh. Incidence of anatomical and physiologic causes. Indian Vet. J. 48: 1007.

3 Kohli, I.S. 1967. A case of aersia cervicitis (white heifer disease) in Rathi heifers. Indian Vet. J. 44: 869

4 Rama Rao. and Rajya,B.S. 1976. A note on the developmental abnormalities of the female genital tract of bovine.IndianVet.J. 53:586

5 Majumdar, M.C., and Dey, B.N. 1985. Studies on White heifer disease in West Bengal – a case report. Indian J.Anim. Reprod. 6:137.

Double vagina and double cervix: This is due to complete failure of fusion. The more common failure of fusion occurs in or adjacent to the cervix. The anterior vagina may be partitioned by a dorsal septum in conjunction with a double cervix. A dorso-ventral band may be present across the external os (double external os), the cervix and vagina being properly fused. The failure of fusion may involve only a part of the cervix, chiefly the caudal part, so that there is one uterine body and the cervical canal which is bifurcated with duplication of external os. The cervix and uterine body may be completely divided and this condition is known as uterus didlephys.

Intersexes: The intersex is an individual with congenital abnormality, where the diagnosis of the sex is confused. Intersexes may be of two types.

1) True hermaphrodites in which gonads of both sexes are present.
2) Pseudo hermaphrodites having gonads of the sex only but possessing reproductive organs in the some characteristic of the opposite sex. Male and female pseudohermaphrodites depending on the gonads present are recognized.

Pseudohermaphroiditism is very common in goats and studied in detail from genetic point of view. It is caused by recessive gene. The incidence of hermaphrodites is Sannenn breed of goats is high and mostly present as male Pseudohermaphroiditism. Intersexes are common in pigs but not to the same degree as in goats. In bovine's intersexes seems to be a rare condition.

Dilations and diverticula of the cervix have been observed as a cause of infertility in heifers. The malformations occur at the level of the 3rd and 4th rugae, and the cervical canal is usually constricted caudal to the defect.

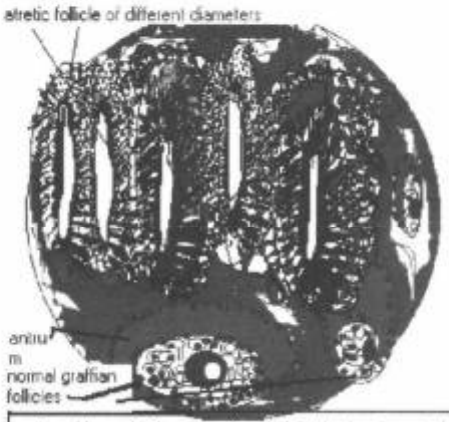
Abnormal presence of Wolffian ducts or Gartner's ducts: Abnormalities of Gartner's ducts which are vestiges of primitive Wolffian ducts or mesonephric ducts in the embryo are rather common in cow.

Disorders of ovary

Disturbances in growth

Ovarian agenesis: Agenesis of one or both ovaries occurs in domestic animals.

Ovarian hypoplasia: This may be total or partial or transitional in types (cited by Setttergen, 1964) [6]. In several studies he stated that in total hypoplasia, the ovary was fusiform, had irregular longitudinal grooves on the surface and contained no follicles. The average dimensions of total hypo plastic ovaries were 18.8 mm long, 7.2 mm broad, and 6.8 mm thick, when one considers the average of ovaries of Swedish Highland breeds who ovarian measurements 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, and efficient in follicles. The tubal pole sometimes contained follicle and corpora leutea. The ovary of



section of hypoplastic ovary of a she buffalo showing atretic graffian follicles surrounded by extensive hyalinised connective tissue and also observe normal growing follicles also

transitional hypoplasia was small and had a smooth surface and a firm consistency. Follicles and corpora leutea bulge from the surface. The average measurements of such ovaries were 19.8 mm long, 13.4 mm broad and 11.3 mm thick. In case of total bilateral hypoplasia, the uterus and mammary gland remained infantile and the pelvis is narrow.

Lagerl of and Setttergen (1953)[8] and Setttergen (1964)[6] observed that in cow of adult ovaries, the tunica albuginea was similar in normal and hypo plastic ovaries. Anovular cords and Anovular follicles were present and there are more in hypo plastic ovaries. They are directly related to the degree of development.

Settergren, 1964, reported in normal ovaries the number of primordial follicles were 50,700, ranging from 6000 to 1, 00,000. In hypoplasia affected ovaries, the number of follicles was ranging from 19,000 to 23,000. In bilateral hypoplasia there were less than 500 primordial follicles and in hypoplastic ovaries, there were no follicles in ovaries. In certain cases it is difficult to locate ovaries or sometimes accord like thickening in the cranial border of ovarian ligament.

In one sided hypoplasia the tubular portion of genital tract develops normally. [7]

The medullary cords in defective ovaries were often arranged in nests surrounded

6. **Settergren.** I. 1964. The ovarian morphology in clinical bovine gonadal hypoplasia with some aspect of endocrine relations. **Act vet scand,** 5(suppl. i): 1-108).2

7 (**Settergren I and McEntte, K.** 1992. Germ cell weakness as a cause of testicular hypoplasia in bulls. **Acta Vet Scand 33**:273-82.

8 **Lagerlof, N. and Settergren.** 1953. Results of seven years control of hereditary ovarian hypoplasia in cattle of *Swedish Highland Breed*. **Cornell Vet. 43**: 52-64;

by circular layer of connective tissue that sometimes contain epitheloid 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 follicle which is usually thousand in normal ovaries considerably reduced. Disturbancesin the development of follicles occurred when there was 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 occur. When the follicle numbers were very low, ovulation did not occur and the follicles leutenised. Interstitial glands were found in hypo-plastic ovaries.

Presence of adrenal cortical area tissues around the ovaries and presence of ovarian tissue in the adrenal gland also has been observed. This ectopic of adrenal tissue is believed to be due to the close anatomical relationship between the adrenal cortex and the gonad is embryological development, both primordia arise in the region of urogenital ridge.

Anovular cords: These are seen in the ovaries of bovines as scattered or in groups in the ovarian stoma. Anovular cords probably originated either from groups or nests of epithelial cells which never had oocytes from normal follicles in the early stages of development replacing the follicles.

Three types of Anovular cords are recognized.

Type I Anovular cords: These are elliptical and surrounded by a thin layer of PAS positive membrane. The cords are filled with 3 to 4 rows of irregularly arranged epithelial cells with no ovum. The nucleus of cells adjacent to basement membrane is oval with diffuse chromatin. The cytoplasm is stained light and contains a network of very thin eosinophilic fibrils.

Type II Anovular cords: These are elliptical or round and slightly larger than type I cords. The cells are arranged in one or two layers of cells. The lumen contain moderate amount of PAS positive material.

Type III Anovular cords: These are larger than type II, the diameter reaching a maximum of 200i. There are two layers of epithelial cells with PAS positive amorphous substance in concentric layers in the lumina. The connective tissue around the Anovular follicles is arranged in several circular layers and in these epitheloid and eosinophilic cells are often found.

Presence of Anovular cords is directly proportion to the severity of hypoplasia of ovaries. In very severe cases type II and III forms are seen. In less severe cases type II and I cords are seen and in early cases of hypoplasia type I cords are predominantly seen.

Folliculoids: Usually these are recognized in ovaries of cattle and buffaloes. Two type of folliculoids are seen, trabecular type and colloid type.

Trabecular type: These have distinct connective tissue and having PAS positive capsule with the invaginations of septa into the lumen dividing it into smaller cavities. The septa are lined on either side by single or double layers of granulosa like cells. These cells are elongated having large vesicular nucleus and scanty cytoplasm. Several rosettes like structures consisting of eosinophilic irregular bodies surrounded by rapidly arranged single or double layers of cells are present in the cavity. These structures have resembled to Call-Exner bodies, characteristic of granulosa cell tumor but the origin and morphogenesis of rosettes is different.

Colloid type: A few irregularly shaped a PAS positive colloid bodies are characteristically seen in the lumina of solitary folliculoids. The cellular elements are few. Two types of colloid bodies are seen. One type is large, irregular in size and shape with laminated appearance. The other type is small and spherical with homogenous structures. Both the types are surrounded by a single layer of granulosa like cells. The common association of Anovular cords with folliculoids and their close morphologic similarity suggest that Anovular cords might be precursors of the folliculoids. Probably under constant stimulation of gonadotrophins, particularly in aged animals, the anovulatory follicles proliferate to form folliculoids.

Ovarian heaemorrhages: Intrafollicular heaemorrhages occur frequently in atretic follicles in young claves but rarely in atretic follicles in cows. The amount of heaemorrhages that occur during ovulation varies in different species. In the cow, a small blood filled cavity in the corpus leuteum will be present for only few days following ovulation. The mare develops corpus hameorrhagicum following ovulation. The mare develops corpus hameorrhagicum in the cow include a fatal hemorrhage, periovarian adhesions, ovarian abscesses, and cystic follicles following repeated enculeations at short intervals.

Ovulation tags: Small clots of blood and follicular fluid attach to the surface of the ovary and proper ligament of the ovary following ovulation and gradually become transformed into fine strands of fibrous tissue. These strands of tissue frequently extend from the ovary and across the ovarian bursa on to the uterine tube and mesosalpinx forming web like adhesions.

Vascular lesions: Degenerative and inflammatory lesions have been observed in the small arteries of the theca interna of the follicles in post partum heifers. Mucoid degeneration of intima and hyalinization of media of large arteries supplying the corpora leutea of pregnancy occur during postpartum period. Similar lesions occur in the arteries of the caruncular stalk during uterine involution. Thrombosis of the ovarian veins has been reported in the mesentery of the bovine ovary. Varicose veins develop on the surface of the ovary. Thrombosed and calcified veins are common in the mares.

Oophoritis (Ovaritis): Eosinophils occur in recently formed corpora leutea in sheep and swine. Ovarian eosinophilic granulated cells may probably arise from

undifferentiated mesenchymal cells. The appearance of eosinophilic granules of the genital tract is in coincidence with increased bactericidal activity, a physiological function from ovarian eosinophilic activity. With viral infections mild interstitial Oophoritis as well lesions consisted of perivascular accumulations of lymphocyte and plasma cells in the ovarian medullas well in the corpora leutea are seen.

Cystic disorders of ovary

A cystic disorder of ovaries implies commonly follicular cysts or leuteal cysts. But close consideration reveals there are 16 different types of cysts. These are normal mature follicle with vesicular fluid normal atretic griffin follicles, cystic graffian follicles, leutenised follicles, cystic corpus leuteum, epithelial (germinal) inclusion cysts, cysts of surface epithelial structures, cystic rete ovarii, cystic epoophoron, cystic paraoophoron, mesonephric duct cysts, cystic accessory funnel, cystic accessory uterine tube, tubo-ovarian cysts, and cystic ovarian bursa.

Mature graffian follicle: It is essential for the pathologist to know the normal follicle size. Cow and mare having large follicles whose diameter may range from 15 mm to70 mm. In sections also normal graffian follicle shows the distinct three layers, the outer most connective tissue, the second of thecal cells, and the third of granulosa cells. The granulosa cells in the developing follicles form a cumulus oophorus, and have distinct cytoplasm and a vesicular nucleus. Theca cells on the contrary either a spindle shaped or that of longitudinal in size with less amount of cytoplasm. The sections invariably contain the follicle which have the antrum, and the fluid which stain with haematoxylin and eosin stains as pink amorphous mass. The discus prodigus may come in sections or may not. In the same way cut sections of ovum may come or may not be seen in sections.

Atretic follicles: Follicular atresia is a normal physiologic process that starts during foetal development and continues throughout the life in domestic animals. Usually four types have been described in cows.

The first type of atresia occurs in the primordial follicles and the smallest of growing follicles. This is characterized by primary oocytes degeneration without hyalinization in the zona pellucida. The degenerative changes start in the oocytes and consist of chromatolysis, disappearance of nuclear membrane, shrinkage of cytoplasm and penetration zona pellucida by macrophages. The degeneration of oocytes is followed by de generation of the grnaulosa cells and disappearance of the entire follicle in to the cortical stroma.

The second type of follicular atresia occurs in growing follicles, which developed zona pellucida and have the small antrum of 1 or 2 mm. Here there is degeneration of primary oocytes with hyalinization of zone pellucida. The zona pellucida increases in thickness and become opaque and hyalinised. The cytoplasm of granulosa cells and the cells outline become indistinct.

The third type of follicular atresia occurs in vesicular follicles that are where

antrum measured from 1 to 6 mm in diameter. Obliterative atresia occurs with primary follicular wall degeneration sets in. Degeneration occur first in the lumen lining granulosa cells. Thecal connective tissue cells extend into the antrum and eventually obliterate the space. Follicular fluid is not there. Cumulus disappears and zonal pellucida becomes opaque. The theca becomes hyalinised. The end project of degeneration is called atreticum.

The fourth type of follicular atresia differs from obliterative atresia in that loss of fluid from antrum doesn't occur. The granulosa cells degenerate. The theca interna become strophic andis poorly delineated form the ovarian stroma. The antrum gradually decreases in volume after being enclosed in the connective tissue capsule. This is called cystic atresia of follicles.

Polyoogonia: Polyoogonia is a condition in which each follicle, which normally contains only one ovum but may contain several ova without disturbing the function of genital organs.

Super fecundation

Super fecundation is produced by a female ovulating two or more ova during an oestrum and copulating with two or more males during that oestrum with ova being fertilized by spermatozoa from each male. Super fecundation is observed in multipara, especially in dogs and cats. In these multiuparous animals that ovulate regularly two or more ova, have long heat periods and opportunities for services by different males.

Superfoetation

Superfoetation is produced when a pregnant female carrying one or more live fetuses come into oestrum and is bread again and a second conception occurs in a uterus already containing a live foetus.

The cumulus and corona cells around zona pellucida of ovum in most domestic animals persist for a few hours or less after ovulation and fellaway in the oviduct. In the dog and cat the corona cells may persist, for several days. The protoplasmic projections fromZona pellucida is withdrawn soon after ovulation and fall way in the oviduct. The cumulus and corona cells die and separate from the ovum aided by ciliary and muscular activity of the oviduct. Inside the zona pellucida is the vitelline membrane similar to plasma membrane of somatic cells.

Life of ovulated ova in domestic animals is 12 to 24 hours, whereas in dog it may remain as fertile up to 4 to 8 days. Under ordinary conditions the fertilized ova or decaying zygote remains in the oviduct until the C.L. is formed. The endometrium under the influence of C.L. secretes progesterone prepares proper environment and nutrition to the zygote upon entering the uterus. Sperm cells live in the cervix for 36 to 48 hours.

Abnormalities of fertilization

The most common abnormalities of fertilization are polygamy and Polyspermy. Polygamy is incomplete maturation of the egg with failure to expel second polar body resulting in triploid zygote. Polyspermy where more than one, usually two sperm cells enter the egg characterized by triploidy.

Cystic ovaries

Cystic follicles: Cystic disorders of ovary;

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The third type of follicular atresia occurs in vesicular follicles, i.e., where the antrum measured from 1 to 6 mm in diameter. Obliterative atresia occurs with primary follicular wall degeneration set in. Degeneration occurs first in the lumen lining granulosa cells. Thecal connective tissue cells extend into the antrum and eventually obliterate the space. There is no follicular fluid. Cumulus disappears and zona pellucid becomes opaque. The theca becomes hyalinised. The end product of degeneration is called atreticum.

The fourth type of follicular atresia differs from obliterative atresia in that loss of fluid from antrum does not occur. The granulosa cells degenerate. The theca interna becomes atrophic. It is poorly delineated from the ovarian stroma. The antrum gradually decreases in volume after being enclosed in the connective tissue capsule. This is called as cystic atresia of follicles.

Follicular atresia is a pathologic when the degeneration is brought about by anoestrous of debility inanition. Follicular growth is independent of hypophyseal gonadotrophins up to the stage of antrum formation. Thereafter, growth and maturation depend on stimulation by hypophyseal gonadotrophins and the ovaries are capable of responding to them. The defect presumably lies in the failure of hypothalamus to produce or discharge gonadotrophins releasing hormone or the pituitary's failure to respond it. The affected follicles may stop to develop at any stage between that of the antrum and that of the finally mature. It is not known how long they may persist before degenerating.

Cystic follicles: Cystic graffian follicles in dairy cows are important in view of the repeat breeding problem. A follicle larger than 2.5 cm in diameter on three successive examinations in a 10 day period is considered to be cystic (Morrow et.al. 1966)[9]. Roberts (1986)[10] found that left ovary was cystic in 23% of cases, right ovary in 33.3% of cases and both ovaries in 43% of cases. Most of the cases showed nymphomaniac symptoms. The behavior of cows with cystic ovaries is variable. The majority of cows with ovarian cysts are anoestrous. The disease arises from the failure of mature follicles to ovulate. It occurs most often before the first postpartum ovulation. Approximately 45-60% of animals which develop anovulatory follicular cysts will reestablish normal ovarian cycles spontaneously. Cystic follicle also may develop after postpartum ovarian cycles have been established, and these cysts are more likely to persist if effective treatment is not instituted.

The cause of cystic ovarian disease is not understood in any species. The disease in cattle occurs more frequently after parturient or post-parturient disease, and there is evidence that intrauterine infection play a role in the pathogenesis of the disease. There is clearly a genetic predisposition of the disease in certain families. The daughter of cows that have had cystic ovaries have substantially increased risk of developing the disease as compared to the general population. The disease

tends to involve primary dairy cows, but it can occur in cattle of any breed if they are withheld for breeding for a prolonged period of time. One of the factors that have made the understanding of the disease difficult is the criteria of the disease itself. Follicular cysts in cattle are usually defined as follicles greater than 2.5 cm in diameter that fail to ovulate and may persist. The cysts may be single or multiple on one or both ovaries. These cysts may persist but during the course of the disease additional cysts may be recruited and some cysts undergo atresia. Patches of leuteal tissue can be seen grossly in the wall of some of the cysts and can be recognized histologically in about quarters of them.

In cystic degeneration of mature follicles, degeneration of granulosa cells occur first, followed by degeneration of oocytes and the theca interna. The grnaulosa cells undergo pyknosis, karryorhexis and slough into the cystic cavity. The theca cells undergo pyknosis and karryorhexis and also slough into the cystic cavity. Leutenisation 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 that is deep in the ovary. The partial leutenisation 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 extra ovarian organs, including the uterine tubes, uterus, cervix, vagina, vulva, mammary glands, adrenals and pituitary. The mucosa of uterine tubes becomes thick and oedematous. The endometrium becomes hyperpalstic with dilatation of endometrial glands. In 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. Abundant mucous is evident in the cystic glands. The endometrial stroma is oedematous. The vulva may be oedematous. The clitoris may be enlarged. Cystic Gartner's ducts as well cystic Bartholin's gland are present. Either may become abscessed. Bartholin's glands, one on each side of the floor of the vulva, undergo cyclic secretory changes during the oestrous cycle and a squamous epithelium on the ducts is normal in oestrous.

Since most cases of cystic ovary are amendable to treatment these extra ovarian lesions are rarely observed.

Because the disease is a dynamic one with new cysts being added and cysts undergoing variable lutenisation and generation, the hormonal consequence is also variable, the peripheral concentration of leutenising hormone, oestradiol and progesterone depending on structural and functional features of the cysts.

Cows which bear follicular cysts for long periods ultimately develop permanent anoestrus. The cysts are then reduced in size and no longer dominate the contour of the ovary, the pressure within the cysts is reduced, and the walls are appreciably thicker. These atrophic cysts are usually multiple and bilateral; histologically they do not differ clearly from the active follicular cysts.

Lutenised follicles: Lutenised follicles develop due to failure of ovulation. This is a lutenised cyst. There is an apparent release of failure of L.H with resulting ovulation failure. Individual lutenised follicles occur occasionally in normal bitches and cows.

Cystic corpora lutea/ (leutenised cyst): A cystic corpus luteum develops following failure of ovulation and appears to be due to premature closing of the ruptured site with the formation of cyst in the centre of the developing corpus luteum. Some workers say that this type of cyst develops when ovulation failure to occur and theca undergoes lutenisation. An ovulation papilla or bulge is present. This differentiates a cystic corpus luteum from lutenised cyst. A cystic corpus luteum has a zone of fibrous tissue between the luteal cells and cystic cavity. Cystic corpora lutea of pregnancy occur in zebu cattle. The cystic corpora lutea with sufficient progesterone production is sufficient to maintain pregnancy.

Lutenised cysts occur more frequently in cattle and swine than in other species of domestic animals. In cattle they usually occur as single cysts. Single lutenised cysts are seen in pregnant sows but multiple cysts are associated with infertility.

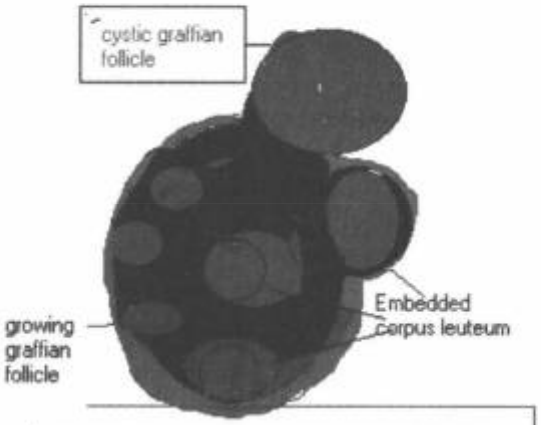
The pathogenesis of lutenised cyst is probably the same as that of proposed for the cystic follicle that is by failure of the hypothysis to release adequate surge of lutenising hormone.

Anovulatory lutenised cysts shouldn't be confused with cystic corpora lutea. A cystic corpus luteum is a corpus leuteum which has formed after ovulation in which a central cavity has persisted in the centre of mass of developing leuteal tissue. Cystic corpora lutea are not evidence of ovarian malfunction. They form after ovulation and do not affect the length of oestrous cycles. Cystic graffian follicles in dairy cows are important in view of the repeated breeding problems. A follicle larger than 2.5 cm in diameter on three successive examinations in a 100 day period was considered to be cystic. Roberts (1955) in his studies found left ovary in cows was cystic in 23% cases, right ovary in 33.33% cases and both ovaries in 43% of cases. Most of the cows showed nymphomaniac symptoms.

Pathogenesis: In cystic degeneration of mature follicles, degeneration of granulosa cells occurs first, followed by degeneration of oocytes and theca interna. The granulosa cells undergo pyknosis and karryorhexis and slough into the cystic cavity. The theca interna cells

Undergo – pyknosis – and

Karryorhexis and subsequently these cells slough into the lumen and subsequent fibrosis results. Leutenisation 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 that is deep in the ovary. The partial leutenisation of the cyst wall ruptures to occur predominantly in the theca interna, but may occur in the granulosa.



OVARY OF A COW SHOWING CYSTIC GRAFFIAN FOLLICLE AND EMBEDDED CORPUS LEUTEUM

Cows with chronic cystic follicular degeneration may have lesions in a number of extra ovarian organs including the uterine tubes, uterus, cervix, and vagina, and vulva, mammary glands, adrenal and pituitary. The mucosa of uterine tubes becomes thick and oedematous. The endometrium becomes hyperpalstic with dilatation of endometrial glands and in 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. Abundant mucous may be evident in the cystic glands. The endometrial stroma is oedematous.

Atrophy of myometrium and endometrium may follow cystic hyperplasia of the endometrium. In these cases, mucoid or watery material accumulates in the uterine lumen. In case of functional follicular cysts, the cervical canal is usually dilated, showing fluid to escape from the uterus. The mucosa of cervix consists of tall columnar cells. Oedema and congestion of stroma occurs. Squamous metaplasia occurs in the base of crypts. Cystic mesonephric ducts (Gartner's) ducts are present in some cases. The vulva becomes oedematous when the cysts are producing oestrogens and the clitoris may become enlarged in long standing cases. Mammary gland development and secretion of thin creamy in nature are common.

The onset of cystic follicle degeneration, delta cells of the adenohypophysis degenerates early in oestrous, whereas delta cells in this won't degenerate. Ovulation is not there. Pituitary gland enlarges significantly. Adrenal glands also increase significantly. The development of hyperpalstic nodules in the adrenal cortex of cows with cystic follicle maybe one of the lesions associated with masculisation, so called adrenal virilism. As the age increases cystic follicular appearance is common.

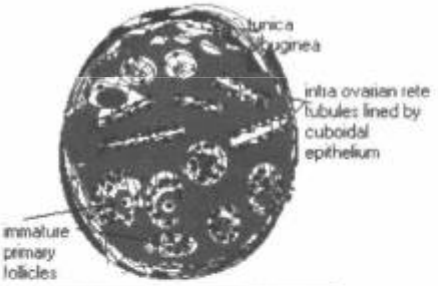
Lutenised follicles: Lutenised follicle develops due to failure of ovulation. This is a lutenised cyst. There is an apparent release of failure of lutenising hormone with resultant failure of ovulation. Individual leutenised follicles are encountered occasionally in normal bitches and sows.

Cystic corpora lutea: A cystic corpus luteum develops following ovulation and appears to be due to premature closing of the ruptured site with the formation of a cyst in the centre of the developing corpus leuteum. An ovulation papilla or bulge is present, and this differentia a cystic corpus luteum form leutenised cyst. A cystic corpus luteum has a zone of fibrous tissue between the leuteal cells and cystic cavity. Cystic corpora lutea of pregnancy occurs in zebu cattle. The cystic corpora lutea with sufficient progesterone projection is sufficient amount to maintain pregnancy.

Cysts of subsurface epithelial structures: These are the tubules and cords located beneath the surface epithelium of the canine ovary. It is an in growth of peritoneal covering of the ovary.

Cystic rete ovarii: Cystic rete tubules occur in all species of domestic animals. The lining of 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 anatomic difference can be useful in differentiating epoophoron cysts from rete cysts. The rete tubules sometimes communicate with the mesonephric tubules and cyst formation may involve both structures. Cyst of the mesonephric tubules (epoophoron) are usually oval or round without in folding of the wall. Cysts of the rete ovarii in domestic animals have been described in the cat. One or both ovaries are affected. They often cause severe compression of the ovarian cortex.

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



Artistic impression of rete ovarii from the section of ovary - H & E x100

Cysts round the ovary

Cysts of mesonephric tubules and ducts: These are Para- ovarian cysts. The term Para -ovarian cyst is commonly used to denote any type of cyst located in the ovary. The mesonephric duct is lined by low cuboidal epithelium which is nonciliated. The nucleus is vesicular and is medially placed and surrounded by two layers of smooth muscle fibers. The mesonephric tubules are highly convoluted than the mesonephric ducts. These also have a layer of muscle fibers but not as thick as that of mesonephric duct. The muscular coat is lost as the tubules approach rete. The epithelial lining of tubules consists of low cuboidal to low columnar. Both ciliated and nonciliated cells are present; the cytoplasm of non-ciliated stains darkly. Their nuclei are usually oval and centrally placed. The paramesonpehric derivatives are also having ciliated and non-ciliated epitheialial cells, as well as thin musculature. The nuclei of epithelial cells of paarmesonephric origin are about 50% larger than those of mesonephric origin.

Cysts of epoophoron: Cysts of epoophoron occur in all species of domestic animals and located between the ovary and Fimbriae of the uterine tube. The lining of cyst consists of a single layer of cuboidal epithelial cells. Some of the cells are secretory and other is ciliated. A thin zone of smooth muscle surrounds the tubules. Cysts of epoophoron are located on the tubal extremity of the ovary. Cysts of paraoophoron are present on the uterine extremity of the ovary. Mesonephric ducts are located close to the uterine tube. Cystic accessory funnels are located on the serosal side of the Fimbriae of the uterine tube.

Tubulo-ovarian cysts: The complete fusion of fimbria of the uterine tube with ovary in cases of salpingitis and perioophoritis results in the accumulation of clear fluid in the proximal part of the uterine tube as the inflammation subsides. The resulting cystic dilatation of uterine tube that is adherent to the ovary is known as tubo-ovarian cyst.

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 distension of the bursa. This condition is seen predominantly in cows as a seqelae to severe inflammatory disease of the uterine tube and ovarian surface. Adhesions following enculeations of the corpus leuteum in cattle may also result in cystic dilatation the ovarian bursa.

Epithelial inclusion cysts: Surface epithelium of the ovary is a modified layer of 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 corpus leuteum or rupture of follicular cysts may induce formation of inclusion cysts of the surface epithelium in cattle. The cysts are lined by a single of layer cuboidal to flattened epithelial ells and contain clear watery fluid. In the mare inclusion cysts of the surface epithelium originate in proximity of the

ovulation fossa and have been called fossa cysts. A large number of cysts can block ovulation and in advanced cases most of the gonad is destroyed resulting in a non-functional ovary. The epithelial inclusion cysts in the mare arise either from the tubal (paramesonephric) epithelium or that of peritoneum. So it may be either a ciliated or pseduostratified ciliated cells.

Cysts of subsurface epithelial structures: These are the tubules and cords located beneath the surface epithelium of the canine ovary. It is an in growth of the peritoneal covering of the ovary.

Cystic rete ovarii: cystic rete tubules occur in all species of domestic animals. The lining of the anastomosing rete tubules consists of a single layer of epithelial cells. No smooth muscle surrounds the retubules in contrast is the mesonephric tubules which are surrounded by a thin layer of smooth muscle fibers. These anatomical differences can be useful in differentiating epoophoron cysts from rete cysts. The rete tubules sometimes communicate with the mesonephric tubules and cyst formation may involve both structures. Cysts of the mesonephric tubules (epoophoron) are usually oval or round without infolding of the wall. Cysts of rete ovarii in domestic animals have been described in the cat. One or both ovaries are affected. These often cause severe compression of the ovarian cortex.

The rete ovarii consist of three parts, an inter-ovarian rete, a connecting rete and extra ovarian rete. The intraovarian rete is located within The tubual 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 extra ovarian rete consists of tubules lined by ciliated columnar cells which end blindly in the periovarian tissues.

Cystic around the ovary: Cysts of mesonephric tubules and ducts.

Para-ovarian cysts: These are para-ovarian cysts. The term para-ovarian cyst is commonly used to denote any type of cyst located in the ovary. The mesonephric duct is lined by low cuboidal epithelium which is nonciliated. The nucleus is vesicular and is medially placed and surrounded by two layers of smooth muscle fibers. The mesonephric tubules are highly convoluted than the mesonephric ducts. These also have a layer of muscle fibers but as thick as of mesonephric ducts. The muscular coat is lot as the tubules approach rete. The epithelial lining of tubules consists of a low cuboidal to columnar. Both ciliated and non ciliated cells are present. The cytoplasm of noncilaited stains darkly. Their nuclei are usually oval and centrally placed. The paramesonephric derivatives are also having ciliated and nonciliated epithelial cells, as well as thin musculature. The nuclei of epithelial cells of para-mesonephric origin are about 50% larger than those of mesonephric origin.

Cysts of the epoophoron occur in all species of domestic mammals and located between the ovary and Fimbriae of the uterine tube. The lining of cysts consists

of a single layer of cuboidal epithelial cells. Some of the cells are secretory and other is ciliated. A thin zone of smooth muscle surrounds the tubules. Cysts of epoophoron are located on the tubal extremity of the ovary. Cysts of paraoophoron are present on the uterine extremity of the ovary. Mesonephric ducts are located close to the uterine tube. Cystic accessory funnels are located on the serosal side of the fimbria of the uterine tube.

Tubulo-ovarian cysts: The complete fusion of the fimbria of the uterine tube with ovary in cases of salpingitis and perioophoritis results in the accumulation of clear fluid in the proximal part of the uterine tube as the inflammation subsides. The resulting cystic dilatation of uterine tube that is adherent to the ovary is shown as tubo-ovarian cyst.

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 in to the bursa causing distension of the bursa. This condition is seen predominantly in cows as a sequel to severe inflammatory disease of the uterine tube and ovarian surface. Adhesions following enucleating of the corpus leuteum in cattle may also result in cystic dilatation of the ovarian bursa.

Neoplastic diseases of ovary

Granulosa-theca cell tumor is the most common tumor. These are usually unilateral. These are observed in young animals. Hyper-oestregenism is characteristic feature with these tumors. Gonadal stroma tumors are tumors of granulosa and theca cells as well as leuteomas. The finding that the stroma of the cortex of the ovary is not a mere supporting tissue but an undifferentiated blastema from which both the epithelium the follicles and non epithelial theca tissue had made histological classification of ovarian tumors difficulty particularly so in animals.

Cyst adenoma: These are seen in cows and seldom in cats. Cell type consists of epithelial appearance with central round nuclei and considerable cytoplasm. In some of these are structures resembling graffian follicle and an occasional specimen may show cells which radially cluster around a tiny open space which may contain an ovum like body the structures are called as Call Exner bodies. In the theca cell type belonged spindle cells are seen resembling theca interna or externa cells.

Granulosa cell tumor: The tumor arises from the cell of variant mesenchyme. This is seen in cows mostly. This has also been recorded in horses, bitches, sheep and fowls. These tumors are seen relatively in young animals. Grossly granulosa cell tumors are usually single and may be very large. In the cow it may attain assize having a diameter of 20 cms. Histologically the tumors may show great variation in structure and all radiating of histological pattern may be seen. Though these and granulosa cells of the ovarian follicles are products of divergent differentiation of undifferentiating ovarian blastema depending upon the predominance of the type of cells, the granulosa cell type tumors show regulars

of or clusters of compact alveoli or in irregular masses of pseudo glands. The cells maybe arranged in rosette like structures reminiscent of Call Exner bodies in the lumen hyalinised acidophilic material is present. Mitotic figures are numerous.

Leuteal cells tumor similar to the usual granulosa cell tumor but contain numerous lipoid droplets.

Arrhenoblastoma: This is a rare tumor present in animals with masculanising effect. In humans it manifests as sterility and atrophy of uterus, enlargement of clitoris and hairiness. Grossly it may be large or small or solid or partly cystic white or yellow. No typical structures are seen, but usually consist of carcinoma like trabaculae and masses with or without suggestion of glandular structures. But when well differentiated they forms structure resembling seminiferous tubules of the testis. It is assumed to originate from the rete ovarii and there is also a view that they originated from follicle forming cells which have served androgenic activity instead of estrogenic production.

Dysgerminoma: These are solid carcinomas of ovaries. These resemble the seminoma of testis without any endocrine effects. These are solid composed of rim with homogenous tissue. Histologically these consist of well define or ill define groups with lumina, large, rounded epithelial cells within connective tissue frame work of variable amount and surrounded by heavy lymphocytic infiltration. They are supposed to arise from the persistence of male tissue in an indifferent bisexual gonad.

Brenner tumor: This is usually small of moderate size and may be cystic or solid and is firm with fibrous structure and coloured yellow. Histologically nests of large polyhedral epithelial cells are seen scatted in dense fibrous stroma. Nests may be solid or may contain well defined cavities lined by stratified epithelium, and or by columnar secreting epithelium. The histogenic has not been clearly elucidated, but it is though to arise from Walthord nests, or it may arise from the ovarian follicles. Recurrence and metastasis is rare. No hormonal disturbance is observed.

Disorders of Uterine tube (fallopian tube) or salpinx

Uterine tube (fallopian tube) or salpinx: The salpinx is divided into four anatomic segments, infundibulum ampullla, and isthmus and uterotubal junctions. 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 third of the tube and is relatively wide. The isthmus is the narrow part of Th tubo proximal totheutero tubal junction. The utero tubal junction is the area of transition from the tube to the uterus.

The wall of the uterine tube consists of three layers namely mucosa, muscularis and serosa. The mucosa! folds are tall and have secondary and tertiary folds in the infundibulum and secondary folds in the ampullla. The longitudinal folds are

short, few in number and lack secondary folds in the isthmus. The mucosa consists of a layer of epithelium and mucosa proper with longitudinal folds. 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 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, mes-ovarium and ovary medially. In most mammals, the transport of ova through the uterine tube requires a about 3 to 5 days, in bitch 6 to 8 days, in cat 5 to 9 days and 2 to 3 days in sow. This delay enables fertilization and early embryonic development, following this zygote passes rapidly to the uterus.

The uterine tube of the mare is 20 to 30 cm long and runs a tortuous course in the mesosalpinx. The Fimbriae of the infundibulum cover the ovulation fossa during ovulation. In the mare, unfertilized ova are retained in the uterine tube for months, whereas fertilized ova pass into the uterus. The uterine tube of the bitch is about 6 cm long takes a tortuous course in the mesosalpinx and almost completely encircles the ovary. During anoestrous and early prooestrous, 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 cells of mid-prooestrous, and by later prooestrous hypertrophy and cytodifferntiation are advanced. Ciliated cells differentiated and become mature more quickly than the nonciliated cells. 60% of the epithelial cells have cilia at prooestrous. By early oestrous 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 hypotrophy until mild oestrous. During the early stage so meteostrous, the process of regression and dedifferentiation begins and by midoestrous the epithelial cells are similar to the basal cells observed during an oestrous (Verhage et.al. 1973)[11]. Ciliar were present in the tubal lining epithelium of cow throughout the cycle and degeneration of cilia was not observed (Nayak and Ellington, 1972)[12] and Nayak et al. (1977)[13].

Major congenital malformation of salpinx which causes reproductive problems in animals are accessory funnels (infundibula); accessory uterine tubes (Hydatid and Morgagni) cystic remnants of mesonephric duct, ectopic adrenal cortical nodules, agenesis, segmental aplasia, accessory osteum and duplication of uterine tubes.

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10 Nayak et al. 1977 about cyclic ultastructural changes in ewe uterine tube infundibular epithelium. Am. J. Vet.Res. 37: 923-33.

11 Verhage et. al. 1973. Development and maintenance of the oviduct epithelium during the oestrous cycle in the bitch. Bio.Reprod.9: 460-

12 (Nayak and Ellington, 1972) Cyclic structural changes in bovine oviduct epithelium. J. Anim.Sci. 35: 250).

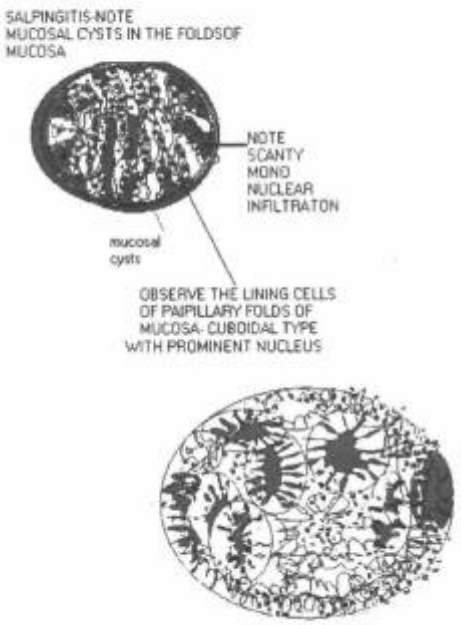
The accessory uterine tubes (Hydatid of Morgagni) are also known as appendix vesiculosus. It develops in the embryo at the extreme cephalic end of the para-mesonephric duct and persists postnatally at a stalked vesicle attached to the caudal portion of the uterine tube. It may consist of a series of linear cysts or a single prominent cyst. It has been suggested that some of the larger cysts may cause infertility in the mare.

Salpingitis: Salpingitis and its Sequleae are the most common diseases of the uterine tubes of domestic animals. Most infectious agents enter the uterine tube via the uterus. Number of organism's especially bacterial species, cause inflammatory lesions in the uterine tube. Most cows recover leaving no residual lesions in the uterine tube. Highly pathogenic organisms like *Brucella baortus, Mycobacterium bovis, streptococci, staphylococci and Mycoplasma bovis* produce more severe lesions and frequently infertility is the result.

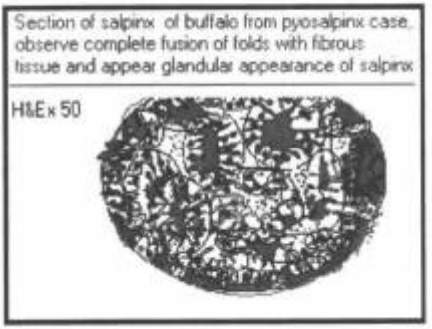
Pyosalpinx is the accumulation of exudates in the uterine tube following obstruction of the lumen due to the presence of exudates, fusion of mucosal folds or the formation of granulation tissue. Mycobacterium tuberculosis and Actinomyces pyogenes are the most common cause of pyosalpinx in cattle. The entire wall of the tube is infiltrated with neutrophils, macrophages, lymphocytes and plasma cells. Loss of epithelium results in adhesion of folds and cyst formation. Surviving epithelium undergoes squamous metaplasia. Bursal adhesions frequently accompany pyosalpinx.

Mucosal cysts: Mucosal cysts develop following the inflammatory denudation of the epithelium on the tips of secondary and tertiary fold of the uterine tube. The areas of denuded epithelium fuse to form cysts lined by tubal epithelium. The cysts occur predominantly in the proximal portion of the ampullla. They can be palpated as bead like structures in the intact tube and can be observed as small cysts in the opened ampullla.

Hydrosalpinx: Hydrosalpinx is the distension of tubular lumen with watery fluid. It may be unilocularis or multilocularis that means the fluid appears as distended spaces. It occurs in association with congenial anomalies of the uterine tubes and more frequently following acquired obstruction of the tubual lumen. In the case of pyosalpinx the exudates is gradually replaced by a watery fluid.



Photomicrograph of pyosalpinx. Observe infiltrating fibrous tissue



Placentation: As the blastocyts increases in size, it can no longer absorb enough nutritive material by diffusion, as it does during the early stages of its sojourn in the uterus. Implantation is a step toward the eventual formation of embryonic membranes that give the growing embryo access to the maternal circulatory system. Thus the transition from embryo trophic nutrition, during which the embryo subsists on uterine milk that is a product of uterine glands to haemotrophic nutrition is made. During haemotrophic stage the placenta is formed. The placenta is intimate apposition or fusion of the foetal organs to the maternal tissue for physiologic exchange.

The different types of placenta found in mammals can be classified in several different ways on of which is on the number of layers or barriers present in the uterus and foetus.

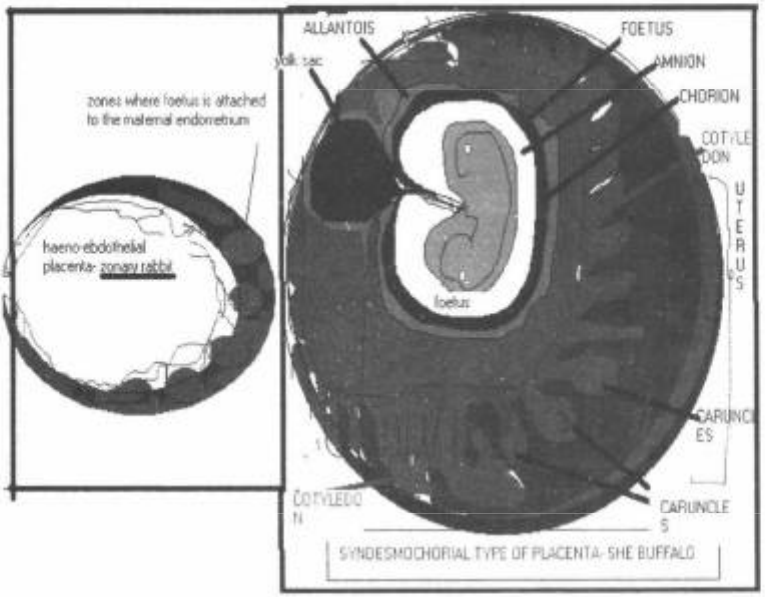
Type of placenta	Species	Number of layers in uterus (mother side)	Number of layers in fetal side	Gross Appearance Of placenta
Epithelio chorial	Pigs, Mares. donkey	Three layers	Three layers	diffuse
Syndesmo chorial	Cows, buffalo, sheep, goat	Two layers	Three layer	cotyledonary
haemo chorial	Cat, dog, human and other primate	Single endothelial layer	Three layers	Zonary--or discoid
haemoendothelial	Rabbit, rat, guinea pig	Single endothelial layer	Three layers	Discoid--or Spheroidal

Of the entire human placenta is a delicate one where the Endothelio chorial placenta is there where placental membrane is still several cell layers thick, and the minimum distance between the maternal blood and the foetal blood is 3.5ì or almost 10 times the distance across the alveolar membranes of the lung. Nevertheless, many nutrients and other substances pass through the placental membrane by diffusion in very much the same manner as through the alveolar membrane of the lungs and the capillary membrane elsewhere in the body.

Disorders of Uterus

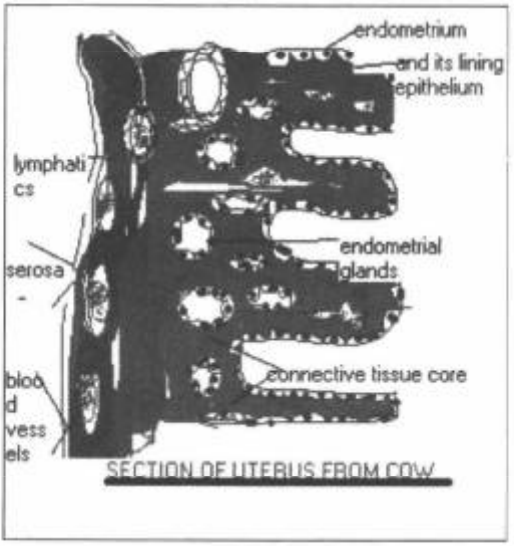
Anatomy of uterus

The uterus of domestic animals consists of cervix, a uterine body and two uterine horns. The body of cervix of uterus extends from 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, cat and mare and are coiled in the cow, ewe, doe and sow. the uterus consists of three layers, endometrium, myometrium and perimetrium. The endometrium is lined by columnar or cuboidal cells. Mucosa or propria consists of simple branched



tubular glands extend from the uterine lumen to the muscularis. Caruncles, which are non glandular portions of the endometrium, are present in ruminants. The caruncle consists of highly cellular connective tissue. The myometrium consists of 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 and the stratum vascularis are continuous with the

broad ligaments that suspend the uterus. The broad ligament contains a considerable amount of smooth muscle. The myometrium is the part of broad ligament that terminates on the horn and body of uterus. The round ligament of the uterus is located in the free edge of this field, which begins near the tip of the uterine horn and bends with the peritoneum over deep inguinal ring.



In cow 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. Uterine glands are absent at birth in normal cows. The surface epithelium of the endometrium is pseduostratified columnar. The surface epithelium of normal claves gradually invades the lamina propria to form glands during postnatal life. The lining epithelium of glands is columnar. The uterine glands are branched, coiled tubular structures that extend to the myometrium. The uterine glands are evenly distributed between the Caruncles and underlying 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 capillaries. The fibroblasts in this area have large, ape staining nuclei. The stratum spongiosa consist of loose connective tissue with many more fibrillar elements than the stratum compacta. The fibroblasts have smaller, dark staining nuclei and the collagen bundles form trabaculae between the endometrial glands.

In oestrous there is oedema of tunica propria of endometrium and the glands are relatively straight. During progestational phase the edema subsides and the gland becomes more coiled and complex. The epithelial cells of the glands reach their

maximum height at about the 8th day following ovulation. During meteostrous the caruncular area of the epithelium remained intact and massive heaemorrhages are observable. Neutrophils are normally seen during oestrous phase of the cycle and rare during progestational phase of the cycle. In prooestrous the number of mast cells increased beneath the lining epithelium and also around uterine glands. In later prooestrous or early oestrous is common. Accumulation of mast cells reached a peak and degranulation become more noticeable. After or during oestrous a sudden diminution of mast cell numbers was observed particularly in the endometrial stroma.

The Caruncles of sheep frequently pigmented from the presence of melanoblasts. During pregnancy the pigment becomes depressed in intercaruncular tissue and reports of reduction in the amount of pigmentation with advancing pregnancy. Pigments of caruncle shave also been observed in goats and certain breeds of cattle.

Endometrial glands are not present in the newborn pig. The endometrial glands begin to develop from the superficial epithelium in the 2nd week of life and reach the basal part of endometrium in the 4th week.

Endometrial cups which are round to oval, gray, elevated areas of endometrium with central concavities that are present in the gravid uterus in the mare between 37 and 150 days of gestation. Their presence is associated with the production of pregnant mare serum gonadotrophins. These endometrial cups develop in that portion of endometrium in apposition to the chorion in the region where the allnatoic vessels fan-out over the allantoin chorion forms the umbilical vessels. The endometrial cup consists of densely packed, large polyhedral cells with abundant pale eosinophilic cytoplasm. Endometrial cups originated from the chorionic girdle portion of the trophoblast. Many of these are binucleated cells. The endometrial cups degenerate from 60th to the 150th day of pregnancy when the necrotic cups are rejected from the endometrium.

The endometrium of bitch consists of three zones, the zone of crypts, the intermediate zone and the basal zone. The crypt zone has numerous short, epithelial line recesses of the uterine lumen, the intermediate zone is predominantly of connective tissue and the basal zone contains glands.

The uterus; Normal postpartum involution: To evaluate pathologic alterations in the postpartum uterus, it is first essential to know the gross and histological changes that occur during normal involution. Involution occurs most rapidly in the mare and sow and least rapidly in the bitch. Post partum periods in the cow starts with parturition and lasts until uterine involution is complete and then animal has resumed regular oestrous cycles with normal oestrous behaviour. The interval from parturition to complete uterine involution is significantly longer in pleurparous than in prim parous cows. This varies between 34 to 41 days. The weight average uterus decreased form 9 kg at parturition to 1 Kg at 30 days and

0.75 kgs and at 50 days. The uterine fluids in cow is from 165 to 1000 ml during first 9 days of postpartum and the average lochia discharge during the every days was around 500ml. Elliott et al (1968) culture uterus for bacteria from 106 postpartum cows. Thirty three species bacteria were isolated. They are Staphylococcus epidemroid, pseudomonas, Corynebacterium spp, Streptococcus fecalsis and Micrococcus. Ellitot.l.Et a. 1968[14].

The gross changes in the normal post partum 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 2nd post partum, irregular wedge shaped red areas are present in the luminal half of the Caruncles. By day 4th the Caruncles are dark red and soft. The dark discoloration extends to the vascular stalk, which is white. By days 9th to 12th, all the necrotic caruncular area has sloughed from the surface of the stalk leaving a granular surface with a few small hameorrhagic foci. It consists to have garnular, nonglistening surface until it is covered by ingrowths of adjacent surface epithelium. The surface epithelium in the intercaruncular area of the endometrium remains intact throughout the postpartum period, giving the surface of the caruncular tissue a glistening appearance. If the epithelium is denuded as a result of endometritis, its surface appears granular and non-glistening. The surface of the caruncle begins to glisten by 15th day and by 30th day the caruncle appears to be normal on gross examination.

The weight of uterus in ewe after immediately parturition weights around 1200 Gms and by 24th day it weights around 100 Gms.

The postpartum uterus of sow involutes by 21st to 28th days. The length of uterus decreased from 240 cm from the day of parturition 120 cm on day 28th. The uterine weight decreased from 2725 gm to 244 gm. The myometrium involution appears to be the result of both cell destruction and atrophy of muscle cells and interspersing connective tissue. The surface epithelium at day one was low columnar to cuboidal and measured 10 to 12 ì in height. The uterine lining was folded and the tunica propria was oedematous. By 14th day, the surface epithelium measures around 15 to 20ì high and is pseudostratified. By 21st day the surface epithelium height was 25ì and the leukocyte migration into the uterine lumen has subsided.

In the case of mare, the uterine involution is well advanced by the 3rd and 4th postpartum and the changes are usually complete by the oestrous period, 7 to 10 days after parturition. After postpartum the uterus weighed around 7 to 9 kgs. And will be reduced up to 2 kgs.

In the case of bitch the reduction in the size of uterus occurred during the second and 3rd weeks. The placental sites were grey tan and contained blood clots. The entire mucosal surface was covered by dark brown mucous. By 5th to 8th weeks the size of the uterus was reduced. The numbers and size of gray nodules in the

placental sites were reduced. By 9th week the uterine horns are uniform in shape and the placental sites were differing entirely from the rest of endometrium by their brown colour.

Pathological conditions

Abnormal uterine bleeding is associated with sub involution of the placental sites. Effusions of maternal blood are characteristic of the margins of placenta alone, but in addition, smaller heaemorrhages takes pace into the substance of the placenta and form the green pockets of central haematomas.

The formation of superficial haematomas is characteristic feature of placentomes of ewe. False heaemorrhages due to rupture of uterine arteries also occurs in the cow. Thrombosis of blood vessels in the placental sites of carnivores and in the Caruncles of postpartum ruminants is normal. The arterial lesions which occur during postpartum uterine involution are a physiological pregnancy sclerosis.

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 are seen. During pregnancy, elastic tissue in the tunica intima of the endometrium of the arteries appeared to disappear and reappear in the postpartum period.

Atrophy

Atrophy of uterus occurs in association with chronic debilitating diseases and following ovarectomy. During period nutritional deficiencies, ovaries become smooth and nonfunctional and uterus atrophies. Cows with mucometra due to secondary cystic follicles wherein the uterine wall is atrophied and where the endometrium and myometrium becomes very thin. The endometrial glands become cystic and the glandular epithelium atrophies. Atrophic myometrial cells are composed predominantly of nuclei with only a small amount of deeply acidophilic sarcoplasms. The mycotoxins, zearalenone induces oedema and multimodal squamous metaplasia of the endometrium of swine. Squamous metaplasia of the uterine surface epithelium is seen in cases of postpartum Pyometra in cows, in association with prolonged cystic ovarian follicles. Oestradiol implantation in pregnancy in bitch showed metaplasia of lining epithelium.

Hyperplasia of endometrium is observed in all species of animals but is more often met within the dog. It is also known as cystic hyperplasia of the endometrium. The cause appears to be increased oestrogen and or progesterone secretion, under the influence of which the endometrium undergoes hyperplasia. The common causes are granulosa cell tumors of ovary, cystic ovaries where oestrogen and progesterone secretions are responsible for this. Feeding in pasture legumes and fodders containing estrogenic principles are responsible for causing hyperplasia of the endometrium in the ewe and cow.

Grossly the endometrium of both horns contains cysts of different size and the uterine glands are filled with mucous exudates and are enlarged hence these condition of Swiss-cheese type. The lumen of the horns may also contain mucous or pus.

Histologically no inflammatory changes are evidenced. Cysts are found in the mucosa and these cystic glands contain a single layer of epithelium. The lamina propria is infiltrated with plasma cells.

Clinically abnormal uterine bleeding, disturbance in oestrous cycles, abortions and finally sterility is noticed. Blood smear examination reveal neutrophilia with shift to left having number of immature neutrophils in blood.

Inflammatory conditions of uterus

Metritis is the inflammation of the uterus. When inflammation is restricted to the endometrium it is called as endometritis. If inflammation is restricted to whole thickens of wall is called metritis. Inflammation of the serosa is known as peri metritis. Chronic endometritis is called as Pyometra.

Endometritis

Causes: Infectious, bacteria like Brucella abortus, vibrio foetus streptococci and staphylococci.

Trichomonas foetus that is infection may occur during coitus. Other bacterial infections spread during artificial insemination or during manual handling of uterus.

Irritants like introduction of too hot fluids or too irritating chemicals into the uterus, thereby injuring the delicate mucosa.

Grossly no lesions are evident. An increased secretion of tenacious mucous may all that is visible. The mucosa is swollen, red and rough, instead of having smooth surface and covered with fragments of necrotic material.

Histologically mononuclear infiltration like lymphocytes and plasma cells is prominent. But not neutrophilic infiltration in mucosa.

Hydrometra and mucometra: Hydrometra is an accumulation watery fluid and mucometra is an accumulation of mucinous fluid in the uterine lumen. The causes for this are congenital malformations of cervix and; uterus and hormonally induced cystic hyperplasia of endometrium. Mucometra with persistent corpus leuteum is common in cows. Hydrometra is also commonly observed in goats with abdominal distensions.

Adenomysosis or endometriosis: The term applies to the presence of endometrial glands places other than endometrium. If these are seen between the muscle bundles of myometrium, the condition is called endometriosis interna or adenomysosis. On the other hand, if the glands are seen in places other than

uterus such as mesosalpinx, ovary, cervix or intestinal serosa and sometimes in humans near the nasal mucosa, then it is called endometriosis externa. The endometrial glands show changes in response to ovarian activity and often there are heaemorrhages. In women these appear as chocolate coloured cysts. Endometrial glands have grown into the myometrium in cow, buffalo, cat and bitch. This is probably as a result of prolonged oestrogen stimulation.

Mummification of foetus: Mummification of dead foetus is seen occasionally in multiparous species and is also in the cow and buffaloes. In horses especially, one of twin fetuses which is mummified.

To have the mummification, the uterine contents should be sterile and there is death of the foetus. In the absence of infection, the fluids are reabsorbed and the membranes become closely applied to the desiccated foetus, the foetus becomes brown or black and rather leathery, moist on the surface with sticky mucous without colour.

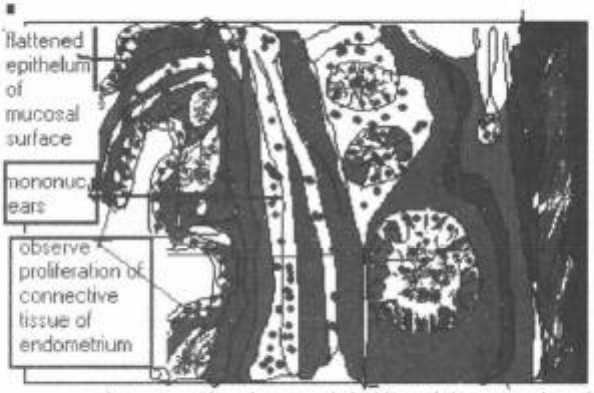
The time required for complete mummification depends on the size of the foetus but probably requires as long as 6 to 8 months in cattle and buffaloes. In uniparous animals, the mummified foetus is usually retained indefinitely or if aborted many only be delivered or into vagina. In the case of multiparous animals, it may be delivered along with the viable foetus. Animals which had and recovered from mummified foetus usually breed normally on subsequent occasions.

Maceration of foetus: Depends on the presence of infection in the foetus as well in the uterus, the foetal membranes disintegrate and only bones will remain. If the early embryo succumbs to uterine or embryonic infection, maceration is usually followed by resorption from the uterus or expulsion along with a small amount of purulent discharge. If the foetus is about three-month as with nine months gestation of domestic animals, complete foetal maceration does occur and the bones are only left as the bones resist maceration. These may be discharged or be retained in the pus of pyometra indefinitely, often near the cervix.

Advanced uterine lesions accompany the macerated foetus. The uterine wall is thickened and the reaction within it varies from acute exudative inflammation to pyometra to more or less complete chronic metritis or sclerosis.

The temporary infertility which is the clinical hall mark of the disease is the result of mild to moderate inflammation of the endometrium and adjacent structures.

Metritis is seqelae to puerperal sepsis as well trauma arises in parturition. The secretion may be scant or abundant and is fetid and is dirty yellow to red-black. Invasion of blood vessels, both arteriolar and venous aggravates the lesions. Thrombosis may extend to the vessels of mesometrium with the usual Sequleae of hemorrhage and infarction.

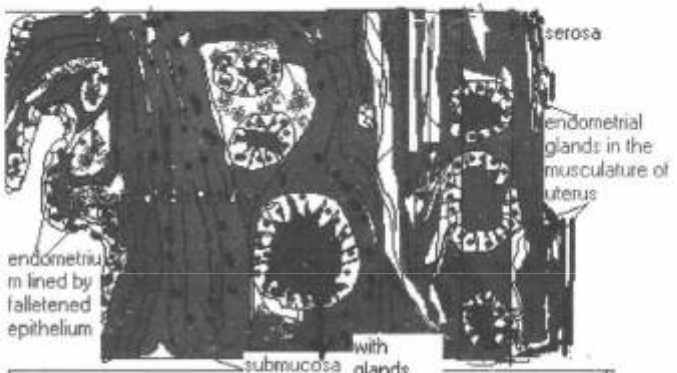


SECTION OF UTERUS OF SHEBUFFALO WITH CHRONIC ENDOMETRITIS. H & E X 20

Chronic endometritis: Recovery from the acute phase of the infection often results in chronic endometrial involvement. Endometrial mucosa is thickened, sloughening of the lining cells as well the glands are depleted, atrophied or cystic with periglandular fibrosis. The lining mucosa may show desquamation or polypoid growths or squamous metaplasia. The exudates in the lumen are serous, catarrhal or frankly purulent.

Chronic suppurative endometritis is called pyometra.

Pyometra.



section of pyometra condition in a shebuffalo showing presence of endometrial glands (adenomyosis interna) in the dilated uterine musculature . H&E x50

Pyometra is an acute or chronic suppuration infection of the uterus with accumulation of pus in the uterine lumen. The escape of the pus is usually prevented by a functionally closed cervix, but the discharges may be prevented by an acquired or congenital cervical stenosis. In horses the gravitational pull of the flaccid, distended uterus over the brim of the pelvis may limit the discharge of pus.

Pyometra is not condition in ewe and the sow. It is relatively common in the bitch, cat, cow and mare.

Pyometra in the bitch: Most cases of pyometra in the bitch are infective inflammation associated with endometrial hyperplasia. This disease occurs in meteostrous period. The corpus leuteum is present in the ovary. The progesterone secretions liberated by persistent C.L. is responsible for this. The cystic endometrial hyperplasia is due to progesterone secretions and consequent bacterial infections like Escherichia coli. The result of bacterial infection being superimposed on an abnormal endometrium it appears that the bacterial infection of the progesterone primed endometrium produces both the pyometra and the cystic endometrial hyperplasia. Most of the Escherichia coli are the strains pathogenic to urinary tract epithelium. Urinary tract infections are common in bitch with pyometra. It seems probably that urinary infections are predisposing to uterine infections.

The clinical signs in affected animals are depression, anorectic frequently vomit and have polyuria and polydypsia. The bitch shows vaginal discharges.

Postmortem findings: There is marked distension of uterine horns. The cervix is completely closed, the serosal surface of the uterus is dark and the vessels are congested.

Histologically there is endometrial hyperplasia and the epithelium is hypertrophied, enlarged, columnar, and vacuolated and has small pyknotic nuclei. Localised papillary proliferations of endometrium are due to obstruction of endometrial glands. Hence this is being called polypoid endometritis. Masses of neutrophilic infiltration is found in the uterus and its mucosa and in glands. As the blood vessels are congested and show thrombosis.

Extra genital lesions: These are found in the dog and cat and maybe due to the toxic effect on other organs as well as to periodical bacteriaemic may occur. The lesions are

1. Extramedullary haemopoiesis like presence of white spots in liver, kidney, spleen, adrenals, lungs and lymphnodes.
2. There is membrano proliferative glomerulo nephritis, tubular generation, heaemorrhages in the medulla, infarcts and pyelonephritis.
3. Congestion and degenerative changes in the liver.
4. Adrenals showed necrotic foci in cortex and heaemorrhages in the medulla.
5. Changes in the lymph nodes are depletion of lymphocytes and infiltrated with neutrophils.

6. There is myeloid hyperplasia of bone marrow. There is increased myeloid: erythroid ratio. There is intense leukocytosis. The total white cell of blood varies form 30,000 to 2 millions/cmm. The shift to left is predominant in the beginning of the case. There is leukemoid reaction in the later stages; there is depletion of immature cells. Infact it is a bad prognostic sign. Until the hysterectomy is done, the bitch cannot recoup from the disease effect.
7. Profound renal hypotension and reduce renal perfusion led to pre-renal uremia.

Pyometra in the cow and

Buffaloes

In cattle and buffaloes pyometra is common due to retention placentas well due to the retention corpus leuteum. The placenta putrefied it is a very good medium for bacteria to thrive. In the cow and buffaloes, the placenta should fall away within 10 to 14 hours after the parturition. When the after-birth is staying beyond this time is called as retained placenta. Variety of causes has been attributed for this.

In the cow uterine diseases causes the corpus leuteum to persist and maintain a high progesterone level. The retention of the C.L. appears to be due to a reduction or inhibition of the synthesis and release of leuteolysis factor, prostaglandin PGF2α, by the diseased endometrium.

Acute endometritis can cause synthesis of PGF2α in large animals that have undergone progesterone priming for 4 to 5 days leading to premature regression of C.L. and shortening of oestrous cycle.

Broadly there are two periods in which a uterine infection can lead to retention of corpus leuteum with the accompanying hormonal effects which convert an endometritis to a pyometra. They are during the early postparturiently period, following dystocia, retained placenta and metritis and at varying times after breeding, as a result of venereal infections with early embryonic death.

The amount of pus retained in the uterus of cow varies form 100 ml to several liters. The cervical has no seal of mucous and though in contracted position, still discharges of pus are seen from the vagina and vulva. The wall of the uterus is thick, doughy and mucometra results. Pyosalpinx and Peir metritis are also result.

Histologically the author has fund out not a single neutrophilic infiltration in the mucosa or submucosa or in fact in serosa of the uterus. There is hyperplasia of endometrial glands and in later stages there is desquamation and sometime the lining epithelium show metaplastic changes. Extensive fibrosis of periglandular and perivascular regions is very common.

Adventitial Placentation: Refers to the development of additional sites of Placentation between adjacent placentomes, in ruminants, usually as the result of

inadequate development of existing placentomes. The condition generally results from an insufficient number of endometrial Caruncles resulting either from a congenital disorder or from loss of Caruncles due to prior episodes of endometritis. Cows normally have 75-120 Caruncles in their uteri, ewes and goats have 40 -125.

Adventitial Placentation results from fusion of adjacent hypertrophied Caruncles with primitive villous attachments between the chorion and the endometrium in intercotyledonary areas. When adventitial placentomes becomes diffuse, Pregnancy may not proceed beyond mid term. Hydrallantois is a frequent complication.

Hydramnios and Hydralantois:

These conditions are characterized by excessive fluid in the amnion and allantoin sacs. At term, cows normally have 15-20 liters of foetal fluid present between the two sacs.

Hydramnios or hydrops amnion is generally associated with malformed fetuses, whereas hydralantois is generally associated with adventitious Placentation or cow varying twins. The quantity of fluid present may exceed 150 liters. When the foetus is not aborted early, dystocia, uterine atony with retained foetal membranes and metritis are common Sequleae.

Amniotic plaques and placental calcification

Amniotic plaques consist of focal areas of squamous epithelium on the inner surface of the amnion. Calcium deposition occurs normally in the allantois and amnion from the end of the first to the middle of the second trimester appearing as a white streaks or these serve as reservoirs of calcium for developing foetus.

Prolonged gestation: In sheep and cattle conditions interfere with the synthesis and release of Adreno cortico trophic hormone by the foetal pituitary and cortisol by foetal adrenal cortex will result in prolonged gestation.

Abortions in animals

Abortion refers to expulsion of an embryo or fetus from the uterus, prior to an age when it could survive with maximal supportive care in an extra uterine environment.

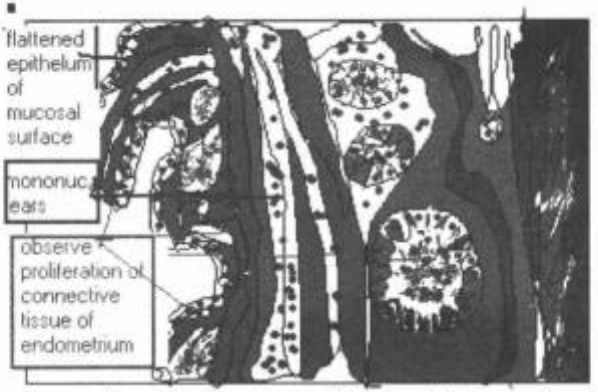
Still births conversely refer to expulsion of dead foetus from the uterus at an age when it could conceivably survive outside the uterus with minimum supportive care.

Predisposing causes for abortions in pregnant animals

Pregnant uterus and its contents the placenta and developing embryo or foetus together referred to as conceptus are more prone to infection than the non-glandular uterus.

The reasons for the pregnant uterus susceptible to infections are

1. Gravid uterus under the influence of progesterone is more susceptible to infections.
2. Chorionic epithelium of placenta secretes substances that predispose the gravid uterus to certain types of infection.
3. Placenta and embryo or foetus is immunologically privileged sites not directly protected from infection by maternal immune system.



SECTION OF UTERUS OF SHEBUFFALO WITH CHRONIC ENDOMETRITIS. H & E X 20

Diagnosis of abortions in cattle

Disease	Clinical features	Abortion rate	Time of-abortion	Placenta	foetus	Isolation-studies
Brucellosis	Abortion	Abortion High-up to 90%	6th month	Necrosis-of-cotyledon, leathery. opaque, placenta	pneumonia	Foetal-stomach-contents, uterine fluid, milk, semen, serum, blood-and ------ agglutination tests
trichomoniasis	Infertility returns to heat at 4 to 5th month, abortion and Pyometra	-30%	2-4 months	Floccular-material, clear serous fluid in uterine exudates	Foetal maceration and Pyometra	Hanging drop exam of slide, Cultural examination-of foetal stomach\contents, uterine exudates within 24 hours, cervical-agglutination test
Vibriosis	Infertility, irregularly moderately prolonged dioestrous	low up to 5 to 20%	5 to 6 months	Semi opaque, little thickening,petic hae and oedema	Flakes of pus on visceral peritoneum	Culture of foetal stomach, contents, placenta-and-uterine exudates, blood agglutination tests after abortion

Leptospirosis	Abortion at fertile stage	5-30%	Late, 6 months	Avascular placenta	Foetal death common	Isolation from pleural fluid, kidney and liver of foetus, direct examination of urine, serum and agglutination tests.
Listeriosis	septicaemia	low	About 7 months	-	No abnormality detectable	Organisms in foetal stomach-contents, placenta, uterine fluids, agglutination titres of sera
Chlamydiosis	Diahorrea / winter	high- 30 to 40%	6 to 8 months	-	Sub cutis oedema and ascites	Stomach contents
Infectious-bovine-rhino tracheitis	uneventful	5-50%	Late, 6 months	–	Autolysed foetus	Culture of placenta

Brucellosis

Synonyms: Bang's disease; Contagious abortion

Brucellosis is the disease produced by a gram negative bacilli or coco bacilli, which are intracellular parasites and affect the animals and humans resulting in chronic infections. In animals usually the reproductive tract is infected resulting in abortions.

Aetiology: The organisms under the genus *Brucella*, which cause disease in animals and man could be categorised into3 classical species, viz., *Brucella abortus, Brucella suis and Brucella melitensis.*These are distinguishable to some extent by biochemical reactions but chiefly serological ones.

Brucella abortus chiefly is an infection of cattle and buffaloes. *Brucella melitnesis* prefers goats and sheep and *Brucella Suis* affects swine. Cross infection, do, however occur and almost all domestic species are susceptible with these organisms. Other species like *Brucella canis* and *Brucella ovis* are recognized. But their infection confines to their respective species.

Bovine Brucellosis: Brucellosis in cattle, previously called contagious abortion, has been recognized since ancient times. It is characterized by inflammatory changes in the foetal membranes, which lead to the premature expulsion of foetus. Source of infection for cattle is an aborted foetus or placenta, contaminated uterine discharges, and the usual route of infection is alimentary.

It has been isolated from the uterine contents of an aborting mare and from an aborted human foetus. It has appeared infrequently in chickens, and dogs. In rare cases abortions are seen in canines. It has been isolated from sub maxillary lymph nodes of swine and also has been found in hygromas of knees of cattle and in inflammations of bursa located beneath the ligamentum nucahe. It causes fistulous withers and poll evil in horses. In man *Brucella abortus* causes a disease

known as Brucellosis or undulant fever. All three species produce the same clinical syndrome in man. *Brucella abortus* produces a generalised disease when injected into guinea pig, rabbit, mice and rats. The organism was first described by Bang in Denmark in 1897 and was recognized in the United States by McNeal and Kerr in 1910. This disease has been recognized nearly all countries of the world where cattle are kept. It is not prevalent in areas of intensive cattle rising. Under range conditions, the disease is often of low prevalence or absent. Growth of Brucella types of organisms in dye (azo dyes)/ media.

It is a small, gram negative, non-spore forming rod. In exudates it is frequently found in clumps. These organisms are microaerophilic. Carbohydrates are not fermented. Gelatin is not liquefied. The growth in selective media and differentiation of other Brucella organisms by growing in differentiated media having dyes.

The favored media are potato dextrose agar, wherein the *Brucella abortus* organisms produce golden yellow colonies.

Brucella Suis can be differentiated from the other types by it ability to split urea. Brucella abortus uses little or no glucose when that sugar is present in the medium, whereas *Brucella melitensis* and *Brucella Suis* utilizes from 4 to 18% of the available supply. Bovine strains require an increased CO_2 tension for the initiation of growth. Neither the porcine nor Caprine varieties have this requirement.

Presence of erythritol stimulates the growth of Brucella organisms. It is present in foetal and placental tissue and fluids of ewe, cow, goat and sow, but is absent from a number of species of laboratory rodents and man.

Strain	Methyl violet	Fuchsine	Thionine
Brucella abortus	+	+	-
Brucella suis	-	-	+
Brucella melitnesis	+	+	+

Transmission: Source of infection for cattle is an aborted foetus or placenta, contaminated uterine discharges and the usual route of infection is alimentary. Infection can occur per vaginum, via the conjunctiva, and through the broken or unbroken skin. Young cattle are relatively not susceptible up to the puberty. Though infected, they throw off the infection in due course. Excretion of the organisms may occur for several days before abortion and a varying period of times after. Brucella organism can survive in contaminated material for days, even weeks if in the shade of protected within a foetus. Infection usually occurs from ingestion of contaminated pastures or water, or by licking a discharging animal, new born calf or placenta. Predators can move a foetus or placenta for several kilometers and thus disseminate infection. Over 90% of cows and heifers excrete Brucella in colostrums and milk, during the first months of lactation. Intermittent excretion of organisms occurs in decreasing proportion of animals

thereafter. Calves are infected in utero or by sucking infected dams. Venereal transmission rarely occurs in bovine brucellosis. However, artificial insemination with infected semen often results in transmission.

Pathogenesis: Infection either by ingestion or by abrasion or by conjunctiva or by venereal transmission, the organisms extend quickly to the lymph nodes in adult animals, there they provoke an acute lymphadenitis. Inflamed glands are enlarged. Spread is chiefly haematogenous and bacteraemia persists for several months. The persistence of organisms depends on the susceptibility or resistance of the host. As the infection becomes chronic, bacteraemia becomes intermittent, stops in some animals and recurs irregularly for at least 2 years in 5 to 10% of animals. Also it tends to recur at parturition. The organisms are not excreted either in the urine or in faeces. Localization in the synovial structures does occur. For this existing inflammatory change may be necessary.

Abortion occurs most often in the 7th or 8th month of gestation. The nonpregnant uterus is not particularly susceptible to *Brucella abortus* and following abortion or parturition, the organism is cleared from the uterus in a few weeks or longer in some cases.

Gross lesions: There is enlargement of lymph nodes of the body viz., supramammary and inguinal are much pronounced. Abortion occurs most often in the 7th and 8th month of gestation. Between the endometrium and chorion in the inter-cotyledonary area, there is more or less abundant exudate which is odorless, dirty yellow in colour. Placental lesions are not uniform. Cotyledons are extensively necrotic, oedematous; organism influences the inflammation of the foetal membranes. By the inflammation, with exudates the circulation of the foetus is interfered with and this way abortion occurs.

Organisms may be found in pure cultures in the alimentary tract and in the lungs of aborted foetuses. Other tissues of the foetus are usually sterile. The location of the organisms suggests that it is taken into the foetus by the swallowing of amniotic fluid rather than through the blood stream.

The foetus is oedematous and subcutaneous fluid is blood tinged; normal abomasal content of the foetus is clear, translucent, thick and viscid. In brucellosis it often becomes very turbid, of lemon yellow colour and flaky. The important lesion in foetus is pneumonia. This may be either catarrhal or fibrinous broncho-pneumonia.

Histological lesions: Besides pregnant uterus, the organisms are frequently recognized in another organ, the udder. Lymph nodes adjacent to the udder and uterus are usually infected where these organs are infected.

In bulls, infection of the epididymis and testicles occur. Abscesses usually develop in these organs.

These intracellular parasites produce granulomatous lesions, and these granulomatous lesions are usually of suppurative in nature. Inflamed lymph glands

show enlarged sinuses and neutrophilic infiltration in sinuses. Remarkable accumulation of plasma cells is seen in medullary sinusoids.

Diagnosis: By clinical symptoms, i.e., abortion waves during the 7th month or afterwards. Recognition of *Brucella abortus* organisms under 10% CO_2 tension as it requires this when compared to other species of Brucella organisms. For this liver agar media is good. The media is added with antibiotics like polymyxin, bacitracin, and crystal violet which inhibit other bacteria in the medium. From the aborted foetus, foetal contents from stomach, intestines or lung could be collected and cultured. If placenta is present the organisms could be isolated from the epithelial cells of chorion. In the uterine exudates, *Brucella abortus* is present in the lochia and within a few days after abortion the organisms disappear from the uterus. Milk, can be procured and intra peritoneal injection of milk into guinea pigs or organisms could be cultured directly from the milk itself. Abscesses if any are present; the material from the abscess is aspirated and cultivated.

Biological inoculation tests: When the organism from uterine exudates or form milk into the guinea pig results in chronic disease in guinea pigs. The lesions in guinea pig with bovine strains are proliferate in character, whereas those due to infection with porcine organisms are both proliferate and degenerative, i.e., the swine organisms commonly causes abscess formation and the bovine does not. The bovine organisms usually will not destroy the guinea pig or only after number of months has elapsed, whereas porcine variety will frequently cause death within 2 or 3 weeks.

Spot serum tests by plate agglutination test by coloured antigen are employed in the field. The spot test positive sera are usually confirmed by tube agglutination test in the laboratory. A titer of 1 in 40 and above is considered as a positive.

Skin sensitivity test by using Brucellin skin intradermal tests can be employed usefully. Abortus Bang ring test can be employed by using coloured antigen on the whey of milk. Complement fixation test is by far the most sensitive and specific. Complement fixations tests are useful in differentiate between reactions caused by vaccinated animals and infected animals. Recent tests by employing ELISA are frequently being used.

In eradication programmes, infected animals are detected by serological tests. The screening tests are the Rose Bengal and Card tests carried out on drops of serum or whole blood. And the milk ring test made on milk from bulk tanks or individual cows. The ELISA test is also being used as screening test in an increasing number of countries. These tests are very sensitive but not always specific. On specific reactions are caused by vaccinating and occasionally by infection with other gram negative bacteria such Yesinia and Salmonella. Paired serum samples are always best tin confirming the test and the second test should be carried out 30 to 60 days later or ideally about 14 days after calving when titers often rise rapidly.

Brucella melitensis

The disease has been name after Bruce who isolated in 1897 from the spleen of resident of the Island of Malta who had died from a disease known as Malta or Mediterranean fever. The disease is characterized by septicemia and death in goats and is caused by *Brucella melitnesis. Brucella melitnesis* share similar antigens to *Brucella abortus* and *Suis.* Three biotypes exist. Cattle and other ruminants may become infected but pigs appear resistant. Man is highly susceptible and the organism causes Malta fever or the undulant fever.

Transmission: Mostly by oral ingestion.

Clinical features: The disease causes septicemia and death. Sheep appear more resistant than goats. The incubation period ranges from 3 to 20 weeks, abortions usually occurring in the 4th or 5th month of gestation. The disease in the goats may become chronic and last many years. The organisms are excreted enormous amounts in the milk. Clinical mastitis is common. Other symptoms include unrthriftiness, bronchitis with hacking cough, lameness and hygromas and orchitis in males.

Lesions: Abscesses in the spleen and costo chondral cartilage may occur. Mild mastitis is present and the milk is of poor quality.

Brucella melitensis is excreted in the urine of infected goats. It is considered that the male plays a greater part in spread of the disease than in the case in bovines. Abortion occurs late in the pregnancy and lameness may be present when bones and joints are affected.

Brucella suis infections

Brucellosis In pigs (Brucella Suis) infection: The causative agent is the *Brucella Suis,* though pigs are susceptible to *Brucella melitensis* and slightly susceptible to *Brucella abortus.* There are 4 biotypes that are responsible for the disease. *Brucella Suis* biotypes 1 and 3 are infections of pigs. Man is susceptible to biotypes 1 and 3. Biotype 2 is found in European hares.

Transmission: Boars are important carriers of infection, organisms can be transmitted venereal and are also excreted in urine and faeces. Sows and gilts liberate organism in milk, foetuses, foetal membranes and vaginal discharges. Alimentary tract in young piglets is common. The usual spread is through contaminated fodder and water.

Clinical features: When first introduced into the herd, the disease runs acute course. It persists in chronic form in adult pigs but is evident as acute condition in subsequent generations. The disease is characterized by abortions, stillbirths or weak piglets, temporary or permanent infertility in both boar and sow. Lameness and posterior paralysis is common.

Boars are usually infected at sexual maturity. There may be bilateral or epiddymo-orchitis, with great enlargement of testis with which contain purulent and calcifying foci. In sows, the gravid or no gravid endometrial is frequently studded with pin-point nodules containing caseous pus. The joints maybe swollen and painful contain increased fluid and may ankylose. Encapsulated abscesses of 2 to 3 cm in diameter are present in the intervertebral discs or vertebrae of lumbar and sacral areas. The disease is of self limiting and may be eliminated in due course.

Pathology: The disease in swine resembles that of seen in brucellosis of man and guinea pig rather than that caused by *Brucella abortus* of cattle in that the infection is found frequently in many organs other than that of genital system. *Brucella Suis* can be readily isolated from blood, spleen, uterus, lymph nodes and other organs in addition to the uterus and mammary gland of sows and testes and *semen of boars.*

Brucella Suis can grow and multiply in phagocytes, and typical granulomatous lesions. Begins with accumulation of histiocytes and epitheloid cells. Perhaps as a response to developing hypersensitivity to the organism, as the lesions enlarges caseous necrosis occurs centrally and fibrous tissue forms a capsule. The granulomas enlarge progressively and the necrotic tissue attracts neutrophils. Giant cells are absent or scarce. Calcium may be deposited in the necrotic foci.

Articular lesions caused by *Brucella Suis* are quite common. They begin as synovitis and affect chiefly the compound and large joints of the limbs. The reaction is purulent or fibrinopurulent. Osteomyelitis in this disease is typically vertebral. Localization is typically in the vertebral epiphysis of lumbar region. There is however, a usual tendency to involve and destroy the intervertebral cartilages. The swollen bony lesions are typical granulomatous with dry caseation necrosis, and the suppurative reaction may extend to meninges or fistulate to produce para vertebral abscesses.

In the uterus and fallopian tubes there are often conspicuous and characteristic lesions which are not dependent or an association with pregnancy. They have been referred to as military uterine brucellosis and as the name implies there are few or very many yellowish white nodules with an average diameter of 2 to 3 mm seeded into the mucosa. Where the nodules are numerous these may coalesce to form irregular plaques and these are associated with thickening of the uterine wall and the structure of the lumen. The same lesion is usually present also in the fallopian tubes when obstruction results in pyosalpinx. Incised, a small quantity of caseous exudates can be expressed from the nodules. The mucous glands are dilated and had lymphocytes in between the glands.

Brucellosis in man

Brucellosis (undulant fever) is transmitted from lower animals to man. The acute

illness is frequently characterized by fever and the chronic form consists of fever, weakness and vague complaints which may persist for months and years. The etiological agent was as stated earlier was discovered by Bruce as long back as in 1886.

The natural reservoir of brucellosis is in domestic animals and the disease is very rarely transmitted from man to man. Majority of cases are acquired through contract and few cases are caused by ingestion of milk. The disease is very rarely transmitted from man to man. Following invasion of the body by Brucella through the oropharynx or through the skin, the organism tends to localize in tissues of reticulo endothelial system such as bone marrow, lymph nodes, liver, spleen and also kidneys. A characteristic but non-specific reaction of tissues to Brucella is the appearance of epitheloid cells, giant cells, lymphocytes and plasma cells. Caseation is the characteristic feature also. The granulomas thus formed are similar to tuberculosis. Brucella organisms are localised in bone, spleen, endocardium and testis. Authenticated version of human abortions is lacking. Orchitis is also rarely seen.

Brucella melitensis infections are contracted from drinking of raw, infected goat's milk or from eating certain cheeses made from such milk. Infections are also contracted from swine and cattle. *Brucella abortus* infections are contracted by drinking raw infected cow's milk. Infection may be contracted by direct contact with infected foetuses membranes and discharges of aborting cows. In USA, this disease is recorded in rural areas, and not in urban areas, people from urban areas invariably drink pasteurized milk.

Species of the organism	Hosts and diseases affection in animals
Campylobacter foetus sub species venerealis	Endometritis, sterility, abortions n cattle
Campylobacter foetus sub species foetus	Abortions in sheep (occasionally in cattle), enteritis in sheep, cattle and swine
Campylobacter jejuni	Abortions in sheep; enteritis in humans, and non human primates, cattle, foals, dogs, cats and other spp. Proliferative enteritis in many spp.
Campylobacter coli	Enteritis in humans, nonhuman primates and other mammals
Campylobacter sputorum sub spp bubalus	Commensal of female genital tract of cattle and sheep
Campylobacter sub spp muusalis	Swine proliferative syndrome, adenomatosis in swine
Campylobacter sub spp Upsaliensis	Enteritis in dogs, cats, humans
Helicobacter pylori (campylobacter pylori)	Anal gastritis in children

Diseases due to Campylobacter spp. in domestic animals

Bovine genital campylobacteriosis

Genital campylobacteriosis or Vibriosis is a contagious disease of cattle caused by a gram negative organism known as *campylobacter foetus*. The infection is confined to the reproductive tract of the cow and the prenuptial sac of the bull and leads to irregular return to service (Repeat breeders) and occasional abortions.

Etiology: The bacteria are common or S shaped or spiral bacteria. It is motile one and having lopotrichous flagella that is the flagella is present at one end. Biochemical and serological variants namely *campylobacter foetus venerealis* and campylobacter foetus intestinalis are described. The first named agent *campylobacter foetus sub sop venerealis* is commonly associated with enzootic infertility and abortions in cows. The later one that is the *campylobacter foetus intestinalis* rarely causes abortions infertility and abortions in cows. The latter one i.e., *campylobacter* foetus intestinalis rarely causes abortions but mostly cause infertility problem. Non-pathogenic campylobacter like *C.sputorum* and *C. faecalis* are present the bull and cows are of not much important in pathogical point of view. *C. foetus sub spp venerelais* is confined to cattle whereas intestinalis is transmitted to the sheep also, but inter species transfer still is a questionable one.

Transmission: The bull is a generally responsible for the introduction of infection, and is mainly due to management practices. Affected bull does not show any lesions though harbouring the organism and being able to transmit it to cows. Infected cows are repeat breeders. Probably there are early embryonic deaths and so animal comes into heat again. Abortion occurs between 4th and 6th month of pregnancy.

Clinical symptoms: Clinical signs in dairy herds which maintain adequate record of fertility are soon evident shortly after the introduction and use of an infected bull. In the natural services, infection may not be suspected until the calving pattern indicates a delaying conception and reduced calf crop.

Pathology: *Campylobacter foetus* produces a diffuse mucopurulent endometritis. There may be small nodules and cystic glands distributed in the uterine mucosa which also reveals lymphocyte infiltration and oedema. Cotyledons and placenta reveal necrotic areas and infiltration by inflammatory cells. The members are opaque and leathery. Purulent exudates are found between the endometrium and chorion. Purulent exudates are found between the endometrium and chorion. In the bulls the organism is located prepuce and does not cause any pathological lesions. They grow in the epithelial crypts of the prepuce and glans penis. Bulls mostly throw off infection, but some may be infective for 3-5 years.

Diagnosis: Examination of the smears from the uterus and the identification of the organism. The oestral mucous is best for culture and may be obtained by either of the first two, flushing out the anterior vagina with phosphate buffer

saline using a multi perforated tube and syringe. The viability of *Campylobacter* in mucous at ambient temperatures is poor. And washings in buffered saline sealed on ice or the sample should be diluted with specific transport media and maintained at ambient temperatures. Preputial samples from the bulls can be either by scraping or flushing the preputial cavity.

Mucous agglutination test: Dieostral cervical mucous is collected from the animals recently exposed to infection by service. Flushing out the anterior vagina by phosphate buffer saline and collecting by syringe or by a tampon and forward to the laboratory on ice. Because the anti-antibody persists for a limited period in animals following infections, the test is essentially a herd test and occasional positives samples indicate for further culturing.

Salmonellosis in animals

Salmonellosis is an infectious disease of man and animals caused by organisms of the genus salmonella. These bacteria are primarily intestinal organisms. Sometimes, therefore either as a consequence of clinical disease or sub-clinical infection they may be found in farm effluents, human sewerage or in any material subject to faecal contamination.

Infection by salmonella is very common among young animals of all species and this is one of the causes for high mortality in dairy farms and piggeries in India. It is proposed that Salmonella has a single species. Enteric, with several subspecies and as many 2200 antigenically distinct serovars which are based on the somatic or O antigens, and H or flagellar antigens. They are usually designated on the basis of the locality, in which the specific type was first isolated or identified, or their host preference and the clinical syndrome they may produce. Salmonella in animals is usually host specific, thus salmonella abortus ovis affects sheep, *salmonella cholera Suis* effects swine, *Salmonella typhimurium* is not host specific.

Salmonella are non-lactose fomenters. The general falling in this group are protease, salmonella and Shigella. Organisms of the genus proteus are readily differentiated from the salmonellae because of their ability to decompose urea. Another characteristic of proteus strains is their tendency to swarm on solid media. This may be defined as progressive species of surface spreading by bacteria from the present colony. Organisms of the proteus group are widely distributed in nature. Salmonella organisms having peritrichous flagella except salmonella pullorum and gallinarum are non-motile. They do not ferment adonitol, lactose and sucrose, liquefy gelatin produce indol, hydrolyze urea or form acethylmethyl carbinol. They regularly attack glucose with gas production. They do not ferment salicin. Approximately 2300 serovars are recognized basing the somatic (o), flagella (H) and capsular (M) antigens. The H-antigens are heat labile and O or somatic antigens are heat stable. Serovars are recognized by combination of O and H antigens. A polysaccharide microcapsule responsible for V1 (virulence) antigen. Phage typing, bio-typing, drug resistance and plasmid profile analysis may be used to identify sites.

Salmonella could be classified under 3 groups. One group specificity for the human host *i.e., Salmonella typhi, Salmonella paratyphi, salmonella schottmuelleri, Salmonella hirschfeldii that is agents of typhoid and paratyphoid fever in man.*

The 2nd group adapted is too specific to animal hosts: These *are S. Arizona (from disease of lambs); 3rd group causes disease both in human and animals.*

Host adapted salmonella: Humans – *Salmonella typhi, Salmonella paratyphi, Salmonella schottmuelleri, Salmonella hirschefldii, Salmonella senadai;* Cattle – *Salmonella Dublin;* Swine – *Salmonella cholera Suis, Salmonella typhi Suis;* Poultry – *S. pullorum, S. galinarum;* Sheep – *S. abortus ovis;* Horse– *S. abortus equi.*

Salmonella usually inhabits intestinal tract and is excreted. Salmonellosis in animal's exhibit in 3 forms viz., enteritis, septicemia and abortive forms.

Transmission and epidemiology: Salmonellosis is primarily an enteric disease and is transmitted principally by the faecal-oral routes. Salmonellae are excreted in large numbers in the faeces of infected animals with consequent contamination of the environment. In an outbreak, the majority of animals will acquire infection by direct contact with faeces or food bedding or water contaminated by faeces.

The introduction infection into uninfected premised maybe but a variety of means, but principally by asymptomatic carrier animals, contaminated feed stuffs or polluted water supplies. Such introduced infection may either remain silent or develops into clinical disease, the outcome being influenced by the both the species and the numbers of contaminated bacteria.

Physiological stress factors, nutrition, management and undercurrent diseases are liable to render animals more susceptible to infection or to activate the latent carrier state. Conditions such as babesiosis, theilerosis, foot and mouth disease, fasciolosis may demonstrate concurrent salmonellosis. Disease is more severe and common in young animals. Salmonellosis sometimes complicates viral disease of carnivores and aggravated food and mouth disease in cattle.

Pathogenesis: The pathogenesis of salmonellosis may be divided into several stages; entry of bacteria into the host and attainment of the primary site of infection, usually the enterocytes attachment to the surface that is colonisation and invasion of enterocytes. In those cases in which bacteria; follows, the organism's be able to survive and replicate in macrophages, and disseminate to other sites. Normally live in, lungs, joints, meninges placenta and foetus. The course and outcome of Salmonella infection is affected by chromosomal and extrachromosomal factors virulence determination of the bacteria and as the response of the host to these factors. For infection takes place 10^7 – 10^9 organism is needed to infect large domestic animals. After ingestion the salmonella must overcome non-specific resistance factors, including bactericidal action of salivary enzymes and the acid pH of gastric juices. Those organisms that survive the non specific resistance factor may colonise and invade the enterocytes. Salmonella

have been demonstrated in the Peyer's patches as early as 6 hours post inoculations. The ability to attach, invade and penetrate enterocytes is crucial to virulence, and the first development of salmonellosis. A number of known virulence factors contribute to the pathogenesis of salmonellosis. Including motility of the organisms, pili or fimbriae, lipopolysacharides and enterotoxins. Motility may enhance the movement of bacteria through the glycocalyx and facilitate the attachment to specific receptor sites one enterocytes. Fimbriae are present on salmonellae, and they may play a role in colonisation of the gut. Adherence takes place in two stages. The first is reversible since the organisms can be washed off easily. Weak ionic and non-ionic interaction; between bacterial and host cell membrane surfaces are thought to be the binding forces responsible for this attachment. The second stage of attachment is irreversible. It occurs after a lag period and is characterized by degeneration of microvillus on the epithelial surface and formation of membrane bound vacuoles containing salmonella. This process is termed as receptor based endocytosis. Lip polysaccharide moiety of salmonella with smooth cell wall consists of an O-specific side chain, a core portion and a lipid A portion. Most Salmonella isolated form animals have smooth cell walls, and this feature influences virulence in several ways. These strains are more invasive and more successful in invading phagocytosis and lyses by phagolysomes after invasion. Lipopolysacharides reduce the susceptibility of the organism to the host's cationic proteins; they stimulate local prostaglandin synthesis and prevent the activation and deposition of complement on the bacterial surface. The main function of lipopolysacharides is to facilitate survival in the intestinal tract and eventual entry into deeper tissues. The lipid A portion of lipopolysachride is responsible for the endotoxin mediated effects of salmonella infection that are seen in the systemic form of the disease. Endotoxemia typically causes fever, leucopoenia, haemoconcentration, lactic acidosis, coagulopathies, hypotension and death.

Invasion of enterocytes especially those in the ileum occurs within 12 hours after oral infection. Large number of organisms is present in the lumen, on the surface of brush border and in enterocytes. There is increase number of neutrophils in the gut. Degeneration microvillus characterized by loss of filamentous cores is associated with close adherence of bacteria. A cytotoxic or verotoxin similar to the shiga neurotoxin produced by *Shigella dysentreriae* has been associated with some serovars of salmonella. Vascular degeneration and thrombosis of mucosal vessels is common feature of Salmonella enteritis. The vascular lesions may be due to action of large amounts of endotoxin absorbed through the damaged mucosa or released locally.

In salmonellas characterized by entertocolitis, the organism usually do not disseminated beyond the mucosa and the mesenteric lymph nodes and the ensuing inflammation remains confined to the intestine. Salmonella are considered to be facultative intracellular pathogens.

Salmonella taken up by resident macrophages elicit a major immune response in the host. There is considerable controversy about the roles delayed by cell mediated and hum oral immunity in the pathogenesis of slamonellosis. Salmonella infection results in the release of lymphokiness by specifically stimulated T lymphocytes; they activate macrophages which pahgocytosise the organism. Once the salmonella organisms have crossed the mucosa, they may enter the blood stream via the lymphatic, perhaps carried in macrophages and cause septicemia or transient bacteraemia or they may remain indefinitely in the gut associated lymphoid tissues and mesenteric lymph. The organism are removed by fixed macrophages that are located in spleen, liver, and bone marrow. They may continue to proliferate in such extra vascular locations and cause another bacteria phase, which may be fatal as a septicemia or result in secondary localization. The carrier state is important in the epidemiology of the disease. Intermittent seeding from the bile or from macrophages in the lamina propria and gut associated lymphoid tissues. The gut associated lymphatic, the cell mediated immunity are responsible for the carrier state. The carrier state is an unstable one for it appears that if the carrier is subjected to some stress or debilitating disease, it may succumb to disease; this often seems to occur in adult cattle. The carrier animal is a potential threat to any other animal it contacts, either directly or through the medium of its excreta, or by products such as bone or meat meal.

Clinical features: Cattle: Calves and post parturient adults often involve. *S. Dublin and S. typhimurium* are involved. In calves there is acute septicemia in neonates and acute enteritis often with dysentery along with fever and inappetance in animals. Affected calves quickly lose condition become dehydrated and emaciated. Pneumonic signs may also be seen and chronic may develop polyarthritis. Adult cows show fever anorexia and enteritis manifested by abdominal pain and dysentery clinically affected animals may abort in the absence of other clinical signs. Calves may show a dry gangrene of the extremities, ears, limbs and tail.

In sheep and goats abortions and death of adult animals either with septicemia or enteritis is common.

Pigs: only young pigs, less than 4 months age are clinically affected. The acute form of the disease is manifested by anorexia, fever and purple discolouration of the extremities with a high mortality. Mild forms of the disease do not show discolouration, but pneumonia or enteritis with fluctuating fever is common. The faeces are often bile stained and; contain necrotic mucosal debris and also blood tinged.

Horses: Abortions are usually associated with S. abortus equi and other salmonella cause mild enteritis in foals.

Lesions: Lesions in cattle, sheep and goats lesions confine to gastrointestinal tract as catarrhal to fibrino-haemorrhagic enteritis with acute inflammation of the

drainage of lymph nodes. Liver contain white foci, popularly called as typhoid nodules and spleen is enlarged and congested and contain white foci. Pneumonia may present in calves. In sheep and goats also enteritis and pneumonic lesions are noticed.

Pigs: Purplish discolouration of the extremities is characteristic. Enlarged spleen, congestion and oedema of lungs and focal necrotic spots in liver. Typically there are few neutrophils and whether the nodules are necrotic or reactive depends on their duration. The chronic enteritis changes of intestines are that of fibrino necrotic enteritis. Pin point haemorrhages are present in the renal cortex. Stomach shows intense red black colour of the severe congestion and venous infarction common in endotoxemia in pigs. Peticheal haemorrhages may occur in the meninges and brain. The pulmonary lesions are also characterised by thrombosis and vasculitis and a largely mononuclear cellular response in alveolar septa. There is flooding of alveoli with oedema fluid.

Leptospirosis

Synonyms: Weil's disease, Stuttgart disease, Rice field worker's disease, Swine herder's disease, Sugar cane worker's disease

Leptospirosis is the disease produced by infection with pathogenic serovars of the genus Leptospira. This is the common zoonotic disease which can affect most mammals. Most infections appear to be sub-clinical, but severe diseases are characterized by hemolytic anemia leading to jaundice, haemoglobinuria and occasional deaths. Milder forms occur with fever, agalactia characterized by mastitis and abortions.

Leptospirosis in the United States of America is considered to be the most important disease of cattle and combined losses in swine and cattle exceed 200 million dollars annually. Leptospirosis is widespread in some countries in South East Asia such as Malaysia and Indonesia. In Malaysia about $1/4^{th}$ of human population and one third of domestic animals and $1/6^{th}$ of wild rodent's exhibit antibodies to one or more strains of leptospirosis. In India the existence of leptospirosis in cattle and buffaloes was recognized. Leptospira were also isolated from bandicoots, swine and from goats. In cattle there is breed susceptibility and higher mortality is seen in European and European crosses with zebu cattle.

Species affected: All domestic animals are susceptible for this infection. The rat is probably a reservoir of the bacteria from which dogs and man may be affected. It is a spirochete zoonosis. Man is affected; in these farm laborers, including garden workers, paddy field workers, swimming military workers, people who keep domestic pets are usually contract this disease.

Etiology: Leptospiral organisms are widely distributed in nature. In this pathogenic and nonpathogenic species are present. Pathogenic species belongs to family Leptopsira interrogans, whereas saprophytic species belongs to the family

Leptospira biflexa. Leptospira have hooked ends. This measures around 0.2 to 0.3 μ in diameter and in length 2.0 to 3.0 μ. They divide by binary fission. Long generation time is required for multiplication, i.e., 6 to 16 hours. The optimum temperature required is around 30°C. Leptospira has been divided into 190 different serovars and 25 antigenic related sero-groups. Inbovines 23 serologically distinct serovars are present. In cattle, infections by strains belonging to the serovar hardjo. Leptospira Pomona cause an acute disease and others are causing less serious diseases. The strains are L. hebdomads, L. icterohaemorrhagiae. In sheep and goats, hemolytic anemia is caused by L. Pomona is seen in lambs and deaths are seen with L. grippotyphosa. In pigs L. Pomona may cause infertility and abortions. Dogs act as a reservoir for L. canicola infections and L. icterohaemorrhagiae also affect dogs. Man is susceptible to a wide range of leptospiral infections and usually become infected from domestic and wild animals. The largest reservoir of Leptospira is in wild animals. Rodents including rats, mice appear the most important carriers of the disease. Foxes, jackals, mongoose, civets, bandicoots, deer, hares and rabbits carry these organisms in their body. Horses appear to be susceptible to a wide range of serotypes.

In India at least 28 serotypes have been so far found to occur among human beings and animals. These include L. icterohaemorrhagiae, L. grippotyphosa, L. Andaman, L. autumnalis, L. Schumer and L. mum rang, L. Pomona and L. Hebdomads. In theory any parasitic leptospire may infect any animal species, but in practice only a small number of serovars will be endemic in any particular region, while each serovar tends to be maintained in specific maintenance hosts. Therefore, in any animal species infection may arise from strains adapted to and maintained in that species of strains maintained by other species of domestic animals.

observe coiled leptospiral organisms with terminal hooks x 100 X

In theory any parasite leptospira may infect any animal species, but in practice only a small number of serovars will be endemic in any particular region, while each serovar tends to be maintained in specific maintenance hosts. Therefore, in any animal species, infection may arise from strains adopted to and maintained in that species or strains maintained by other species of domestic and wild animals.

Transmission: Either by ingestion, or through coitus, through abrasions of skin,

through intact skin, conjunctiva, nasal mucosa, trans-placental transfer and through predation. Leptospires are excreted in urine for a variable period, depending on the infecting serovar and the age of the animal. In rat urine, in dog's urine the organism are excreted for a long period. It is common in India in rainy season when drainage water rare overflowing in the streets prevalence of jaundice with leptospiral infections are common. In cattle, the organisms are excreted through urine for at least 18 months. The organisms are also seen in post calving uterine discharges for up to 8 days. Rats have been shown to excrete L.icterohaemorrhagiae for at least 220 days. Direct infection may occur when animals are herded together. The organisms may survive for months in water saturated soil. The optimum environment conditions for leptospirosis are warm, wet conditions with a pH value close to neutral. These conditions occur all the year round in parts of the tropics, where rainfall is seasonal, and transmission of incidental infections may also seen. Leptospires cannot tolerate desiccation, excessive sun light, pH values other than neutral, salinity and many kinds of chemical pollution.

Other routes of infection are bites from rodents, venereal spread, (from bull's semen), predation, especially wild animals and transplacental infection. During acute phase, the organisms may be voided in the milk and so calves may get infected by drinking such milk.

If the animal does not die during septicemia phase, the organisms settle down in the liver, kidney, and the pregnant uterus. The acute form is common in calves, piglets and lambs. In sheep and goats, the organisms localize in the central nervous system producing encephalitis. During the acute phase, jaundice is seen in all animals due to intravascular haemolysis and hepatic necrosis. Anemia, icterus and haemoglobinuria are noticed.

Pathogenesis: From the point of entry the organisms invade the blood stream and multiply rapidly producing septicemia. Primary multiplication is in liver and secondary multiplication in kidney and brain tissue. During this period, the temperature rises. This phase lasts for several days. If the animal does not die during the acute septicaemic phase, the organisms settle down in the liver, kidney and in the pregnant uterus. The acute form is common in calves, piglets and lambs. In sheep and goats, the organisms localize in the nervous tissue producing encephalitis. During the acute phase, jaundice is seen in all animals due to intravascular haemolysis and hepatic necrosis. Anemia, icterus and haemoglobinuria are noticed.

In the animals that survive the disease runs a sub acute course in which the liver and kidney are affected. Leptospirae are found in the urine. This is called immune phase. Albuminuria is present due to interstitial nephritis which may be either focal or diffuse. Uremia may supervene and death is common. When the organism localizes in the gravid uterus abortion results and there are degenerative lesions in the epithelium of the placenta.

Symptoms: In cattle: 3 forms are seen. Namely acute, sub-acute and chronic forms. The incubation period is 2 to 10 days. Though mortality is low as 5%, it may lead to 100% in some cases. In acute form, there is septicemia wherein rise of temperature up to 107°F is there, followed by anorexia, congested mucous membrane, haemoglobinuria, jaundice and anemia. Due to anemia there is tachycardia and dyspnoea. Cutaneous ulcers are common. In lactating animals strips of blood is present in the milk and there is reduction in the yield of milk. In sub-acute form, the reproductive tract is more affected. Abortions are common. In chronic form no symptoms are seen. Abortions occur. Aborted calves usually die. Premature live birth of weak calves may occur up to 3 months, and occasionally longer, after the acute phase of infection. In apparently infected animals greatly outnumber than clinically affected cases. These void the organisms in urine for a considerable period of time. When animals recover there is a prolonged convalescent period.

In lactating animals, the milk yield falls considerably or stops completely. The milk secretion is yellowish, thickened and even bloody. Udder remains soft and pliable. Pregnant animals frequently abort. Thus acute form in cattle causes septicemia, hepatitis, nephritis and meningitis, whereas chronic forms are characterized by abortions, stillbirths and nephritis.

The aborted foetus does not show any specific lesions but for oedema in the umbilical cord, pericardium, in subcutaneous tissue and peri-renal tissue. There may be interstitial focal nephritis. The foetus may be in the advanced stage of putrefaction suggesting thereby that it was dead for some time prior to abortion. Placenta is retained. Placenta shows lesions of placentitis. The Leptospira can be found sometimes in the foetus.

Sheep and goats: Infections are less common in sheep and goat. In sheep the disease may be per acute, some may be found dead. Others may show jaundice besides dullness and may die in 12 hours. Abortions may occur in the acute form. In goats abortions may be noticed besides icterus. Heavy mortality is common in outbreaks of leptospirosis.

Pigs: L. Pomona is the chief organism producing a comparatively mild chronic disease. Abortions may occur as well as birth of weak piglets. Some animals may manifest nervous symptoms. Urine of sow and aborted fetuses contain the organisms. Recovered animals are carriers for a long time and excrete the organisms in the urine. The renal lesions are focal interstitial nephritis.

Horses: Acute form of leptospirosis is characterized by fever, anorexia, polydypsia, oedema of legs and parts of the body. Periodic opthalmia of horses is supposed to be caused by L. Pomona. This disease in horses is characterized by conjunctivitis, keratitis, photophobia, intense lachrymation and iridocyclitis. Leptospira may also produce mild sub acute disease with fever, abortion, icterus and

haemoglobinuria. The course of the disease is brief and the animals do not remain as carriers.

Dogs: Leptospira canicola affects most dogs and this is transmitted from dog to dog, whereas L. icterohaemorrhagiae occurs from rats to dogs. Per acute form is common in puppies wherein septicemia characterized and death occurs within 2 to 3 days. The symptoms seen are fever, weakness and hemorrhages giving rise to epistaxis, haematemesis, and melena. Mucous membranes reveal petchiae. Icterus may not develop at this stage.

Acute form: This is manifested by fever, anemia, icterus, diarrhea, vomiting, dehydration, and emaciation, acceleration of erythrocyte sedimentation rate, albuminuria, leukocytosis and foul odors from the animal. The infection occurs in young dogs up to 3 years of age and the infection is contracted by close contact with rats or their urine.

Sub-acute or mild form: When the organisms localize in the kidney, the symptoms manifested are those of progressive renal failure. Uremia may develop and death supervenes. There is dehydration, emaciation and death.

Man: Man is susceptible to a wide range of leptospiral infections and usually becomes infected from domestic or wild animals. Although severe cases occur with L. icterohaemorrhagiae most cases are milder. The disease should be suspected in any case of pyrexia of unknown origin, if there are suspicious circumstances. The disease occurs in two phases. The first one is acute leptospiremia and the second one occurs in a chronic or immune phase. Icteric leptospirosis is characterized by hepatomegaly, spleenomegaly and rhabdomyolysis. Kidney is involved and proteinuria is seen. Leptospira are found in the first 10 days in the blood.

Lesions: Gross: At postmortem examination, severe jaundice, when present striking as the entire carcass appears yellow. There may be ulcers or hemorrhages in the abomasal mucosa of cattle. In dogs, hemorrhagic gastroenteritis is prominent with hemorrhages throughout the organs but prominent in lungs and heart. Kidneys are swollen and show numerous grayish white spots on the surface. Liver shows necrotic foci on the surface. In canines, horses and pigs, petchiae are present on the cortex and in chronic cases it is difficult in peeling off the capsule. The kidney may contain innumerable white foci. Urine in the bladder may be coloured red or black.

Histological lesions: Liver architecture has been disrupted and dissociation of liver cords is common. Liver cell show degenerative changes. The nuclei becomes pyknotic and hyper chromatic and the cytoplasm becomes granular and eosinophilic. There is hepatocytomeglay; with mitotic figures and appearance of binucleated cells are common indicating regenerative changes. Bile canaliculi are plugged with bile pigments and Kupffer cells are loaded with haemosiderin. In

the histological sections, spirochetes can be stained by silver impregnation techniques like Levaditti's on sections.

Kidneys show focal or diffuse interstitial nephritis. Histological sections by silver impregnation techniques reveal spirochetes in the lumen. The lumen may contain eosinophilic debris and presence of RBCs. In some tubules regeneration of epithelium is evident. There are focal aggregates of lymphocytes and plasma cells in the form of nodules indicating antigenic challenge at the sites. Tubules in the sections of medulla are dilated and contain hyaline casts.

Uremia is seen in dogs due to the destruction of kidney. When uremia develops, extra renal lesions are common. These are gastric hemorrhages and ulcers in the stomach. Calcium deposition on the gastric mucosa and in the walls of the aorta, large arteries, laryngeal mucosa, endocardium of the left auricle and the costal pleura are common. Even there is change in the bone and there is osteodystrophy exhibited in the form of soft bones of jaw known as popularly as rubber jaw syndrome.

Leptospira canicola also causes nervous symptoms associated with hyperemia and petchiae of brain and spinal cord. Purulent lymphocyte meningoencephalitis is seen.

Diagnosis: By characteristic symptoms namely icterus, anemia, haemoglobinuria, abortions, petchiae on mucous membranes. Leptospires may be detected in plasma, urine or organs including foetal tissue by using dark filed microscopy, fluorescent antibody techniques or by a number of silver staining techniques cited above. The common silver staining techniques applied on section is Levaditti's stain. Smears could be stained by War thin-starry stain. This organism cannot be differentiated or identified by morphological examination. Only serological tests are useful.

Leptospires are very fragile and do not survive long in a decomposing carcass. Cultures are most readily obtained from the liver and kidneys of animals recently dead or slaughtered for examination. A selective medium like Ellinghausen McCullough Johnson-Harris medium containing fluorouracil is beneficial in isolation of organisms from urine. Modified Korthoff's medium (oleic acid or albumin medium) is also good for cultural examination of leptospires. In serological tests, agglutination test and agglutination lysis test are useful. Inoculation into guinea pig intra-peritoneally from the blood, milk or urine collected from ailing animals at the height of the disease and recovering from the disease. Demonstration of the organisms in the blood of the guinea pig is possible. Leptospiral infections in aborted fetuses may be demonstrated by combination of foetal serology, isolation of leptospires and immunofluoresence. The kidneys, lungs and pleural fluid of the aborted fetuses should be examined for the presence of the organisms.

Differential diagnosis in cattle consists of distinguishing the acute form of the

disease from other causes of jaundice and haemoglobinuria including anaplasmosis and babesiosis which may be intercurrent or secondary. Clostridium haemolyticum is also present in the picture which causes bacillary haemoglobinuria in cattle. Kidney lesions in cattle could be looked for theilerosis. Azoturia and infectious equine anemia is to be distinguished in horses; babesiosis and anaplasmosis in sheep and poisoning by a variety of toxic plants could also be looked for.

Chlamydiosis

This is a disease of man and birds caused by an organism known as *Chlamydia psittaci*. Chlamydia is classified in *monogeneric ricketssial* order, *the chlamydiales*.

Chlamydia organisms are minute (0.2 to 1.5μ) bacteria that propagate within host cells of vertebrates including humans, other mammals and birds. The organisms are non motile, spherical and gram negative and they have a cell wall. The basic unit termed elementary body, which is a spherule measuring 0.2 to 0.4 μ in diameter. It contains an electron dense nucleus and ribosomes surrounded by a trilaminar wall.

The elementary body is infectious form of the organism, which attaches to host cells, presumably through specific receptors, and enters the cell in phagosome. The phagosome does not fuse with lysosomes. Once inside the cell, the elementary body undergoes morphologic changes. It becomes larger (0.6 to 1.5μm) and gains more ribosomes and the nucleus becomes laky or reticular and is termed reticulate body. Reticulate bodies divided by binary fission and ultimately reorganize into elementary bodies which are released from the cell. The replication cycle again has been discussed in detail in subsequent paragraphs.

All Chlamydia affecting animals are considered to be strains of *Chlamydia psittaci* and two biotypes are recognized, one of which causes disease in birds and man and the other which infects a wide range of domesticated animals. The avian and mammalian biotypes do not cross react serologically. The disease in man and psittacine birds (parrots, parakeets) is known as Psittacosis while the disease is manifested in pigeons, fowls, turkeys and ducks known as ornithosis.

Within the mammalian biotypes there are two serovars, one attacks the alimentary, respiratory and reproductive tracts and the other causes polyarthritis, conjunctivitis and encephalitis.

Chlamydiosis or psittacosis or ornithosis is the disease due to minute bacterial organisms that propagate only within host cells of vertebrates including man, other mammals and birds. The infective elementary bodies of *Chlamydia psitttaci* are tiny coccid under electron microscope and measure 300 nm in diameter. Rickettsia contain RNA, they sub divide by binary fission and intracellular obligate parasites. They look like small cocci. They turn light blue with Giemsa and bright red with modified Ziehl-Neelsen stains. They are heat labile and survive pasture on several days.

The organism are no motile, spherical and have developmental stages, the elementary body, the initial body and in the intermediate body is a form of Chlamydia contains an electron dense nucleus and many ribosome's surrounded by multi laminated cell wall. The name of Chlamydia has come as it appears a cloak that is the outer garment. The infective elementary body is the infectious form of organism is taken up into host cells by phagocytes. Elementary bodies have a cell wall that is made rigidly disulfide bonds rather than by cross linked peptidoglycans found in bacteria. Therefore, *Chlamydia* is not susceptible to penicillin. Chlamydia has adhesins on their surface which bind to microvilli on host columnar epithelial cells. The infective elementary body is infectious form organism and is taken up into the host cells by phagocytosis. The initial body is a large spherule, 0.8 to 1.5μ in diameter, with a thin wall containing nuclear fibrils and ribosomal structures. The initial body is the vegetative form, which divides by fission within the cells. The intermediate body is a transition stage between the initial and elementary bodies. These bodies are gram negative.

Developmental cycle: The cycle consists of basically five major phases. Attachment and penetration by the elementary body. Transition of the metabolically inert elementary body into metabolically active reticulate body. Chlamydia life cycle consists of Multiplication of the reticulate body by binary fission, producing many progeny (Chlamydia) and maturation of noninfectious reticulate body into infectious elementary body and release of elementary bodies from the host cells.

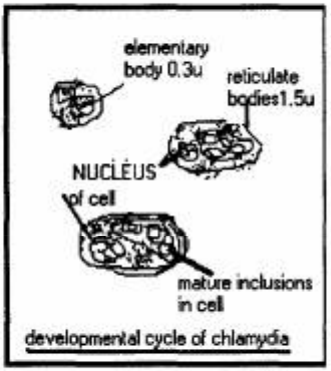
After phagocytosis by a host cell, elementary bodies enlarge to become initial bodies, which divided by fission within a cytoplasmic vesicle formed by invagination of host cell wall. Daughter cells of the initial bodies continue to divide, then develop laminated walls and a dense nuclear mass (intermediate form), then decrease in size to become the infectious elementary bodies. Rupture of the cytoplasmic vesicle and cell wall releases the elementary bodies, which may infect other host cells.

As already stated the cell walls of Chlamydia are gram negative. The intracellular organisms may be stained with Giemsa, Machiavelli's, Gimenez's or Castaneda's methods. They may also be demonstrated in unstained preparation of infected cells with a phase contrast optical system.

Chlamydia depends upon host cells for energy and do not grow outside such cells. Multiplication is inhibited by tetracyclines, penicillin and 5-fluorouracil.

Currently *Chlamydia* is classified in monogeneric ricketssial order, the chlamydiales. There are two species, *Chlamydia trachomatosis and c. psittaci.* Three biotypes of the Chlamydia are existing and cause disease in man and one biotype infects mice.

All *Chlamydia* affecting animals are considered to be strains of *Chlamydia psittaci,* and the two biotypes recognized are those that cause disease in bird and man and the other which infects a wide range of domesticated animals. The mammalian



and avian biotypes do not cross react serologically. Within the mammalian biotype there are two serovars. Type I serovar attacks the alimentary, respiratory and reproductive tracts. The type II serovar causes polyarthritis, conjunctivitis and encephalitis. Diseases induced by serotype I and II have not been observed to occur simultaneously under natural conditions.

Diseases caused by Chlamydia

Diseases due to Chlamydia trachomatosis

Name of the organism	Species affected	Disease produced
Chlamydia trachomatosis	Human	Trachoma, inclusion body conjunctivitis, Urogenital inflammatory--disorder, lympho-granuloma venereum, pneumonia
Chlamydia trachomatosis	Mice	Pneumonitis
Chlamydia psittaci	Psittacosis (ornithosis)	Humans, birds
Chlamydia psittaci	Cattle	Sporadic--bovine encephalomyelitis
Chlamydia psittaci	Cattle, sheep, horses	Polyarthritis
Chlamydia psittaci	Cattle	Enzootic bovine abortion
Chlamydia psittaci	Sheep	Enzootic bovine abortion
Chlamydia psittaci	Horse, swine	abortions
Chlamydia psittaci	Cats	Feline Pneumonitis
Chlamydia psittaci	Cattle, sheep, goats, horses, dogs, rabbits	Pneumonia
Chlamydia psittaci	Sheep, cats, guinea-pigs, hamsters	conjunctivitis
Chlamydia psittaci	Sheep, cats, guinea-pigs, hamsters	conjunctivitis
Chlamydia psittaci	Cattle, pigs, musk rats	enteritis

In humans that affected psittacosis (ornithosis) showed febrile illness, upper respiratory tract involvement, pneumonia and severe debility. Infected birds show sleepiness, listless and refuse to eat. They show drooped wings and feathers can be pulled out easily. Nasal and ocular discharges are greenish and further more below these have been discussed in detail.

A few lambs are infected in utero, but most are infected orally at birth or shortly thereafter through contact with injected placentas and foetal fluids. An inapparent enteric infection follows and persists for years up until the 4th month of pregnancy. Then these organisms take chlamydaemia and invade the reproductive tract resulting in abortions. This type of Chlamydia (psittaci group) is being called as type I organisms.

The type II Chlamydia causes polyarthritis, encephalitis and conjunctivitis (non-enteric disease). These Chlamydia cause enteritis both in young calves and lambs. This results in mucoid watery and bloody diarrhea. The recovered animals act as carriers and shed the organisms. These will lead to fresh outbreaks or human infections.

The intestinal tract is the natural habitat for Chlamydia. Most infections probably are in apparent, but the intestine may be an important portal of entry in the development of systemic infections leading to hepatitis, arthritis, encephalitis, pneumonia and abortion in ruminants. Judging from world literature, mammalian Chlamydia types are certainly not as infectious for humans as avian Chlamydia. There has never been a major zoonosis attributed to the mammalian type. Reports of occurrence of nonhuman mammalian origin of Chlamydia can multiply in man and produce disease.

Avian Chlamydia isolates are responsible for latently and systemic disease in birds and Pneumonitis in man (psittacosis). Strain differences do exist within avian isolates. Latency is also a dominant feature in avian Chlamydiosis and is responsible for its endemicity. Man is an incidental host. Members of both chlamydiales species are sensitive to penicillin. Avian isolates are to a lesser degree susceptible than mammalian agents. *Chlamydia psittaci* are sulfonamide resistant. Tetracycline's are the most effective inhibitors, and are the drugs of choice in treatment of almost all chlamydial infections.

The first Chlamydia isolation from the poultry was made in 1939 from a flock of white leghorn chicken. Chlamydial infection in ducks and poultry as well human infections are reported from Eastern Europe, Austria and Germany. It is generally agreed that man is an incidental host of *Chlamydia psittaci* and avian species are the primary hosts.

Levinthal (from Germany), *Coles* (from England), and *Lillie* (from USA) observed characteristic elementary bodies (basophilic) in the cytoplasm of reticulo-endothelial cells of affected humans and birds. However it was Bedson and co-

workers in London conclusively established the etiology of psittacosis by transmitting the agent from man to parrots and mice.

Avian Chlamydiosis (Psittacosis, ornithosis, parrot fever)

Chlamydiosis is principally an inapparent or latent infection in animals. However, per acute, sub-acute, chronic infections do occur in most species. There are no pathognomonic lesions or signs that occur in systemic disease. Mortality is higher in parrots, than parakeets. Per acute form is common in parrots. In adult birds, a sub-acute or chronic form occurs with intermittent overt signs followed by asymptomatic period.

Avian Chlamydiosis spreads by direct means when birds are in close contact, and indirectly through fomites, and also by biting insects, and mice and lice. The source of infection includes birds in the incubation stage of infection, sick birds and carriers and infected inanimate material. *Elementary bodies* are found in faces and also in respiratory excretions. Spread occurs mainly through inhalation of infected contaminated dust. Elementary form of the organism is highly resistant outside the host and can survive in dried faces for months. Stress brings about flaring up of the disease. Among domestic poultry, turkeys are most susceptible and then ducks and pigeons, while chicken are rarely affected. Currently 6 serotypes of *Chlamydia psittaci* are known to infect birds. Avian strains of *Chlamydia psittaci* can infect humans, and precautions should be taken when handling infected birds or contaminated materials. The disease inhuman contracted from turkeys is usually more severe than that from psittacine birds. Avian Chlamydiosis in birds is usually systemic and sometimes fatal.

The **pathogenesis of Chlamydiosis** that occurs after oral administration of the agent has been studied in turkeys. Events in this experiment stimulation those that would most likely occur in an outbreak, caused by a virulent strain in a crowded aviary or poultry confinement. After aerosol infection occurred, Chlamydia multiplies primarilyin the lungs, air sacs and pericardial sac within 24 hours after exposure. At 48 hours after infection, Chlamydia was detected and the agents were present in various somatic organs such as liver, spleen and kidney. Chlamydia is also found in nasal turbinate and cloacal contents.

Air sacs are involved and the air sacs are thickened with fibrinous or fibrinopurulent exudates. Fibrinous pericarditis, perihepatitis and the exudates is also seen on intestines. Pronounced congestion of liver and spleen is common. Liver is mottled and the surface is colored and contains necrotic foci. There is enlargement of spleen and rupture and death of fowls are there. Catarrhal enteritis with yellowish green faces is observed.

Histological examination shows proliferative changes as well necrotic changes. Carrier animals show proliferative changes. Proliferation of lymphoid tissue in the periportal region and interstitial nephritis and enteritis are commonly observed.

Signs: In acute form, birds show bilateral conjunctivitis with serous to purulent exudation, nasal discharges, anorexia and reluctance to move. Diarrhea is present. Faeces may turn to yellowish. As the infection progresses, eyes may become dull and sunken in, corneas may become cloudy, egg production decreases drastically and feathers are lost. Birds tend to remain in a fixed position and when forcibly moved, may stagger and shown signs of paralysis. Sub-acute form, birds show chachexia and these birds are carriers and shedders of Chlamydia.

Zoonosis aspect: Affected humans show fever up to 102°F, anorexia, sore throat, photophobia and severe headache. Pneumonia with consolidation of lungs, encephalitis, meningitis and death is common. Since the advent of effective antibiotic treatment with tetracyclines, human Chlamydiosis of avian origin has come down.

Chlamydia psittaci of mammalian origin: Chlamydia has been recovered from eye infections of domestic animals viz., guinea pig, cat, dog, sheep, cattle and piglets. The animals under observations sowed photophobia, conjunctiva, and the enlarged sub mucosal lymphoid follicles. The disease in sheep is bilateral. It is unilateral in cats and in sheep and apart from eye joints are also affected. Transmission: A few lambs are infected in utero, but most are infected orally at birth or shortly thereafter through contact with infected placental and fetal fluids. An unapparent infection follows and persists for years until the 4th month of pregnancy, where it moves from alimentary tract to the reproductive tract and invades the cotyledons.

Systemic infections: In sheep it causes enzootic abortion or kebbing. Here placentitis and consequently late abortions, stillbirths and premature delivery of weak lambs are common. Infected ewes remain carriers but rarely abort. Fetal membranes show characteristic changes. Necrosis of the cotyledons and abortion is manifested by accumulation of red creamy discharges. Histological lesion is characterized by palettes with loss of epithelial cells and progressive necrosis of the underlying villi and tip of the caruncular septa. Chlamydia multiply within the cytoplasm of the trophoblastic epithelium and inclusions are visible in the foetus, surprisingly the uterus is unaffected. Abortions are also common in the last semester of gestation of cattle, rabbits, pigs, and goats. In chronically affected flocks the abortion rate is around 1 to 5%. Following abortions ewes usually recover without complications except occasional retained placenta. In cows, on the other hand, retained placenta is common. Joints are also affected in ovine, equines, bovines and humans also.

Laboratory diagnosis: Organisms could be recovered from pericardial fluid, lungs, liver, spleen or intestinal tract and from faces of live animals; organism could also be recoverable from intestinal mucosa liver kidney, heart of dead animals. From synovial tissue, in case of polyarthritis cases, and from aborted material, in cases of abortions in ewes and cows, and also from faces of dams. Placenta and fetal organs and fluids are rich in Chlamydia organims. In cases of human Chlamydiosis,

Pneumonitis, sputum and tracheal swabs or washing, blood and vomits may yield chlamydiales. Postmortem material including lung is collected in buffer containing sucrose or protein for Chlamydia isolation. The most widely used indicator hosts for isolation of Chlamydia are seven day old chicken embryo (embryonating egg), tissue culture, mice and guinea pigs. Mice have been used for isolation of *Chlamydia psittaci* of avian origin, mice can be injected with intraperitoneal, intranasal or intracerebral routes. Death may occur within 2 to 3 days or it may take as long as 14 days. Bloated abdomen, spleenomegaly, liver necrosis and peritonitis are common. Stained smears reveal elementary bodies in the cytoplasm of cells. Intracerebral inoculation of mice results in paralysis and somnolence and die within 1 or 2 days. Chlamydiae could be demonstrable from impression smears of meninges. Examination of brain material reveals meningoencephalitis and perivascular cuffing.

Guinea pigs have frequently been used to isolate *Chlamydia psittaci* strains of mammalian origin. Avian isolates induce les pathogenesis. Intraperitoneal injection result in febrile response and death of the animals within 5 to 10 days. Prominent lesions are fibrinous peritonitis, spleenomegaly, and hepatic necrosis. Complement fixation test with a titer of 1: 16 agglutination test and demonstration of Chlamydia antigen by agar gel precipitation test are also employed for demonstration of organisms or their effects. Serological test like complement fixation test, ELISA, immunofluorescent and gel diffusion tests are also useful. Antigen could be demonstrable by fluorescent antibody or immunoperoxidase staining and DNA polymerase techniques to demonstrate Chlamydia DNA.

Listeriosiss

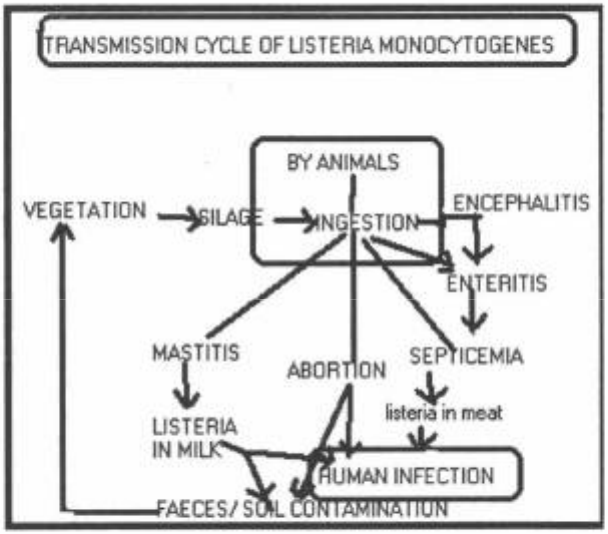
Synonyms: circling disease

This is an acute infectious disease of man and animals caused by Listeria monocytogenes, a gram positive rod shaped non-sporulating motile organism where in septicemia, nervous affections and abortions are of common occurrence.

Species affected: Sheep, cattle, goat, swine, rabbit fowl and man. Rats, guinea pigs, fox and dogs are affected. Rats are suspected to be reservoirs. Birds may be affected and may transmit the disease to other animals.

Etiological agent: It is a gram positive rod shaped nonsporulating motile organism. The flagella are at one pole, lopotrichous flagella and in movement it takes tumbling motility.

It resists pasteurization and can thrive in the soil for one year. By phage typing 8 types of Listeria have been isolated. Five serotypes have been isolated. Alkaline conditions in silage (spoiled) encourage bacterial multiplication. Listeria is commonly found on plants and in soil. Organisms are found on top soil, river and sewage sludge. For human listeriosis the apparent source of infection is ingestion of foods of animal origin which becomes contaminated by L. monocytogenes from various environmental sources. However there is evidence of L. monocytogenes may infect humans and animals by the oral, ocular, cutaneous, respiratory or urogenital routes. Virulence of various serotypes of L. monocytogenes is multifactorial. Theseinclude haemolysins, phophatidyl inositol, catalase activity, super oxide dismutase and iron transport system. Some surface antigens, secreted proteins and monocytosis stimulatingactivity are also involved.



Routes of infection and disease manifestations: Bacteria multiply in silage when the pH is below 4. A large proportionof healthy sheep and goat are latent carriers. Listeria organisms are excreted in stress in faeces and milk. High % of humans acts as healthy carriers. Bacteria are widespread in nature. Nutritional deficiency and excessive feeding of silage have been attributed as the predisposing factors in flaring up of listeriosis infection in animals. The faeces of healthy animals often contain L.monocytogenes and fecal carriage rate of Listeria spp. has been reported to be in the range of 3.1% to 45.8%.

Animals may manifest three distinct syndromes namely meningo-encephalitis or nervous form, abortion and septicaemic form. These three may overlap or may occur independently. Pathogenesis depends on the method of infection. The nervous form is supposed to arise when infection is through nasal mucosa or through conjunctiva. Infection via trigeminal nerve from mouth is also suggested. Ingestion may cause the visceral form of the disease and in pregnant animal's abortion. Transmission through coitus may also result in abortion. Outbreaks of the disease have been encountered when silage was fed. It is thought that bacteria may be viable in the silage where the pH is below 4. Organisms are excreted through faces and milk, thus in turn the contaminating the vegetation. Listeria is presenting the meat and milk and in that way this poses a problem to the human beings, as it is a zoonotic disease. Fever and abortion are common in the human beings and high percentage of humans form as healthy carriers. Dogs eat the flesh of animals, suffer with various forms and surviving one will become carriers.

Pathogenesis: The organisms are voided in the faeces, urine, milk, uterine discharges and aborted fetuses. When ingested the organisms penetrate the intestinal mucosa, enters the blood and a state of bacteraemia is set in.

Though number of authors have described different forms, viz., meningo-encephalitis in ruminants, septicemia without meningitis which has been reported in monogastric animals including young ruminants and abortions wherein placenta of pregnant animals are affected. The author has observed in buffaloes the three combined forms.

But experimental infection by installation into nose or conjunctiva wherein infection of meningoencephalitis results. The organisms are present only in the brain and nowhere else.

Listeria monocytogenes produce a potent haemolysins with lipase or phospholipase activity. This leads to red cell destruction. Though the non-toxic, non-antigenic lipid material is associated with cell wall which is responsible for the monocytosis and monocytosis is not consistent feature in ruminants, especially in cattle and buffaloes. But reports say that haemolysins produced by the bacteria acts on pace maker and contractile cardiac muscle fibers are affected leading to a faulty conduction and arrest of the heart in septicaemic phase. The different forms of listeriosis occurring in sheep, goat, and cattle are, encephalitis (circling disease),

abortion, still births and neonatal deaths, septicemia in unweaned animals, mastitis, diarrhea and septicemia in ewes and purulent conjunctivitis. In other animals like swine, horse and fowl also the disease condition has been recorded. In swine meningo-encephalitis and abortions, in horse's encephalitis and septicemia and in fowl myocarditis, hepatitis and nephritis have been recorded. Listeriosis has also been recorded in healthy adults andchildren. The most vulnerable groups include pregnant women, infants, elderly and immuno-suppressed persons. Symptoms are variable and depend on the individual susceptibility. Disorders associated with L. monocytogenes are meningo-encephalitis, influenza like low grade septicemia in prenatal period, infectious mononucleosis like syndrome, septicemia in adults, pneumonia, endocarditis, localised abscesses, popular or pustular cutaneous lesions, conjunctivitis, urethritis and abortions.

Symptoms: Nervous form: Adult ruminants show meningoencephalitis form. With this death occurs in cattle and buffaloes by 2 to 3 weeks, whereas in sheep death occurs in 3 to 4 days. There is pyrexia, the animal is dull, has a stiff gait, and arched back, rough hair coat, constipation and weakness. Wry neck or torticollis is common. Animal makes several rounds and circles, naming this disease as circling disease. There may be one sided paralysis of the face with drooping of the ear, eyelids and lips. Finally animal becomes recumbent and die of respiratory failure.

Visceral form is observed in young animals and monogastric animals. In dogs, the author has observed dullness, emaciation, vacant look and continuous moaning. Abortions occur in all animals. Unsolved abortions must be attributed to listeriosis.

Mastitis may be acute, chronic or the mastitis exhibits as symptom less and organisms are excreted in milk as long as 2 to 6 weeks.

In rabbits and rodents distension of belly, progressive emaciation and sudden deaths are seen.

In humans minor skin infections particularly in farmers or veterinarians after handling bovine calving or abortions have been recorded. The symptoms such as headache, vomiting, fever, malaise, pneumonia, conjunctivitis have also been seen. The meningitis characterized by high temperature, stiffness of neck, often ataxia, tremors, seizures, and fluctuating consciousness. The onset is reported to be sudden and death may follow within 24 to 48 hours.

In swine the disease is seen acute form and is characterized by meningoencephalitis. Some affected animals show dyspnoea, cough and abortion.

Gross lesions: In nervous form, congestion of meningeal vessels is common. In visceral form congestion of internal organs including liver and gastrointestinal tract mucosal congestion is seen. In the viscera, where the organisms have settled, small granulomas with necrotic foci are common. The cerebrospinal fluid where the organisms settle, the fluid is turbid. Mesenteric lymph nodes are congested.

There is necrosis of myocardium. In abortions, retained placentais common. Fetus is infected in utero. Military granulomas are found in all organs and tissues. The fluid contains plenty of organisms. Under microscopic under high power or under oil immersion lens one can examine the darting movement of the bacteria.

Histological lesions: focal necrotic spots are common in the central nervous system; there is gliosis and perivascular cuffing. Perivascular cuffing occurs with infiltrating lymphocytes, histiocytes and eosinophils. Infection may spread to meninges through the spaces of Virchow-Robin. The meninges are heavily infiltrated by lymphoid cells-lymphocytic leptomeningitis. Macrophages or monocytes are rarely seen especially in the central nervous system and visceral organs of bovines. In the viscera, where the organisms have settled, small granulomas with necrotic or purulent centres form. Organisms could be demonstrable in these places.

In fowls, sporadic cases occur. Nervous symptoms are not noticed in birds. Massive necrosis of myocardial muscles, pericarditis with increased pericardial fluid and enlargement of the liver with necrotic foci, fibrinous peritonitis and enteritis is common. Organisms can be cultured from abdominal organs and blood.

Diagnosis: Symptoms, by circling movements.

Histopathological examination of brain wherein gliosis and perivascular cuffing is a feature.

Culture of the organism could be done from blood and from brainstem in acute stages Brain stem is to be collected and to be kept in ice or refrigerator for 2 to 3 weeks, and then the bacteria is cultivated on blood agar plates. Thus in the meningoencephalitis form brain is preferred. In septicaemic form liver, spleen, kidney and lung tissues are collected and stored in 50% glycerin or these organisms could be collected in 0.05% in potassium tellurite agar. In pregnant animals the lochia and the foetal stomach contents and foetal tissues are to be collected and to be transported. Among earliest method for the isolation of Listeria from food and environmental samples was use of cold enrichment. However drawback of this method was long duration up to 3 months, is required for identification of the organism. More recently incorporation of certain specific selective agents such as nalidixic acid, acriflavin, lithium chloride, phenyl ethanol etc. into enrichment and plating media has sown to reduce time required for isolation. Various selective broths used for enrichment of Listeria are university of Vermont, Fraser broth, polymyxin-acriflavin, lithium chloride, ceftazidine aesculin, mannitol, egg yolk, broth, thiocyanate, nalidixic acid, broth. Plating media for isolation of Listeria organisms are lithium chloride, phenyl ethanol molxalatum agar, Dominguez Rodriguez agar, Polymyxin acriflavin lithium chloride ceftazidine aesculin mannitol agar, oxford agar.

Biological test (Anton) is preferred. Drop infected material on the eye of a rabbit.

The rabbit develops purulent conjunctivitis. Intracerebral injection of suspected material into rabbits and kill these animals after2 to 3 days and isolate the Listeria organisms from these animals. Chick embryo inoculation is useful wherein necrotic focal lesions are found on the chorio-allnatoic membrane.

Mice can be inoculated wherein intraperitoneal injection results in death of mice after 7 days.

Fluorescent antibody test can be done and with this the antigen in the suspected tissues can be detected in a rapid way. Other methods for diagnosis of Listeriosis include detection of organisms by polymerase chain reaction, nucleic acid probes in clinical specimens, sero diagnostic methods such as ELISA, complement fixation test, agglutination, and precipitation tests.

Differentia diagnosis: Listeriosis should be differentiated from influenza, tuberculosis, meningitis, brucellosis, Pasteurellosis, taxoplasmosis, especially when abortions have been reported. Nervous symptoms should also be differentiated from rabies, acetonemia and lead poisoning. In pigs it should be differentiated from hog cholera, Pasteurellosis, and Aujeszky's disease and middle ear infections and in sheep from pregnancy toxemia and enterotoxaemia infections.

Toxoplasmosis

Toxoplasmosis is a disease of man and animals and is one of the important zoonotic diseases caused by protozoan parasite *Toxoplasma gondii,* which is intra cellular parasite capable of infecting a wide variety of tissues in a wide range of mammals and birds. Infection is probably extremely common, but clinical toxoplasmosis is relatively rare. It uses the members of the felidae as definitive hosts is optionally heteroxenous. Cats may be infected directly by ingestion oocysts or due to ingestion of asexual stages in the tissues of prey species. It is important as a human disease and a cause of ovine abortions. It has been estimated that about 500 millions of human beings are having the antibodies of *Toxoplasma gondii.* The organism can infect virtually any cells of the body and a wide spectrum of clinical disease may be produced in man, especially in congenitally infected children and imunosuppressed individuals.

This was first observed in the African rodent, the gondii; but since then it has been found in a very large variety of mammals and birds. The causal organism is *Toxoplasma gondii* is an intracellular protozoan parasite found in many types of nucleated cells. The life cycle is very complicated but the parasite has a simple coccidian life cycle in the final host, the cat. The cat is the only known host in which *Toxoplasma gondii* completes its life cycle and produces oocysts. Infective sporulated oocysts ingested by the intermediate host, which can be from a wide range of other mammals and birds, result in the rapid multiplication of the parasite (tachzoite) in a variety of tissues. A few weeks later, the parasites localise in certain tissues (brain, muscle, lungs, and placenta) and their multiplication slows

down (bradyzoites) as they become contained in a cyst and the infection becomes chronic.

The proliferative stages or trophozoites in the intermediate hosts are crescentic in shape, 4-6μ long, one end being more rounded than the other and the nucleus is centrally placed. In fixed and stained preparations, the parasite appears more rounded. Movement is by flexion of the body and gliding.

Toxoplasma is crescentic shaped 2-4 μ width and 4-7μ in length. It has a nucleus, most clearly demonstrated with Giemsa stain, located near one pole of the cell. Its cytoplasm contains mitochondria, microtubules, endoplasmic reticulum, ribosome, Golgi apparatus, and number of organelles unique to protozoa. Among the latter structures are called rhoptries which are osmophilic, dense, vase shaped gland like structures with their narrow portion at the pointed end of the organism and broader base near the basis. Toxoplasma has 4-6 rhoptries. Convoluted tubules or fibrils called toxonemes or micronemes are also present. Toxoplasma lack kientoplast.

Life cycle: By eating infected oocysts or cysts which are present in any organ of the animals like cattle, sheep and goats, the cats get the infection. The bradyzoites come out of the cyst and infect the intestine of cat.

Five stages of asexual development are recognized in the intestinal epithelium of cats infected with tissue cysts from intermediate hosts. The gametocytes also develop in the epithelial villi, especially the ileum. In heavy infections, exfoliation of infected epithelium from villi is associated with the development of villous atrophy and occasional spontaneous cases of diarhoea in kittens. In intermediate hosts and in cats, extra intestinal asexual development occurs in a variety of organs and tissues. Rapidly dividing forms (tachyzoites) may be endodyogeny proliferate in cells in many sites for an indefinite number of generations, and are the stages associated with acute toxoplasmosis in cats and other species. Eventually, tachyzoites induce formation of a cyst wall in a host cell, and divide slowly, forming bradyzoites, which reside in quiescent tissue cysts.

Here oocysts are produced in cats. Ingestion of sporulated oocysts by intermediate hosts results in initial rapid multiplication of tachzoite in a wide range of tissues. During this stage, the parasite can be transmitted to other intermediate hosts and cats by various routes, namely congenitally via the placenta in pregnant animals in excretions and secretions including milk, and by carnivorism. Later, when infection is chronic and the parasites are contained as bradyzoites in host tissue as cysts, transmission by ingestion of infected tissues is possible.

In cats the enterointestinal cycle and systemic infection occurs simultaneously, in other animals the tachyzoites are the first stages of infections after the invasion of the lamina propria by sporozoites released from the oocysts, or by Brady zoites released from the tissue cyst digested from food in the intestine.

Dissemination of toxoplasma occurs in lymphocytes, macrophages, granulocytes and as free forms in plasma. From the intestine the organism may follow two routes, it may spread via the lymphatics to the Regina nodes and from there in the lymph to the blood stream or it may pass in the peri-portal circulation to the liver and from there to the systemic circulation. Further dissemination occurs to a wide variety of organs. Tachyzoites actively invade or are phagocytose by host cells and are surrounded by a parasitophorous vacuole. Tachyzoites proliferate destroying the host cell and cell to cell transmission may occur within the infected organs.

Life cycle of *Toxoplasma gondii* is completed in two classes of hosts where cats including felidae namely mountain lion, bob cats, Bengal tigers etc., act as definitive host. Whereas man, rodents and other non feline hosts like sheep, goat, pig, cattle and birds act as intermediate host. The three principle modes of transmission of toxoplasmosis are faeco-oral, carnivorism and congenital.

The cat is crucial for the perpetuation of the infection as a cat is capable of excreting millions of oocysts in its faeces. Moreover, the oocysts are very resistant and can survive in the environment unto 18 months and are remarkably resistant to most disinfectants. Epizootiological studies suggest that cats become infected soon after they begin to hunt or share the food hunted by their mother during the pre weaning period. Cats usually become infected by preying birds, rodents and small mammals having *Toxoplasma gondii* infection. Aborted foetuses, foetal fluid and membranes are also a good source of infection for carnivorous birds and mammals.

Small proportion of congenital infection occurs in man and the mother of congenitally infected children do not give birth of infected children in subsequent pregnancy. In India, where majority people are vegetarians or meat is usually cooked thoroughly, food and drink contaminated with oocysts may be the main source of infection.

Transmission: Oocysts shed in the faeces of the final host sporulated within 2-3 days and become infectious to other cats and all intermediate hosts. Ingestion of sporulated oocysts by cats results in a typical direct coccidian type life cycle in the intestine, resulting in further faecal excretion of large number of oocysts. Ingestion of sporulated oocysts by intermediate hosts results in initial rapid multiplication of tachzoite in a wide range of tissues. During this stage, the parasite can be transmitted to her intermediate hosts and cats by various routes, namely congenitally via the placenta in pregnant animals, in excretions and secretions including milk, and by carnivorism. Later when infection is chronic and the parasites are contained as bradyzoites in host tissue cysts, transmission by ingestion of infected tissues is possible.

Clinical feature and pathology: Although infection appears to be common and widespread and are symptom less or mild. Clinical signs depend on the tissues

infected and three stages of the parasite namely; acute disease results from rapid multiplication of tachzoite. Symptoms are exceeding varies and include pneumonia, endocarditis, febrile exanthema (rash) and neonatal mortality. The pattern of abortion depends on the stage of pregnancy when animals are infected. Infection early in pregnancy that is 40 to 45 days of gestation results in foetal death and apparent bareness or abortion for a mummified foetus. Infection in pregnancy causes placentitis. The cotyledons have multi necrotic lesions.

Immune animals develop a chronic form of Toxoplasma infection, which's characterized by the formation of cysts, containing bradyzoites. These are mainly located in the brain, skeletal muscle and myocardium. The formation of cyst is accompanied by disappearance of tachyzoites from the circulation and visceral organs. Cyst formation takes place as early as 1 to 2 weeks, after infection and they may persist for months, possibly years. Intracellular encystment protect the bradyzoites, from both cellular and humoral mechanisms in inflammation is not usually associated with cysts. When cysts rupture due to immunosuppression severe inflammation which is hypersensitive in character may develop, apparently released bradyzoites may rarely survive to infect other cells.

Systemic toxoplasmosis has been reported in most species of domestic animals. This is characterized by interstitial pneumonia, focal hepatic necrosis, lymphadenitis, and myocarditis and non-suppurate meningoencephalitis. Pulmonary lesions are more consistently seen and also symptoms of central nervous system infection.

Eye may be infected in human adults. The lesion is one of granulomatous chorio-retinitis.

Gross lesions in lungs consists of gray foci of necrosis on the pleural surface to hameorrhagic pneumonia with confluent involvement of the ventral portions. Focal necrosis and mottling of liver with oedema of gall bladder is seen. Spleen is enlarged and pale areas are seen on myocardium and skeletal muscles. Occasionally pancreas is also affected.

Histologically pulmonary lesions are characterized by diffuse interstitial pneumonia, alveolar septa are thickened and mononuclear cell infiltration is common with occasional presence of neutrophils and eosinophils.

In liver necrotic spots contain variable amount of tachyzoites in heptocytes and Kupffer cells. Moderate lymphocytic reactions found in the periportal areas. Tachyzoites are also observing in the epithelial cells of the bile duct. Pancreatic acini show necrosis and numerous tachyzoites are found in the epithelial cells. In the heart and skeletal muscle necrosis and focal mononuclear infiltrations seen.

Brain lesions consists of nonsuppurative meningoencephalitis with multi focal areas of necrosis and often malacic spots. There is marked perivascular oedema and hyperplasia of periepithelial cells.

Lambs born to infected ewes have congenital infections alive for some time and die after few days. Infection of sheep outside pregnancy is asymptomatic but result in immunity.

In pigs symptoms are variable, ranging from latent to severe, and include Pneumonitis, encephalitis and abortion.

In cattle the parasites quickly eliminated from infected tissues, and the milk of infected cows is of negligible importance in transmission.

Diagnosis: Clinical symptoms are abortions in flocks. The parasite can be isolated from infected animals by various means, the most sensitive being the intraperitoneal inoculations of suspected material into mice which are highly susceptible to infection. Parasite cysts can also be isolated direct from infected tissue by centrifugation, a discontinuous density gradient of a colloidal silica solution.

Various serological tests for detection of infections are there. These are detected by measuring Toxoplasma antibodies. These tests are the complement fixation test, the indirect fluorescent antibody test, the latex agglutination test and the indirect haemagutination test, all of which to ascertain extent have supersed the dye test. These ewes can be used to detect Toxoplasma antibodies in foetal fluids from aborted materials.

Thus the diagnosis of Toxoplasma gondii infection is mainly based on isolation of the parasite, histological examination and serodiagnositc methods.

Impression smears from lesion of tissue biopsy or at necropsy is useful for rapid diagnosis severe infections.

In histological sections of tissue stained with haematoxylin and eosin, tachzoite can be differentiated easily and tissue cysts are found occasionally of which Brady zoites are strongly PAS (per-iodic acid Schiff stain) positive.

A variety of serological tests are in use for diagnosis of Toxoplasma gondii infection. Sabin and Feldman dye test is still used in many laboratories. Due to the inherent hazards in dealing with the live parasite as antigen in the dye test, it is now being replaced by other tests in which are agents are non infective and more standardized. Among them indirect haemmagglutination and complement fixation test and an enzyme linked immunosorbant assay. Molecular methods of diagnosis such as DNA probe hybridization and PCR assays are the emerging and reliable techniques.

The preventing is cat should never be fed with raw or uncooked met and prevents them for hunting. Cat should not be kept for rodent control. Cat shouldn't be allowed nearer to pregnant women or sheep and goats. Animal caretakers should wear mask and protective clothing during cleaning cat litters and removal of cat faeces everyday before oocysts become infective. Cats shedding oocysts should be quarantined and treated with combination of sulphonamide and pyrimethamine.

Genital Trichomoniasis

This is a specific contagious venereal disease of cattle caused by the flagellated protozoan Trichomonas foetus and is transmitted at coitus.

The organism is roughly pear shaped, 10-25μ long by 3-15μ wide. It moves with a characteristic vigorous jerky movement. The nucleus is anterior, there is a cytosome which's difficult to discern and a sausage shaped parabasal body. Three anterior flagella are present and the posterior flagellum extends back along the undulating membrane and trials behind the organism. The undulating membrane runs the full length of the body, the Costa is prominent, the axostyle is well developed and it merges from the end of the body through a chromatic ring. Multiplications by longitudinal fission. No sexual process or encystations has been observed.

Infection in the bull remains in the preputial cavity and must be considerd, in the absence of effective treatment, as permanent. In early infections, there is balano-posthitis of moderate severity with preputial swelling and a slight purulent discharge. As the infection becomes chronic, the inflammatory reaction disappears and the organisms become fewer in number. There is tendency for them to concentrate in the glans penis adjacent areas of the prepuce, but they are quite difficult to find in preputial washings and may be detected only by test mating suspected bulls to susceptible heifers.

Females aren't readily infected, if at all, except by service or experimentally by implanting a culture of the organisms into vagina. A few days after infection, an acute vaginitis with swelling of the vulva develops, and there is a moderate amount of mucoid floccular discharge from vagina. The protozoa may be easy or impossible to find in the exudates. The vaginitis resolves shortly and the infection localizes in the uterus and cervix. Immediately prior to the oestrous which follows the infective stage, large number of organisms is from the exudates aspirated from the cervix, but as oestrous advances, the number of protozoa is greatly reduced.

The manifestations of established trichomoniasis is female are cervicitis and endometritis which result in repeat breeding abortion or Pyometra. The inflammatory changes in the endometrial and cervix are relatively mild and non-specific although the exudates, mucopurulent in character may be rather copious. Discharge of exudates into the vagina may be more or less continuous or intermittent and the numbers and activity of the organisms in the discharge vary considerably over short periods. The discharges may be presented apparent at the vulva.

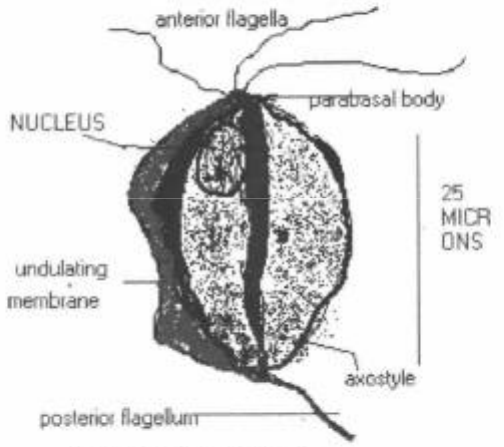
The pattern of repeat breeding trichomoniasis in cows return to service occurring at irregular

Intervals, which indicates that fertilization and implantation are followed by

embryonic death. When the embryo or foetus dies it may be resorbed, aborted or retained with the development of Pyometra. Abortions due to trichomoniasis may occur at anytime but mainly in the first half of the pregnancy. There are no specific gross foetal lesions but large numbers of protozoa may be found in the foetal fluids. The placenta is severely altered as in brucellosis, it maybe covered by white or yellowish flocculent exudates in small amounts, thickened and slightly tough, and heaemorrhages without much necrosis may be evident on the cotyledons.

On histological examination, the placenta is oedematous with a light diffuse infiltrate of mononuclear cells and mild spotty necrosis of chronic epistle. Many tirchomonads may be present in the stroma of the chorion. In the lung, there may no changes or there may be marked bronchopneumonia. Many large multinucleated giant cells maybe present and some of these contain trichomonads and meconium. Tirchomonads are present in the alveoli and airways. The organism can readily identifiable in the abomasal and intestinal contents some cases, in the lungs and placenta. Pyometra is characteristic feature in cow at least 5 to 6 liters of pus is seen coming with watery floccules from uterus without any odors and organisms are seen even in low power field of microscope itself.

There is little evidence that bulls become immune to infection. Usually the organism persists in them for life and the animal is continuous source of infection for cows. In the cow immunity to reinfection commonly follows abortion and it is unseal for more than one abortion to take place; however a recovered cow may not always be cleared of the organism. Despite the development of immunity to the parasite permanent sterility may result if there has been extensive involvement of the uterine mucosa.



TRICHOMONAS FOETUS

Dourine: Abortions are common in horses in dourine infections. It is a venereal disease of horse caused by a protozoal parasite, Trypanosoma equiperdium. It is transmitted by coitus and both sexes are affected. Following infection the organisms invades the sub mucosal lymphatics where it proliferates and evokes a purulent vaginal discharges, hyperplasia of lymphoid follicles and eventually chronic proliferative vaginitis. Trypanosomes enter the blood stream and become disseminated to many part of the body where they also cause lesions. Large painless cutaneous swellings often occur as a part of disease. Animals eventually die of degenerative lesions involving the cranial and spinal nerves that lead to paralysis.

Viral causes

Variety of viruses exclusively causes abortions in animals. The viruses that take systemic infection will set a viremia resulting in pyrexia and death of the foetuses and with resultant abortions. The examples are Rinderpest in cattle and buffaloes, herpes viruses in cattle, horses and pigs, hog cholera or swine fever in pigs, parvovirus infections in variety of domestic animals. The common viral infections that cause abortions in animals are as follows.

Rinderpest (paramyxoviridae), cattle, Multiple organs of foetus affected, resulting in abortion; Infectious bovine rhinotracheitis (Bovine herpes virus-1), Cattle, sheep, swine. Multiple organs of foetus including central nervous system, eye are affected with resultant abortions; Bovine Parvo virus, Cattle , Multiple organs of foetus are affected including central nervous system; Blue tongue(reo viridae), Sheep, cattle, Central nervous system of foetus affected, malformations in foetus; Japanese B encephalitis (flavi viridae), Swine, Central nervous system of foetus is affected growth retardation and malformations of foetus; Porcine Parvo virus, Swine, Central nervous system of foetus is affected and malformations in foetus; Hog cholera(togaviridae), swine, Central nervous system of the foetus is affected abortions, growth retardations, mummification and malformation of foetuses; Equine viral abortion (herpes virus-I) , Horses, Multiple affects on foetus resulting in abortions; Equine viral arteritis (togaviridae), horses, Multiple effects in foetuses resulting in abortions; Canine herpes virus, dogs, Defects in central nervous system of foetus, eye and multiple organs resulting in foetal death and abortion; Canine Parvo virus, Dogs, Multiple defects in foetal organs, foetal death and abortions; Caprine herpes virus, goats, Multiple defects in foetus with resultant abortions; Foot and mouth disease (Picorna viridae), Cattle, buffaloes, sheep, goats and pigs, abortions and death of the foetuses.

Viruses that cause abortions in animals

Name of the virus	Species effected	Effect on the foetus
Rinderpest (paramyxoviridae)	Cattle	Multiple organs of foetus affected, resulting in abortion
Infectious bovine rhinotracheitis (Bovine herpes virus-1)	Cattle, sheep, swine	Multiple organs of foetus including central nervous system, eye are affected with resultant abortions
Bovine Parvo virus	Cattle	Multiple organs of foetus are affected including central nervous system
Blue tongue (reoviridae)	Sheep, cattle	Central nervous system of foetus affected, malformations in foetus
Japanese B encephalitis (flavi viridae)	Swine	Central nervous system of foetus is affected growth retardation and malformations of foetus.
Porcine Parvo virus	Swine	Central nervous system of foetus is affected and malformations in foetus.
Hog cholera (togaviridae)	swine	Central nervous system of the foetus is affected abortions, growth retardations, mummification and malformation of foetuses.
Equine viral abortion (herpes virus-I)	Horses	Multiple affects on foetus resulting in abortions.
Equine viral arthritis (togaviridae)	horses	Multiple effects in foetuses resulting in abortions
Canine herpes virus	dogs	Defects in central nervous system of foetus, eye and multiple organs resulting in foetal death and abortion
Canine Parvo virus	Dogs	Multiple defects in foetal organs, foetal death and abortions
Caprine herpes virus	goats	Multiple defects in foetus with resultant abortions
Foot and mouth disease (Picorna viridae)	Cattle, buffaloes, sheep, goats and pigs	Abortions and death of the foetuses

(Picorna viridae) Cattle, buffaloes, sheep, goats and pigs, abortions and death of the foetuses

Hog Cholera

Synonyms: Swine fever

It is an acute febrile highly contagious and often fatal disease of pigs caused by a RNA virus (pesti virus). The disease is having high mortality rate and majority of the animals survive only up to 14 days after showing the first signs of illness. Acute, chronic and in apparent forms of disease are existing.

Etiology: Hog cholera is a member of pestivirus and the family of togaviridae and the genus of flavi viridae. The pestiviruses differ from all other Flavi viridae viruses by being non-arthropod borne viruses. They are related serologically. Only one type of hog cholera virus is known, although strains vary widely in virulence. The virus is relatively stable and will survive in frozen carcasses for years and in cured or salted pig's meat products for months. The RNA genome is packed into a capsid shell with icosahedra symmetry and surrounded by an envelope of lipoprotein. The virions of these viruses are 40 to 70 nm in diameter and contain isometric cores. Frequent deviations of the spherical shape of the virions are believed to be caused by conformation of loosely fitting envelope.

Occurrence: The first outbreak had come from America in 1830 in imported European breeds and now is seen throughout the world.

Transmission: The disease spreads by direct contact of infected animals with susceptible pigs. The virus is present in the urine, faces, lachrymal and nasal secretions of infected pigs. With less virulent strains, the virus may be excreted in the urine for a period up to 3 months. Fomites, insects are also infected.

There are four gradations of viral virulence. Highly virulent strains produce features of classical acute disease in pigs wherein morbidity is 100% and mortality is 90%.Low virulent infections produce mild chronic disease with a protracted course and chronic illness. Avirulent or immunogenic strains produce little or no disease. A strain of persistent infection in young pigs also exists. It is very difficult to differentiate between chronic and persisting infections.

Natural occurrence of viral strains of reduced virulence that cause chronic disease occurs in population. These strains may cause abortions, disease in baby pigs or clinical signs in older pigs as a part of mixed infection with pathogenic bacteria.

Persistent infections are the important mechanism by which hog cholera is perpetuated in domestic; pig populations. As result of Trans placental transmission of hog cholera virus and to a lesser extent postnatal contact, persistent infections may develop with or without chronic illness, resulting in retardation in growth and runting.

Meyer et al (1981) recognized 3 typical groups of piglets belonging to infected litters. The first group consisted of still born or aborted fetuses with typical lesions or demonstration hog cholera virus. The second group consisted of piglets with congenital viremia lasting from birth to death and later developed runting and animals died within 3 to 8 weeks of age. Third group of piglets comprised those not infected at birth.

By chronic infections, hog cholera virus is persisting in the flocks. Chronic hog cholera has been defined as a lethal form with duration of 30 or more days with pigs having persistent viremia and an impaired antibody response to the viruses.

Congenital-infections acquired mainly in utero by transplacental transmission of hog cholera virus can result in life long or at least long lasting persistent infections.

Transmission spread: The pig is the only domestic animal which is naturally infected by the virus. The infection is usually acquired by ingestion, but inhalation is also possible route. In case of infection with virulent virus, all excretions and secretions and body tissue of affected pigs contain the virus. The virus is excreted in the urine for some days before clinical illness appears, and for 2 to 3 days after clinical recovery. The virus is a resistant one and survives outside for a considerable time, as it is resisting to chemical and physical influences. Birds and humans, also act as physical carriers of the virus. Transplacental transfer of virus is there. Postnatal infection occurs either directly through close contact between sick and healthy pigs. A common source of new outbreaks is the feeding of infected meat scraps. Once the disease is established within a herd, its spread is hastened by mosquitoes and tabanids.

Pathogenesis: The tonsil is the primary site of virus invasion following oral exposure. Primary multiplication of the virus occurs in the tonsils, beginning with several hours after infection. The virus multiplies in the tonsilar epithelium. The virus is then transferred through lymphatic vessels to lymph nodes of cervical region and enters blood capillaries, results an initial vermeil at approximately 24 hours. At this time the virus can be found in the spleen and other sites such as peripheral and visceral lymph nodes, bone marrow and Peyer's patches. The virus exerts its pathogenic effect on endothelial cells, lymphoreticular cells, macrophages and epithelial cells. The virus multiplies in the cells of lymphatic system. After 3 to 4 days, the virus invades endothelial cells and epithelial mucosa, gastrointestinal tract, gall bladder, pancreas, salivary gland, uterus, adrenal and thyroid.

The vascular endothelial cells swell, proliferate and occlude the lumen. The walls of the blood vessels undergo hyaline degeneration with infiltration of lymphocytes, macrophages and plasma cells. These changes of the blood vessels are the causes of hemorrhage, necrosis, and infarction found in the various organs. The virus is also capable of causing inflammation of lungs, thereby producing corpous pneumonia.

In the intestines especially in the caecum and colon, are found the characteristic button ulcers. These are formed from Peyer's patches and solitary follicles. To begin with there are hemorrhages in the follicles as a result of which the follicle becomes necrosed and form small grayish yellow nodules which are surrounded by a ring of sero-hameorrhagic mucosa. Subsequently this mucosa also become necrosed and with the fibrin and a coagulated exudates forms a diphtheritic yellow raised patches over the follicles. These changes are primarily due to occlusion of the blood vessels causing infarction and so hypoxia. The rim of the nodule is slightly raised. Secondary bacterial invasion intensifies the process and the lesion expands concentrically, producing concentrically lamellae or thickening. Later the central necrotic area becomes softened cast off and an ulcer results covered with thick purulent exudates and raised borders resulting in the typical button ulcer. Granulation tissue may fill the ulcer and the scar may be covered by epithelium covering from the sides.

Clinical findings: Clinical signs usually appear 5 to 10 days after infection, although longer incubation periods of 35 days or more are recorded. At the beginning of an outbreak young pigs may die per acutely without clinical signs having been evident. Acute cases are the most common. Affected pigs are depressed do not eat and stand in a drooped attitude with the tail hanging they are disinclined to move and, when forced, so with a swinging movement of the hind quarters. They tend to lie down and burrow into the bedding, often piled one on top of the other. High temperature of 40.5°C to 41.5°C is usually seen. Other early signs include constipation followed by diarrhea and vomiting. Later a diffuse purplish discoloration of abdominal skin occurs. Small areas of necrosis are sometimes seen on the edges of the ears, on the tail and lips of the vulva. Conjunctivitis is usually seen wherein eyelids are stick together by dried purulent exudates.

Nervous signs are often observed, characterized by circling, incordination, muscle tremors and convulsions. Death occurs within 5 to 7 days after the commencement of illness.

Infection with *Salmonella cholera Suis* also occurs and concomitant infection potentates the two diseases with resultant high mortality.

With low virulent strains, the incubation period is longer than normal and there is emaciation and the appearance of characteristic skin lesions including alopecia, dermatitis, blotching of the ears and a terminal, deep purple coloration of the abdominal skin. Pigs may apparently recover following a short period of illness but subsequently develops clinical diseases and die if stressed. Pigs infected with low virulent strains of hog cholera virus appear more susceptible to undercurrent bacterial diseases. Reproductive failure can be significant feature of hog cholera infections. Infection of the sow results inno clinical signs, other than mild pyrexia. But it may be followed by high incidence of abortion, low litter size, mummification still births and anomalies in piglets. Congenital abnormalities are associated with cerebella hyperplasia.

Clinical pathology: A valuable antemortem examination is the total and differential leukocyte count. Pig in early stage of hog cholera show pronounced leucopenia falling from normal range of 14,000 -24,000 of leukocytes /cmm to 4,000- 9000 leukocytes/ cmm. In the later stages due to bacterial infections leukocytosis may develop.

Lesions: The lesions vary depending on the acute or chronic course of the disease and also by the presence or absence of secondary bacterial infections. In swine fever not complicated by secondary infection by bacteria, septicemia changes are only seen. In per acute cases in animals that die suddenly early; in the disease no postmortem lesions are noticed. The mucous membrane may be congested. Petichae may be found on the kidneys, mucous and serous membranes. Lymphatic glands are hyperemic and swollen.

In acute cases the carcass is dehydrated, emaciated and soiled with diarrhea and faces. The condition is that of septicemia with widespread hemorrhages all over the body. Hemorrhages are found on the serous membranes, subcutaneous fat, underneath the skin, pericardium, the pleura and pulmonary tissue, larynx, on the bladder as well in the bone marrow. In the kidney, when the capsule is removed, may be found peticheal hemorrhages on the cortex extending deeply into the parenchyma giving a characteristic turkey egg appearance to kidney. The lymph nodes are usually affected and are swollen and are red in color. Hemorrhages are found in the periphery and so the zone just under the cortex is red. The skin of the ventral surface of abdomen and thorax and of the ears and internal aspects of thighs, the perineum and snout shows erythematous patches resulting form changes the blood vessels sometimes these areas may be found oedematous, necrotized and shows sloughing. Sloughing in the gastrointestinal tract may be found diffusely with catarrhal and charactereristic lesions resembling button ulcers. In the spleen due to the proliferation of the endothelium, thrombosis occurs with resultant infarction of the organ. Furthermore the wall undergoes hyalinization and necrotic changes. The spleenic infarcts are wedge shaped and found on the edges of the organ and are brownish in colour.

The pathological changes in the spleen are non-purulent meningo-encephalitic changes. Both gray and white matter is affected. The lesions are confined to the blood vessels and their supporting mesenchymal tissue. The most conspicuous lesion is per vascular cuffing that is accumulation of lymphocytes, monocytes plasma cells and local histiocytes in the peri vascular space of Virchow-Robin space. Neutrophils are seldom seen. The lymphocytes, monocytes, plasma cells are derived from the blood while the histiocytes of the locality proliferate by mitotic division. There may be degeneration of the vascular endothelium and fibrinoid changes of the wall of arteries. Nodules of microglia accumulations and are also seen around the blood vessels. In the lungs diphtheritic pneumonic changes

are seen. The pleura over the affected lungs are covered with fibrinous deposits.

Some acute cases may survive and turn to chronic and later they may die. In the intestines button ulcers are common. There is spleenomegaly and serofibrinous peritonitis is seen.

Diagnosis:

1. Intense leucopenia and thrombocytopenia in the affected animal is characteristic feature;
2. by symptoms and lesions;
3. Inoculation into a healthy pig and study of the symptoms and lesions thereby produced;
4. Agar gel precipitation test by taking sera from the affected animals or antigen from the spleen. A presumptive diagnosis therefore must be confirmed by the detection of the antigen. The samples required are tonsil, kidney, spleen, ileum, submandibular and mesenteric lymph nodes and brain.
5. Fluorescent antibody test either for antibodies or for antigens. Blood is collected in an anticoagulant and is transported on dry ice to laboratory for isolation of virus.

Herpes viruses

Herpes viruses are well known cause of outbreaks of abortions in cattle, horses and pigs. Abortions due to herpes virus infections have also been described in goats and dogs. Lesions in affected foetuses include lymphoid necrosis, together with multiple, small foci of narcosis, mild acute inflammation and intranuclear inclusion bodies in parenchymal cells especially in liver, lungs and adrenal glands. The foetal liver is enlarged and focal lesions appear as point white areas. Vascular lesions comprise endothelial swelling, but may cause pleural and peritoneal effusion, and subcutaneous oedema. Pulmonary lesions include bronchiolar epithelial hyperplasia with some necrosis and epithelial cell desquamation. The placenta is oedematous.

Equine herpes virus-1: important virus in horse that cause abortions. Infection of the uterine endothelial cells play as major role in the pathogenesis of abortion. The lesions include multiple areas of thrombosis; perivascular infiltration by lymphocytes, neutrophils and monocytes perivascular oedema and necrosis of endometrium. The fluid that escapes the damaged endometrium causes separation of maternal and foetal placenta, and can allow virus from maternal leukocytes and lysed endothelial cells to enter to the foetus. Foetal endothelial cells are also targets for the virus, and also number of parenchymatous organs.

Pesti viruses

Pesti viruses in cattle, sheep and pigs are capable of causing foetal death, or

malformation. Pestiviruses include viruses of bovine virus diarhoea in cattle, swine fever in pigs. In the horse, equine viral arteritis causes abortion but no foetal lesions.

Equine viral arteritis caused by togaviridae abortions is common. Strains of the virus vary in virulence. Consequence of infection range from sub clinical to mild fever; ocular and nasal discharges, oedema around the eyes, legs and scrotum; skin rash and in severe forms diarhoea, respiratory distress and rarely death. Sub clinical infections are very common. 80% of the pregnant animals abort or deliver still born foal. Aborted foetuses may be fresh or Autolysed but gross and histological lesions include moderate arteritis with necrosis and mononuclear cell infiltrate has been reported in the myocardium of foetus. In the mare there is multifocal necrotizing metritis involving muscular layers of uterus.

Parvo virus

Parvo virus in pigs is an important cause of embryonic and foetal loss, causing death and mummification. Foetuses have widespread necrotizing lesions, along with inflammation and inclusion bodies, especially in the liver, lungs, kidneys and cerebellum. Damage to the foetal circulatory systems lead to oedema, haemorrhage and the accumulation of sero-sanguineous fluid in body cavities.

Bovine Parvo virus is widely distributed in cattle. It is reported to cause enteritis and diarhoea in young calves and abortion and birth of weak calves. Aborted calves show cerebella hypoplasia and intranuclear inclusions in Hepatocytes and adrenal cortex cells and in the epithelium of intestinal crypts.

Blue tongue virus: The consequence of infection during pregnancy depends largely on the stage of gestation when infection occurs and on the virulence of the virus. Infections in pregnancy up to 50 days of pregnancy may result in death of embryo, placental infection and necrosis resulting in abortion.

Lesions in bovine foetus up to 70 days of gestation infection may cause in utero death and resorption or abortion of the foetus.

Blue tongue

Synonyms: Fever Catarrhal du mount; Catarrhal; fever of sheep; Sore muzzle of sheep.

Blue tongue is culicoides borne virus disease of sheep and goats caused by double stranded RNA virus belongs to orbi virus group under reo virus family. This causes fever, ulcerative Stomatitis, muscle edema and lameness. Cattle may be infected but the disease in them is not as severe as in sheep. Cattle may act as reservoirs. Sheep, cattle and buffaloes suffer with this disease. The rate of infection in buffaloes is higher than those cattle. Serum neutralization tests have differentiated 24 serotypes with some cross reaction between them. Blue tongue is most severe in sheep. The severity of the disease depends on the strain of the

virus and breed of sheep. Goats and deer are also susceptible to infection. The virus also has been recovered from bovine semen.

The prominent changes in the animals are congestion of buccal and nasal mucosa. Lameness due to coronitis, degeneration of skeletal muscle fibers is also seen. All orbiviruses are very stable and survive for years at most shade temperatures.

The disease was first recognized in South Africa in 1902. Now it has the widest global distribution. Blue tongue is endemic in India. Being a culicoides borne virus, there is a seasonal prevalence associated with the periods of maximal activity by the vectors.

Transmission: Biting insects of genus culicoides transmit the disease.

Incubation period is less than a week.

Pathogenesis: Following infection, viral replication is believed to initially occur in haematopoietic cells. This results in viremia and subsequent replication in endothelial cells throughout the body. Endothelial cell damage is responsible for the widespread gross and histological lesions. Endothelial cells become swollen and later become necrotic, causing oedema, hemorrhages, thrombosis and infarction of the respective organs. Affecting haemopoieitc tissue anemia and leucopenia is caused.

Symptoms: First there is rise in temperature (105 °F), with associated reddening of the nasal and oral mucosa and excessive salivation. A watery discharge from the nostrils later become mucous, and may dry to form crusts. Oedematous swelling appears in the lips, tongue, ears, face, and inter-mandiubular space. Oedema and cyanosis of the tongue (blue tongue) are so striking that the name of the disease stands. On the nasal and oral mucosa may be found Petichae and thickening. By shedding of the epithelium at these places, ulcers are produced which may be subsequently infected and become gangrenous.

As the fever subsides, flushing or reddening of the skin and feet appears, so that the coronets are warm and the periople which should be pink in turn turns as deep red. The animals therefore go lame as the condition is painful. There may be streaky zone parallel to the periople like the lines seen in laminitis. The mucosa of tongue becomes necrotic and show hemorrhages. There may be oedema under the skin on the neck and abdomen.

There may be pneumonic lesions and gastro enteritis with pronouncing of diarrhea which are the offshoots of spread of infection down the respiratory and digestive tracts from the oral lesions. Wool may be shed.

The disease finally terminates with extreme emaciation, chachexia_and muscle weakness. There may be torticollis. Death occurs mostly due to pneumonia and occurs after the 6 days after commencement of symptoms. The morbidity may range from 5 to 50% and the mortality may be less than 10%. Mortality is higher

in lambs. Pregnant cattle may abort. Infections during pregnancy may cause congenital deformities in the fetus.

Lesions: The lesions at postmortem are seen around the mouth and these include hyperemia, edema, cyanosis, multiple hemorrhages and swelling of the epithelium and this result in erosions and ulcers. Ulcers on the tongue may be found on the lateral surface, adjacent to the teeth. Due to infection by saprophytes, gangrene may occur. In the foot there is congestion of the skin papillae together with edema and neutrophilic infiltration producing lesion is similar to laminitis. It is the pressure on the sensitive laminae by infiltrating cells that causes pain and lameness.

In the skeletal muscle may be noticed hemorrhages and necrotic foci. In the muscle fiber that is affected show hyaline degeneration with loss of striations and pyknosis of sarcolemmal nuclei. If the sarcolemma is intact, regenerating is possible. Otherwise the degenerate karyoplasms are removed by macrophages and scar tissue forms. Sometimes dystrophic calcification of the affected muscle occurs. Hemorrhages may be found on the mucosa of abomasums and duodenum as well as in the myocardium. Pericardial space is filled with serosnaguinous fluid. Liver may show fatty changes while in spleen may be noticed congestion and swelling. Edema of lungs and develops into pneumonia.

Blue tongue virus infection during pregnancy may result in foetal infection and abortions. This causes severe cerebral abnormalities in both sheep and cattle. The nature and severity of the disease in fetus depends on the stage of pregnancy. When fetus has been exposed to 40 to 60 days of pregnancy and 60 to 120 days, a necrotizing encephalopathy occurs in fetus, which at birth is seen as that of hydraencephaly. Later pregnancy causes porencphaly that is cavities in brain. A retinal Dysplasia is also seen apart from encephalitis changes in calves and lambs born at later stages of life.

Diagnosis of Blue tongue disease:

1. Symptoms and lesions
2. Isolation of virus by inoculation on embryonating eggs and identification by inoculation into young lambs in which temperatures rise to 106°F by 4th or 5th day. Then temperature drops followed by swelling, hemorrhages and vesicles of the lips. Virus is present in the blood during fever but not when temperature drops.
3. Cherry red colour of embryonating chicken eggs, when these are injected by intravenous or yolk sac route.
4. The virus can be grown in lamb kidney cell culture. Identification of the virus can be done on serum virus neutralization in culture. Antigenically different viruses occur in nature with variable virulence. As 24 strains of blue tongue virus have been identified.
5. Diagnostic techniques based on serology include AGPT, complement fixation test.

6. The sample required for diagnosis from live animals coagulated and no coagulated blood.
7. Postmortem examination gives a clue to this diagnosis of the disease. The tissues to be harvested from dead animals are spleen and mesenteric lymph nodes. Spleen specimens are also to be collected from aborted or deformed congenital fetuses. All these specimens are to be sent at chilling temperatures to the laboratory.
8. Ecchymotic hemorrhages underneath the tunica media of pulmonary arteries.

Infectious bovine rhino-tracheitis

(Infectious pustular vulvo vaginitis)

Infectious bovine rhino-tracheitis or infectious pustular vulvo vaginitis is due to bovine herpes virus1.

This belongs to herpes family viridae and subfamily alpha herpes virinae. It has been associated with two or more or less distinct disease syndrome names a respiratory disease, infectious bovine rhinotracheitis and a genital disease, infectious pustular vulvo vaginitis.

Some isolates of the infectious bovine rhinotracheitis sub group are more virulent than most strains of either respiratory or genital origin, and these variants in addition to sever upper respiratory disease can because endometritis, Oophoritis, mastitis, dermatitis, and fatal diarhoea in young calves. Both respiratory and genital strains cause foetal disease and abortions.

Transmission: Cattle to cattle transmission are the principal method of spread and the virus spreads through respiratory, ocular or vaginal discharges. Live vaccines are also transmitting the disease.

In pregnant animals when attached virus enters the mucosa of the respiratory or genital tract. It multiplies at that site and is carried to the rest of the body by infected leukocytes and in blood to the uterus. After reaching the caruncle, the virus passes through the trophoblast to the interstitium of villi thereby infecting endothelium, mesenchyme and then trophoblast.

Abortion rate in the affected herd is around 25%. Most cows infected virus does not abort until 3-6 weeks following the initial infection and most of them abort between 5-8 months. It is the virus that stay prolonged period in the placenta before actually the abortion has taken place. As the virus invades, the foetus dies and expulsion occurs 3-5 days following foetal death.

Gross lesions in the foetus are usually absent or masked by autolysis. The lesions are white to tan foci of necrosis measuring 1 to 3 m in diameter under the liver capsule and more rarely on the surface of the lung. Heaemorrhages, occur

preferably in the perivascular region of the cortico-medullary junction of the kidney.

Histological examination of kidneys sections, focal necrosis with minimal cellular infiltration. Similar focal mononuclear infiltration is seen in liver, adrenal lymph node lung and spleen. A necrotising vasculitis in the small vessels of placenta villi is commonly seen.

Diagnosis: Fluorescent antibody techniques on frozen sections of tissues are helpful. For this kidney, liver and placenta of the foetus could be useful. ELISA to identify the antibodies to IBR in cows is also useful.

Mycotic abortions

Abortions due to mycotic agents generally occur sporadically in herd rather than an outbreak. Aspergillus is the most common cause of mycotic abortion in cattle and horses, followed by Absidia, mucor and rhizopous species. In cattle infection of the gravid uterus occurs via haematogenous route, usually by dissemination of the organisms from either the respiratory or alimentary tract of the dam to the placentomes of gravid uterus. Infected cows commonly have ulcers in the gastrointestinal tracts colonized by the same fungus causing lesions in the placenta. In mares, mycotic placentitis. The begins in the region of placental scar that is portion of the placenta covering the internal os of the cervix, thus it is regarded as an ascending infection from the cervix and vagina. Abortion and stillbirths generally occur late in gestation and are characterized by prominent lesions in the placenta and occasionally in the foetus. The placenta is frequently retained. In advanced cases in cows, leathery thickening of the placenta is evident and involves both the cotyledonary and intercotyledonary tissues. Edges of the cotyledons are thickened and gray tan in color. Numerous mycotic hyphae can be demonstrated in necrotic tissue.

Foetal skin is usually involved. The aborted calf is small and undernourished. Circular patches of skin are present near the head and neck region. Most cows clear the infection from their uteri following abortion and unless endometrial damage has been severe fertility is not permanently impaired.

Abortions due to use of poisonous chemicals.

Poisoning on administration of ergot: Use of ergot derived products results in violent contractions of uterine muscle with resultant abortions. Previously it was being used extensively in veterinary medicine and other well synthetic drugs are being put into use now-a-days.

Hormonal-abortifacient drugs: Progesterone maintains the pregnancy while oestrogen terminated the pregnancy as it induces forcible uterine contractions.

PGF2 α is frequently used in animals to bring about abortions as this is leuteolytic in most of the domestic animals by annihilating corpus leuteum.

Poisons: Chlorinated naphthalene and purgatives and nitrates through ingestion of plants are abortifacients.

Deficiency diseases that brings about abortions. Nutritional deficiencies of minerals and vitamins bring about abortions in animals.

Vaccination of mother during pregnancy against bacterial and viral diseases results in abortions. This has been discussed in detail.

Hereditary predisposition also causes abortions in animals. Both mother and foetal causes have been attributed for this.

Causes of sterility in uterine diseases

Sterility occurs in salpingitis and metritis for the following reasons: the ciliated epithelium and contractile muscle necessary for transport of ovum are destroyed, preventing the movement of the ova to the uterus. The inflammatory exudates are toxic to the spermatozoa causing their death. Exudates or proliferating cells may occlude the lumen of the tubes and fibrosis in chronic salpingitis and endometritis may cause occlusive stenosis.

Toxic products that come from uterus due to infections are lethal to zygote, hence death of embryo results. While usually fertilization takes place in most species in the distal 2\3rd portion of the salpinx, any effete products of salpinx kills the zygote, thus sterility is the common factor.

Miscellaneous disease conditions of uterus

Sclerotic metritis: It is characterized by complete destruction of endometrium as a result of severe chronic endometritis. A thick dense connective tissue layer replaces the endometrium. The foci of infection in the connective tissue layer are responsible for purulent exudates in the uterine cavity. The uterine caruncle sane endometrium appears hard and firm and the cervix is thickened.

Peri metritis and para metritis are terms wherein varying amounts adhesions between uterus and broad ligaments, with other pelvic and abdominal organs are seen. The adhesions are resultant of severe metritis, douching with strong irritant solutions, perforation of rectum with leakage of its contents, torsion of uterus and vaginal and cervical ulcerations, during abortions or parturition, excessive bleeding, following nucleation of corpus luteum or vigorous massage of infected uterus. The conditions results consequent to caesarian operations as well as due to laparotomy with resultant septic peritonitis or tuberculosis of the genital organs.

When uterus is infected with saprophytic organism's gas gangrene results and the resultant conditions of affection of uterus with gas accumulation and inflammatory changes are known as **physometra**. This is common in black quarter conditions in animals with clostridial organisms.

Diseases of cervix

Malformations: These occur more frequently in the cervix, than in other parts of the reproductive system.

Varying degrees of persistence of the median wall of the Mullerian ducts which are destined to develop into cervix results in the formation of a complete or partial duplication of cervix.

Incomplete double cervix occurs much more frequently than a complete duplication and usually involves the protin of the cervix adjacent to vagina. In the case of both incomplete and complete double cervix, if the insemination is done pregnancy may occur but it may result in dystocia.

Absence of external os may be commonly encountered. In this case, the expulsion of uterine secretions cannot occur resulting in accumulation of fluids in uterine horns resulting in Hydrometra.

Double external os: Presence of a dorso-ventral band adjacent to external cervical os giving an impression as though two cervical openings are there. It may not interfere with conception or pregnancy but may cause dystocia occasionally. The foetal membrane maybe aught on this dorso-ventral band. This is an inherited condition and acquired by a single recessive gene with low penetrance.

Hypoplasia of cervix: The cervix may be very small and there may be deficiency in number of cervical rings. Such cervix is usually defective in protecting the uterus against bacterial invasion from vagina.

Tortuosity of cervical canal: Extreme degrees of tortuosity of the cervical canal may be a cause of infertility in heifers. There may be S- shaped kink and insemination pipette cannot be inserted into cervix.

Cervical dilatation and diverticula: Dilatation and diverticula usually occur in heifers at the level of the third and fourth cervical rings. The cervical canal is usually very small anterior to the defect so that it maybe difficult to insert insemination pipette. With age tenacious mucous tends to accumulated in the area of the defects.

Prolapse of the uterus occurs fairly commonly in ruminants, exceptionally in other species. Predisposing causes in the cow are essentially those which cause, or are associated with uterine hypotony and probably also with dysrhythmia of involutionary contractions. Among the most common associations in the cow are prolonged dystocia relieved by forced traction, retained placenta and post parturient hypocalcaemia. Uterine polyps may lead to prolapse of the involved horn in the bitch. In ewes intake of legumes containing high content of oestrogen in fodder.

In any species usually only the previously gravid horn prolapses. In the cow and

ewe, the non gravid horn and sometimes intestine and bladder also may be present within the everted horn. Congestion and oedema are followed by heaemorrhages, necrosis and sepsis. Gangrene may supervene.

Prolapse of cervical rings: This is condition which usually develops with age following repeated parturition. Lacerations and heaemorrhages occur during parturition results in the formation of excess fibrous stromal tissue. This also results in enlargement of cervical rings, vascular embracement and occasional squamous metaplasia of the affected rings. The first and sometime the second cervical rings prolapse into the vagina.

Cervicitis is the inflammmation of the cervix and normally follows abnormal parturition such as abortion, premature birth, dystocia, retained placenta, postpartum metritis, pneumo vagina and vaginitis. Cervicitis also occurs whenever metritis or vaginitis is present since cervix is located between these two causes include mechanical injuries as occurring during parturition, copulation and injuries caused by variety of agents. Cervicitis is also seen consequence to disease of uterus and vagina.

Cysts: Retention cyst of the cervix is seen in cows. These is usually small and bigger ones may partially occlude the cervical canal. Cystic dilations of Gartner's ducts and Bartholin's glands is common in cattle. Gartner's ducts are remnants of the embryonic Wolffian ducts; they lay one on each side of the floor of the vagina, beneath the epithelium. They become cystic in cows poisoned with highly chlorinated naphthalene's in cows and in cows with ovarian follicular cysts and occasionally following vaginitis.

Neoplasms: Squamous cell carcinoma is the common tumor seen in most of the domestic animals. Transmissible venereal tumor is another common tumor seen in dogs and extends up to the cervical canal.

Vulvo vaginitis or vulval tumefaction of swine: vulval tumefaction of vulva is physiological response to oestrogens. This may be a development consequent to persistence in hyperoestrogenism. Vulval tumefaction in swine is due to mycotoxins. A distinct syndrome characterized by vulval hyperemia and oedema occurs in swine associated with feeding of moldy grains. The mycotoxins that causes this estrogenic effect is zearalenone or F-2, which is produced by at least four different fusarium species of which *Fusarium graminearum* being the most common.

Inflammatory diseases of vagina and vulva: The mucous membrane of the vagina and vulva shares with mucous membranes in general sensitivity to irritants, bacterial and viral infections. Although the vagina is of Mullerian duct origin, the original epithelium is replaced by stratified squamous epithelium from the urogenital sinus. This epithelium proliferates and matures under the influence of oestrogen and is then more resistant to infection. This enhanced resistance may

be due to mechanical factors in the thickened keratinized epithelium and to local production of lactic acid from the glycogen which is deposited in the epithelium under the influence of oestrogens.

Specific types of vaginitis and vulvitis:

1. *Granular venereal disease (Granular vulvo vaginitis):* Popular eruptions of the vulval mucosa are common in most domestic species but is common in cattle and buffaloes popular called granular vulvovaginitis. The term vaginitis is a misnomer, as the papules are strictly limited to the vulval mucosa and are not found in the vagina, although in acute cases there may be an associated nonspecific vaginitis. These are that is vulval granules are prominent in heifers bred naturally. They are much less common in pregnancy and are almost never present about the time of parturition.

In severe cases, the papules may be found on all aspects of the vulval mucosa, but usually they are clustered in the ventral commisures about the clitoris as pale or pink elevation a few millimeters in diameter and covered by a normal intact vulval mucosa. When numerous they are likely also to be more active, larger often coalescent, congested and red with a covering catarrhal vulvitis and vulval swelling. The overlying epithelium is then easily injured and bleeding occurs freely from the papule. The resting papules are composed of respectively organised lymphoid follicles. When the vulval mucosa is irritated these become congested with small Intrafollicular heaemorrhages and edema and hyperpalstic. In these epithelium the mitotic frequency being quite high. The same lesions occur on the penis and prepuce of the bull and so those of the vulva often persist for many months. Experimentally mycoplasmal infections have been attributed and reproduced in herds. The development of subepithelial lymphocytic foci is a characteristic response of mucous membrane to mild persistent or recurrent irritation.

2. *Infectious bovine cervicovaginitis and epdidiymitis (Epivag):* This is a specific infectious disease that has been an important cause of infertility. Bovine herpes virus 4 group has been incriminated. The slow growing virus from these infections differs to those of bovine herpes virus -1 of infectious bovine rhino tracheitis (IBR).

Natural transmission is solely by coitus. Experimental transmission is easy of infective discharges are placed in the vagina or prepuce. After incubating for a few days, diffuse purplish inflammatory streaks or patches develop in the anterior vagina to be followed by the development of a copious amount of tenacious creamy discharges in which there are large numbers of neutrophils but few or no organisms. The infection spreads readily from the vagina to the cervix and uterus. There is production of large amounts of pus. About 25% of infected animals are sterile because of the development of chronic salpingitis with Hydrosalpinx and bursal adhesions. In the bull there is early but slightly palpable enlargement of

the spermatic cord and epididymitis. The disease usually commences in one epididymis but later involves both organs and spreads from the tail of the epididiymitis to the head of it and ultimately to the testicles. The lesion is apparently an interstitial epdidiymitis with the production of excessive peritubular fibrosis and tubular obstruction.

3. *Infectious pustular vulvovaginitis of cattle;* This is due to infectious bovine rhinotracheitis of Herpes virus 1. As a rule nasal and vaginal infections behave epidemiologically as distinct diseases, although occasionally the syndromes occur together in individual animals. The infections can be transmitted to sheep and goats; producing vaginitis. *Infectious pustular vulvovaginitis is highly contagious.* It is frequently transmitted by coitus, but it can also be transmitted by other mechanical means and is contagious by close contact. It may involve individuals or few animals in heard. The disease subsides in a few days leaving immunity which is fragile and transient. *The incubation period is 1 to 3 days.* Ht lesions are restricted to the genital tract but a viremic phase probably occurs because there is early fever and leukopenia. *Initiallly there is* hyperemia of the vaginal and vulval mucosa with focal heaemorrhages in the lymphocytic follicles of the submucosa. The severity of the vulvo vaginitis increases rapidly and edema of the vulva and mucopurulent vagnial discharge develop. The focal lesions replace the hemorrhages over the lymphoid follicles and consist of small 2 to 3 mm pock like foci, .slightly elevated, pale, soft and friable. The focal lesions being related to the lymphoid follicles may be in short linear arrangements. The epithelium in the focal lesions erodes or ulcerates so that in few days the foci are flat, gray semitransparent plaques the size of the original lesions. Reinfection can occur but early reinfection produces only a mild disease. Intranuclear inclusion bodies are found in the epithelium and these inclusions are slightly acidophilic and large and they can be found for 3 to 4 days. By this time the lesions has reached peak and start healing. The parasitized cells undergo necrosis, and epithelial disruption and ulceration occur accompanied by an intense infiltration of neutrophils. Vesicles are pustules do not form. Acute inflammation occurs in the lamina propria, with hyperemia and oedema and exudation of numerous plasma cells and lymphocytes. Many of the small vessels are occluded by adventitial and endothelial swellings. The lymphoid follicles are remarkably hyperpalstic. Resolution occurs in about 8 days with hyperpalstic lymphoid follicles and slight epithelial thickening as residue. The virus produces similar lesions on the mucous membrane of the penis of infected bulls. Since virus shedding occur in most of the herpes infections under stress, inapparent infections can also transmit the disease.

4. **Necrotic vaginitis and vulvitis:** It is primarily due to trauma with contamination, often the result of bite wounds by pigs or dogs. This is also a complication of parturition and is observed chiefly in ewes and cows as a consequence of dystocia.

5. Lesions of genitalia with **Dourine in horses:** As already discussed *Trypanosoma equiperdium* is responsible for this. This is a primarily venereal disease. Natural transmission is by coitus. This is seen in mares. Following natural infection the organisms are common in vaginal discharges and male urethra. The organisms penetrate the intact mucosa at the site of implantation and proliferate in the submucosally lymph space. The incubation period is; much prolonged even months together. From the initial lesions, the organisms are disseminated in the blood to the other parts of the body, and oedematous swellings occur where they localise. The resistance of the host is modified by climatic conditions, physical conditions, intercurrent disease, and nutritional status.

The signs of dourine can be divided into genital, cutaneous, nervous and general manifestation, which occur separately or concurrently. The initial signs are usually genital but may be nervous or cutaneous. The incubation period of the genital signs varies from several days to several months during which the organisms are present in genital discharges or washings. The external genitalia are swollen and doughy, but characteristically the swelling are neither hot nor painful. The swellings are so severe that may extend to the perineum and ventral abdominal wall. The lymphoid follicles of the mucosa is hyperpalstic and ulcerates. In stallions there is balanitis and posthitis with prolapse of urethra and penis. In virulent infections, flat circulars ulcers develop in the glans penis. Healed ulcers in both males and females remain often as depigmented scars. Cutaneous lesions are manifested by uriticarial rashes which are circular occur on the skin especially on the side of the body and croup. The swellings may enlarge up to 15 cm. in diameter and painless. There are local disturbances of sweating and pigmentation occurs.

Nervous manifestations develop late in the course and usually lead to death. There is acute loss of sensation which may be a generalised or localised to the distribution of particular nerves. There is paresis or paralysis of individual motor nerves. Commonly facial nerve as well nerves of hind limbs is affected.

The general manifestation are chiefly of continued or intermittent fever, emaciation and severe anemia. The large nerve trunks are transformed into fibrous cords, which are fused with surrounding muscular fascia. Histologically there is oedema, mononuclear infiltration and fibrosis of the perineum. Changes are also seen in ganglia.

Tumors of genitalia: Leiomyoma or uterine fibroid occurs in the genitalia of the bitch. It rarely occurs in the bitch earlier than middle age and is frequently associated with ovarian follicular cysts or oestrogen secreting tumors and often also with endometrial hyperplasia, mammary hyperplasia and mammary neoplasia. The genital Leiomyoma may grow to be as large as 10 to 12 cm in diameter but not invasive. On cut surface they have a watered silk appearance and the colour usually fleshy or white depends on relative amounts of muscle and connective tissue. The tumor is not encapsulated. Histologically the tumor is composed of

whirling bundles of smooth muscle cells with abundant stroma but scant intercellular connective tissue. The nuclei of muscle fibers are short, plump and fusiform while those of fibroblasts are longer, slender and curved.

Canine venereal tumor: Canine venereal granuloma or histiocytoma or Sticker's sarcoma. Bitches are more susceptible. Since the tumor is transmitted by transplantation of tumor cells during coitus, it is found on glans penis and on the prepuce in the male and in the vagina in the bitch. Rarely the scrotum and perineal regions in male show the tumors. The tumors may also occur occasionally, on the skin of other parts of the body. Ocular lesions occur as flesh coloured masses attached to the iris and protruding to the anterior chamber of the eye. The tumor cells can also spread by aberrant metastases in organs like liver and brain. The tumors also spreads by transcoelomic way.

There are two morphological types of cells in culture namely spindle reticular and often round cell type. Canine transmissible venereal tumor cells have 19 muticentric or and 40 to 42 acrocentric chromosomes. The total number of chromosomes usually may vary from 59 ± 5. The normal number of chromosomes in the dog is 78.

The tumor can be transmitted from one animal to another not only by coitus but also by injecting the intact cells, subcutaneously or rubbing them on a wound on the skin or a mucous membrane.

Histologically the tumor varies depending on the stage of growth or regression. During the early stages of growth, the tumor is composed of round, oval or polyhedral cells with indistinct boundaries and a poorly stained or clear cytoplasm. The nuclei are large in proportion to cell size with a single, well defined nucleolus and many chromatin granules. Mitoses are frequent. Desmoplastic reaction characterized by fibrous tissue proliferation is common in haling tumors. The tumors are in association with low grade epidermoid carcinomas of the vulva and vagina. Wheather the infiltration of tumor cells of venereal granuloma brought about the anapalstic changes on the surface epithelium is to be probed. In most of the cases usually vagnial squamous epithelium is not breached, but in some cases where squamous cells carcinomas are common there is ulceration skin epithelium.

Fibropailloma of the vulva of bovines are very common in heifers. Histologically the bulk of the tumor consists of interlacing bundling of fibrocytes are seen. Mitotic figures are common. These fibroblasts are plump and spindle shaped and has large bizarre nuclei as well nucleoli. Collagen formation from the stroma is progressive with progress of time.

Diseases of mammary gland

Summary

Diseases of mammary gland – Embryology of mammary gland – Inflammatory diseases of mammary gland – Mastitis Chronic fibro sign glalcothophoriectasis of

mammary ducts. Summer mastitis: *Corynebacterium pyogens*—Bovine tubercular mastitis: Caseous tubercular mastitis: Mammary tumors—Hisotgenesis of mammary-gland—tumors—Classification—of—mammary—neoplasms

Diseases of mammary gland

The mammary glands are modified cutaneous glands with the important roles providing nourishment to immature young ones and providing to the new born of any protective antibodies to the neonate.

The duct system of mammary gland in cattle and buffalo teat is divided into three parts namely streak canal, Furstenberg's rosette and teat cistern.

Streak canal is the primary defense barrier against udder pathogens as majority of the organism enters the gland through streak canal. Streak canal is lined by stratified squamous keratinized epithelium both in cows and buffaloes. The epithelium appeared thicker in buffaloes than in cattle which provide an extra resistance against penetration of pathogens through epithelium. As the stratum granulosum contained higher amount ofkerato-hyaline granules in buffaloes than in cow. The kerato hyaline granules may probably contribute in formation of large amounts of keratin in lumen of streak canal that particularly occludes the lumen. It inhibits bacterial penetration by providing physical barrier. Fissures in the keratin have been reported through which organism travel into teat cistern. Kertain can not only act a physical barrier for entry of bacteria but also liberating certain fatty acids and protein like ubiquitin which have bacateriostatic properties. This ubiquitin inhibits the growth of variety of bacteria through binding inactivating negatively charged bacterial cells by inducing alteration in osmo regulatory mechanisms leading to swelling and lyses.

Furstenberg's rosette: The mucosal epithelium of Furstenberg's rosette is stratified cuboidal or columnar and sub epithelial connective tissue is thrown into folds which are rich in blood vessels. The aggregates of lympho-reticular tissue in the form of lymphoid nodules were seen in sub epithelial stroma, which is the site for antibody production. The antibodies may act by inhibiting the attachment of bacteria to epithelial surface or may also neutralize bacterial toxins. The lymphocytes interact with macrophages and neutrophils to stimulate phaogcytosis of bacteria. The large surface area provides by connective tissue filled fold rosette provides more surface for infiltrating leukocytes.

Teat cisterns: Teat cisterns mucosa is lined by stratified cuboidal to columnar epithelium which has fewer folds than that of rosette both in cows and buffaloes. Some lymphoid aggregations are also present in sub epithelial stroma. The cells observed are neutrophils, mast cells, monocytes and macrophages.

The mammary gland however provides a source of infection by bacteria such a Mycobacterium paratubuerculosis and Brucella, which arrive in the gland by haematogneous route and provide minimal pathologic changes. Pasteurella spp.

and streptococcus also come during the course of agalactogenic infections and inflammation. A number of helminthes parasites have adapted their life cycles in ways that ensure their transfer to neonates in milk. Toxins of virus sources may be excreted in milk.

The major pathological changes are those of inflammatory response (mastitis) in large animals and neopalstic changes in dogs and cats.

Embryology of mammary gland: It is a specialized form of sweat gland. The myo epithelial cells are thought to be of epithelial origin, and the relationship to sweat gland possibly accounts for the structural and behavioral similarities and their participation of myoepithelial cells in mammary and sweat gland carcinomas in the bitch.

The glands form on the mammary line provided is detectable in the ventro-lateral ectoderm of the embryo. The ectodermic cells of ridge, which are destined to develop into the mammary glands, congregate in specific areas, and number and location appropriate to the pieces, to form the mammary buds. From the buds primary sprouts push into the mesenchyme, the number of sprouts for each bud determines the number of openings. These will eventually develop in each teat. Only one primary teat sprout develop from each bud in cattle and is destined to form this streak canal and teat cistern and proximally the gland cistern. Secondary sprouts develop from the primary sprout to form the early milk ducats. In species such as cattle, sheep and goats with one teat orifice, the gland is a single large secretary structure, but ectopic mammary tissue may form into the wall of teat canal. There are usually two streak canals in horses and pigs, 3 to 7 in cat and 8 to 14 in dog. In species with multiple teat orifices, mammary gland is in reality a composite gland, the number corresponding to the number of streak canals, and each is autonomous and separate from its neighbors.

Mammary gland development in males is generally similar that in females in the embryonic and fetal stages. The males which do not have teats or nipples, the primary sprouts separate from the surface epithelium of the mammary bud under the influence of androgenic hormone and regress. The male mammary gland is susceptible to hormonal stimulation but is not sensitive as the female. Alveolar structures are not present and the enlargement which occurs under the influence of estrogen is due to cystic ductal hyperplasia. This is seen most often in dogs with estrogenic secreting tumors of the testis.

Inflammatory diseases of mammary gland

Mastitis is inflammation of the mammary gland and thelitis is the inflammation of the nipple. Any injury can cause mastitis but the common causes are microbes. The route of invasion is haematogneous as already states either but tuberculosis or brucellosis or it may be per cutaneous or complication of local dermatologic conditions of the skin or a teat, but the usual route of invasion is through the teat canal.

Infections of mammary gland are most frequent and cause the most economic loss in dairy cows. Infection agents known also to invade and colonize mammary gland include, numerous bacterial organisms, certain species of fungi, Mycoplasma and algae and even few viral agents.

Most pathogenic organism enters the mammary gland via the streak canal of the teat, although few are known to enter via the haematogneous route.

The udder of dairy cows is predisposed at invasion by pathogenic organisms due to high incident of trauma to the teat orifice, sphincter or streak canal of the teat.

In cows the orifices of the teats and streak canals are normally lined by stratified squamous epithelium and are partially occluded by coagulum consists of keratin like material from the epithelial lining and a waxy component of milk which together are referred to as smegma. This waxy plug serves as a natural barrier to ascent of microorganism into the more vulnerable cistern portion of the gland and its associated ducts and alveoli. Trauma to the teat may cause break of natural barrier and render the cows more susceptible infectious. Cows are susceptible streptococcus agalactiae. Mastitis is common in cattle as age increases. Humoral and cellular factors are responsible for the enhanced resistance end inhibit microbial growth, other factors like lactoferrin, iron-binding protein that inhibits growth of bacteria that require iron, immunoglobulin and lactoeparoxidase. Streptoocccus agalactia, dysglacatia and uberis a recommon causes of streptococcal mastitis in dairy cows.

Streptococcal mastitis is responsible for showing fever, inappetance and malaise. With time the exudative stage subsides and macrophages, lymphocytes and fibroblasts dominate the residual inflammatory processes.

On clinical examination of affected portions of gland are swollen, firm and painful to palpation. Infection may recur to subsequent episodes and spread to the glands or teats and eventually these become atrophic and fibrotic.

Chronic fibrosing galactophorectasis of mammary ducts: This is common in older bitches; cystic ducts are often filled with protein rich fluid which appears clear to reddish brown grossly. Epithelial cells lining the affected ducts can vary from low cuboidal to squamous type.

Staphylococcal mastitis is predominantly an infection of the younger age groups, and there is no increase in susceptibility with age. Pathogenesis strains of staphylococci are always of human or animal origin and persist as permanent inhabitants of the skin and mucous-membranes. The ability of a strain at produce catalse and haemolysis is the best single criteria of pathogenicity for animals. Coagulase positive staphylococci responsible for this. This is due to the presence of α-toxin. Catalse positive staphylococci are the primary cause of mastitis in cattle.

Clinically staphylococcal mastitis may be per-acute and fulminating. The acute

form of the disease occurs shortly after parturition and tends to produce gangrene of affected quarters and a high mortality. The affected quarters are swollen and tense hot and firm and are very painful. Brownish blood stained or straw colored watery fluid can be expressed from the teat. Unaffected quarters of the same udder are also swollen and tense and the secretion is reduced but otherwise normal, and effect probably due to the diffusion of toxins through the vascular bed of the gland.

Gangrene usually affects first the teat and adjacent portion of the udder and may not be more extensive or it may extend even to involve the whole quarter. The tissue becomes blue and eventually black and is softer and insensitive and cold. There is pitting edema of the inguinal area, flank and ventral portions and in a day or so the necrotic skin begins to exude serum and to slough and crepitating as bubbles develops beneath it. Natural separation of the gangrenous areas begins about a week after the onset but proceeds slowly with the development of a suppurative surface and fistulate.

Coliform mastitis: The bacteria group under this category is Escherichia coli and species of the genera of Enterobacter, Klebsiella, Citrobacter, and Proteus and Serratia.These produce acute mastitis with systemic reaction especially with Escherichia coli septicemia. Lameness may also be expressed. This mastitis is common for lactating gland. The organisms enter whenever there is trauma suppuration results. The destruction to mammary tissue is due to end toxin liberated by the bacteria. The galactogenic cisterns and ducts are affected. The infection is limited to one quarter and the inflammation is serous with much edema or it may be severely hemorrhagic. The secretion in the cistern is scanty oar watery or cloudy and blood stained and contains floccules of fibrin and coagulated casein. There is severe edema of sub cutis.

Histologically the inflammatory reaction is seen to be centered on the ducts. The lining of larger ducat sis destroyed and replaced by fibrino-cellular exudates. The Intralobular ductular lining is destroyed and the acini are filled with a serous fluid wherein desquamated epithelial cells are seen. Interlobular septa are widened by edema fluid and the lymphatic are greatly dilated and contain plugs of fibrin.

Summer mastitis: Corynebacterium pyogenes causes sporadic cases of acute mastitis. It is a necrotizing galactophoritis with slight primary involvement of the acinar tissue. Grossly visible abscesses form and the exudates remain stagnant in the ducts. The wall of the teat canal and cisterna is thickened by granulation tissue and the mucosa is ragged. The teat canal is stenotic.

Mycoplasmal mastitis: Mycoplasmal bovis is the frequent organism found in these infections. The disease is characterized by sudden onset of agalactia. The mammary gland is swollen, firm and painless. Arthritis and lameness is seen. Affected quarter is in the active stage and is swollen and firm but later becomes slack as rapid involution occurs. The altered secretion and glandular enlargement persists for

several weeks. Recovered animals are chronic carriers.

Bovine tuberculous mastitis: Disseminated tuberculosis of udder results as part of early generalization of tubercular organisms. Tubercular nodules of 1 cm or so in diameter project about the cut surface. The tubercle is not evenly distributed, and present in deep mammary tissues. The interlobular ducts are so extensively involved and the dilated lumen is filled with cellular exudates. Supramammary lymph nodes are involved and contain many typical tubercles.

Chronic organ tuberculosis: Regional lymph nodes are not usually involved. The mammary tissue is firm and cuts readily. The lobulated structure is exaggerated and when cut projects above the surface of the organ, giving a smooth bumpy appearance and indentation into the interlobular tissue. The lobules which are affected and most of them tend to be varying from grayish red to white and the surface is dry. The lesions begin as one or more foci of granulation tissue within the lobules, and they expand and coalesce to involve the entire lobule. Affected tissue breaks down and caseates.

Histologically the lobular outlines are retained and interlobular septa are not involved. Typical tubercles do not form although the type of cell involved in the reaction is usual.

Caseous tubercular mastitis; Greater enlargement of the affected gland is seen but not nodules. The caseous areas are large and irregular. The dry yellowish caseous appearance and hyperemic margins are suggestive of ischemic infarction. Histologically changes area characterized by inflammatory exudation of fibrin and numerous leukocytes. The caseated areas are surrounded by a zone of hyperemic granulation tissue of the hemorrhages in it occur frequently.

The gland is progressively increased in size and firmness. Infected gland progressively enlarged. Milk may be physical abnormal thought it contains the bacilli. In the later stages of other dies either is reacting in the amount of the secretion, and it is converted to thin whey like fluid which contains floccules of caseous exudates and very large number of bacilli.

Cryptococcus mastitis is caused by Cryptococcus neoformans. There usually involvement of more than one quarter. With the acute stages, rather severe swelling and increased firmness of the gland and subcutaneous edema which when chronic condition produces tight adhesions of the skin to the gland. Change in the milk occurs after 2 to 3 weeks. The milk become watery and flaky and large number of organisms excreted in the milk. The disease tissue is abnormally flesh, firm and grayish in the acute stage and the cut surface is very shiny with viscid grayish secretion that makes the gland hard to handle. Later the tissue become involutes and gray and contain numerous small granular masses.

The histological picture is variable in several affected areas there tends to be compete liquefaction affecting epithelial cells, and the acini, on consequence

becomes distend confined only the skeleton of connective tissue. The organism represents in very large numbers and produce multilocualr cystic acini. Lymph nodes are greatly enlarged and the lesions are to those in the udder infection also spreads to the lungs.

Mammary Tumors

These are commonly seen in dogs and none in cows. (Cotchin.E. Neoplasm's of the domesticated animals. A review. 1956. Common Wealth Agricultural Bureau). The cell becomes neopalstic is that of either epithelial or mesenchymal, i.e., myoepithelial. These myoepithelial cells are located external to the lining epithelium and internal to the basement membrane. Presence of myoepithelial cells in mammary gland links its morphogenicity to sweat glands. They are elongated cells with fewer processes and are strongly positive to alkaline phosphatase staining. In this connection, it is interesting to observe Bloom's statement that serum of dogs with mammary neoplasms in 63.6% of cases showed a high alkaline phosphatase activity.

Table showing the type of epithelium and the type of tumor with respect to mammary tissue

Name of the tissue	Name of Benign tumor	Name of malignant tumor
Luminal epithelium (glandular epithelium)	Adenoma	Adenocarcinomas
Myoepithelim	Mucoid tissue (Myxoma)	Mucoid-sarcoma (Mycosarcoma)
Basement membrane	Chondroid tissue	Chondrosarcoma
Intralobular connective tissue	Bone	Osteosarcoma

Histogenesis of mammary gland tumors: a). *embryonic cell rest theory*: epithelial cells can undergo dysembryogenic transformation into cartilage or bone. b). Metaplasia *of fibrous tissue*: The production of mucin, which is related to normal physiology of gland, accumulates because it is not destroyed out at a normal rate. Cotchin.E has opined that myoepithelial cells play a significant role in mammary neoplasia, and he believes that osseous tissue is a product of endochondral ossification of preformed cartilage by intra-membranous ossification, in the Chondroid tissue. Cochin, furthermore states that myoepithelial cells though of neuroectodermal in origin is accepted to have the power of forming tissue of mesenchymal type.

Classification of Mammary Neoplasms (Cotchin.E, 1960)

Benign Malignant

A. Simple benign

1. Connective tissue type A. Simple Malignant

2. Epithelial type

1. Carcinoma

B. Complex benign or mixed tumor

a. Squamous cell carcinoma

b. Duct carcinoma

c. Adenocarcinoma

d. Sclerosingcarcinoma

e. Anaplastic carcinoma

2. Sarcoma

3. Complex malignant tumor

The mammary glands are modified cutaneous glands with the important roles of providing nourishment to immature neonates and the weight of evidence supports the derivation of mammary glands as specialization from sweat glands. The myoepithelial cells are thought of to be epithelial origin.

The glands form on the mammary line. Ectodermic cells congregate in specific areas to form the mammary buds. From the buds, primary sprouts push into the mesenchymal, the number of sprouts from each bud determining the number of off springs that eventually develops in each teat. In species with multiple teat orifices, the number of mammary glands corresponding to a number of streak canals, and each is autonomous and separate from its neighbors.

In the mare, ewe, sow and cow, tumors occur rarely and are generally benign. In bitches, the mammary tumor occurs more commonly in older groups. It is strange to notice that the udder of the cow with great functional activity and development is seldom the seat of neoplasia. It is only in the bitch and to a lesser extent the cat that is of importance. Spaying bitch prior to first oestrous reduces the incidence of mammary gland tumors. No inhibitory effect on mammary tumorogenesis has been detected if the bitch is spayed after two and half years of age or from four oestrous cycles. Early pregnancy lessens the risk of getting mammary tumors. Dogs aged between 7 and 14 years show the incidence as 78%.

Bitch possesses five pairs of mammary glands and tumors arise usually in 57% of cases, by involvement of posterior glands. Next in frequency are the anterior two while the central pair is least affected. The reason for the posterior pair to be more frequently affected is probably because they are more prone to trauma.

Estrogens play a distinct role in the genesis of mammary tumors. The low incidence of mammary neoplasia in ovarectomised bitches lends to support the same. In mammary neoplasms, the tumor cells contain more estrogen receptors compared to that of progesterone.

Grossly the tumors are soft or firm depending upon their fibrous tissue content. They may be cystic or those containing bone or cartilage are hard and these tumors are grayish white in colour.

Histologically canine mammary growths fall into five main groups. Those showing dyspastic changes, mixed tumors, and benign tumor other than mixed type, carcinomas and sarcomas. The tumors may be benign or malignant. If the glandular epithelium is alone is effected, it is called simple tumor. However, if the connective tissue also proliferates, then the tumor is known as mixed tumor.

Simple mammary tumor: Duct Papilloma: This tumor arises from the lining epithelium of the canal or larger ducts. Tumors or localized and may be single. The cells are cuboidal or columnar and these form papillary projections into the lumen of the dilated ducts, which contain eosinophilic material. These must be differentiated from duct Papillomatosis that are more common in the cat.

Malignant duct Papilloma or intraduct Papilloma: In this condition, the cells are anaplastic and show Hyperchromasia. These are arranged in acinar or multiacinar formation, but sometimes in solid sheets also. More commonly a papillary arrangement can be noticed wherein the cells are one to several layers thick. A delicate fibrous tissue core is present in which blood vessels are found.

Lobular carcinoma: In this, the cells of the acini of mammary gland proliferate and arrange in solid sheets or as acini with Lumina. This variety is called true adenocarcinomas of the mammary gland.

Mixed mammary tumors: These are far more numerous than the simple variety. Besides the epithelial cells, the connective tissue elements and myoepithelial cells may also be involved. In the benign variety, the tumor consists of papillary growth of the ductal epithelium. The acinar cells in some parts may also proliferate. It is not uncommon for the epithelium of the ducts to show metapalstic change to squamous type. Very often, the myoepithelial cells that are situated between the epithelial cells and the basement membrane may also proliferate to a thickness of several layers. These cells are spindle shaped with tapering ends and have elongated nuclei. They can be converted into hyaline cartilage.

Stromal tissue also proliferates and this may be transformed into Myxomatous, cartilaginous, or osseous tissue. Hence, the tumor may be a mixture of all these tissues to merit, depending upon the tissues present, the name like fibro-myxo-adenoma or fibro-myxo-chondro-adenoma etc. Since pronouncing such name will be difficult, a collective term of mixed tumor is applied.

Malignant mixed tumor: In this variety, the epithelial cells are malignant. The connective tissue part may also be malignant or it may be benign. Thus, one can find variety of elemental tissues like chondro-osteo-adeno-carcinoma. Myoepithelial cells may also show malignancy. These cells become pleomorphic and may form multinucleated giant cells.Mitotic figures are numerous in all types of tissues. Fibrous tissue frequently shows metaplasia to cartilage and bone. Metastasis into lung, liver and kidneys are frequent. It is observed that neoplasm affecting the anterior three pairs of glands first metastasizes into auxiallry lymph nodes while those of the posterior two pairs into the inguinal lymph node.

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Chapter 7

Diseases of Male Genital System

Summary

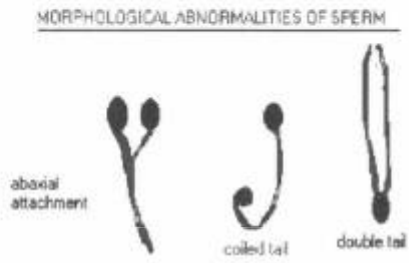
Structure of testis- gross and histological-Testis- Classification basis on the germ cell maturation- Testicular descent-Tubuli recti- Mediastinum testis—Testicular hypoplasia Cryptorchids- Complete agenesis—Accessory adrenal cortical tissue Cystic rete testis Testicular degeneration—Causes:-Epididymis—Disease of penis and prepuce—. Uroliths—Tumors-of—testis—Seminomas—Sertoli cell tumors—Interstitial cell tumors—Canine Venereal tumor—Tumors of prostate—Hyperplasia of prostate

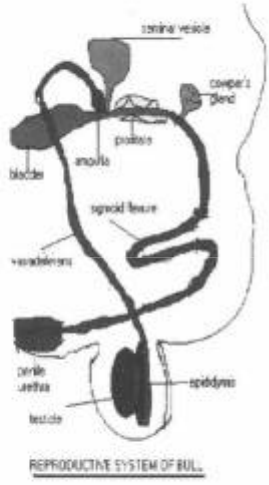
Male Genital system

The reproductive system of the male consists of paired testes, paired accessory glands, and the duct system, including the copulatory organ. The indifferent gonads of early embryo differentiate in females into ovaries and in males into testes. In all species the testes develop in the vicinity of the kidneys, in the region of primitive ridge. In mammals the testes undergo an elaborate descent, ending for most species in the scrotum. In birds the testes do not descend but remain approximately in the position in which they originate. The function of testes is two fold; they produce the male sex hormone, androgen, and they form the male gametes, the sperm.

The sperms are produced in the seminiferous tubules, which make up over 90% of the testicular mass. The tubules are extremely convoluted, each testis contain tubules that would be several miles long if they are stretched out.

The histology of the tubule changes progressively with age. In young males the tubules are simple, the germinal epithelium consisting only of spermatogonia and Sertoli cells. In older males the spermatogonia give rise to primary spermatocyte, which after the first meiotic division gives rise to the haploid secondary spermatocyte. Thus in turn becomes spermatic, which after a series of transformation called as spermatogenesis and gives rise to sperm cells consisting of head, middle piece and tail. The Sertoli cells, which are found along the basement membrane of the tubules, are called sustentacular cells or sperm nourishing mother cells. The other major function of the testis is secretion of male hormone by the interstitial cells or cells of Leydig.


MORPHOLOGICAL ABNORMALITIES OF SPERM
abaxial attachment
coiled tail
double tail
proximal cytoplasmic droplet


seminal vesicle
cowper's gland
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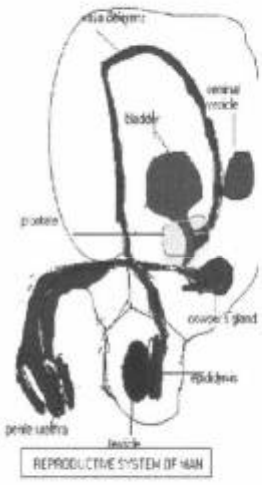
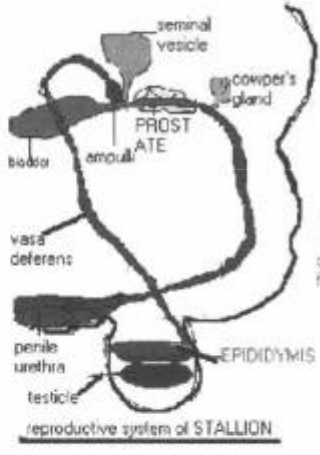
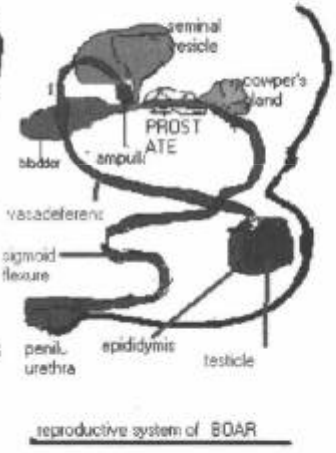
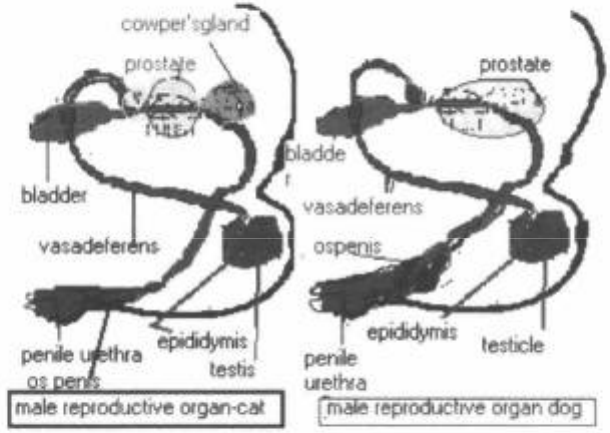
ampulla
bladder
sigmoid flexure
vasadeferens
penile urethra
epididymis
testicle
REPRODUCTIVE SYSTEM OF BULL

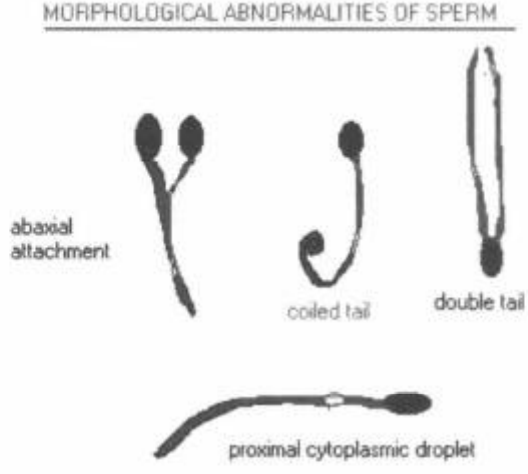

vasa deferens
seminal vesicle
bladder
prostate
cowper's gland
epididymis
penile urethra
testicle
REPRODUCTIVE SYSTEM OF MAN


seminal vesicle
cowper's gland
PROST ATE
bladder
ampulla
vasa deferens
penile urethra
EPIDIDYMIS
testicle
reproductive system of STALLION


seminal vesicle
cowper's gland
PROST ATE
bladder
ampulla
vasadeferens
sigmoid flexure
penil. urethra
epididymis
testicle
reproductive system of BOAR



Compare the relative sizes of the various accessory glands, and note that all these species have the prostate; that the dog and cat have no seminal vesicles, that the dog has no Cowper's gland; that the cat, the boar and man have no ampullla swelling; that the bull and the boar have the sigmoid flexure of the penis; that the dog and the cat have the os penis; that only the boar has the preputial pouch. Urine accumulates in this pouch and is responsible for the strong male sex odour of boars, which permeates even their meat and accounts for its disagreeable odour.



Embryology of male reproductive system

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. The gonads originate as thickenings and known as gonadal ridges on the medial side of the mesonpehros. The gonads originate

as thickenings and known as gonadal ridges on the medial side of the mesonpehros. The gonadal ridge is the mesenchymal thickening covered by mesothelium. The mature male and female germ cells are direct descendants of the primordial germ cells, which in human embryos appear in the wall of the yolk sac at the end of the third week of development. These are endodermal derivatives. These migrate to the gonadal ridge through mesentery, and the overlying cuboidal epithelium which is superficial, invades the underlying mesenchyme. Thus at this stage, germ cells, which arise from the endoderm of the yolk sac of the embryo, have migrated to bilateral swellings of pelvic mesoderm (genital ridges) overlying the mesonpehros (primitive kidney) to form paired bipotential gonads. At about the same time, small mesonephric tubules from the mesonpehros also grow caudally and fuse to form a pair of ducts the paarmesonephric ducts (wolffian ducts). At about the same time a second pair of ducts, paarmesonephric ducts (Mullerian ducts) forms on the ventral aspect of each mesonpehros. The caudal most portion paarmesonephric duct fuse with each other on the mid line, and form y shaped configuration.

The cranial most portion of the duct becomes convoluted and forms the oviduct. Unfused portions of the uterine horn and fused portion as body of uterus, cervix and cranial part of the vagina. The various adult uterine shapes found in different species are based upon the extent of the fusion of the para-mesonephric ducts, greatest amount in the horses and least amount in the pigs. The greater the fusion the greater the part of the uterus that comprises the body.

The critical stages of genital development involve differentiation of the bipotential gonads into testis and ovaries. Upon entering the genital ridges, after migrating from the yolk sac, the primitive germ cells increase in number by mitosis in the superficial mesenchyme of the bipotential gonads. During the period of active proliferation, the germ cells loose their mobility and become somewhat smaller and thus are transformed into oogonia or spermatogonia.

Gonadal definition is determined genetically and involve the expression, or lack, thereof a gene normally found on the y-chromosome of the male. The genes referred to as the SRY gene or sex determination region of the Y –chromosome and codes for a protein referred to as testicular determining factor (TDF).

The male reproductive tract arises primarily from the Wolffian ducts, which in turn have differentiated from the genital ridge of the early embryo. Sex organs of the embryo are discernible by 45th day of gestation. Testis develops within the abdominal regions near the kidneys. They commence their descent from the abdomen into scrotal pouches during foetal development. This migration normally results from the shortening of gubernaculum testis, a fibrous cord of connective tissue and muscle attached to the tail of epiddymo and the inguinal region of the abdominal wall of the foetus which is destined to the scrotal pouches. The shortening is a result of differential growth and intra-abdominal pressure.

Migration is normally complete soon after birth. The present authors found the migration to be complete in a 130 day old foetus but in a 70 day old foetus. However one or both testis may fail to descend to scrotum in cryptorchid condition.

The scrotum, the two lobes sac carrying the testis. This is situated in the inguinal region between thighs just posterior to rudimentary teats. Scrotal sac is made upon several layers. Skin which is covered with fine hairs, possess large sweat and sebaceous glands

1. Tunica vaginalis which is an extension of peritoneum is reflected back over the testis and then is drawn by them down into each scrotal pouch at the time of decent from the abdomen. Thus the tunica vaginalis has two layers, visceral layer forming the coat of testis and epiddymo and a parietal layer lining the scrotal cavity. It passes through the inguinal ring wherein spermatic artery; vein, nerves and lymphatics all forms spermatic cord. The tunica vaginalis secrets a lubricating fluid. The external cremaster muscle which aids lifting the testis, originates at the internal orifice of the inguinal canal, and is striated and attached to the exterior of tunica vaginalis. The testis are suspended in the scrotum by means of testis mesorchium and ligamentum testis.

2. Temperature of abdominal cavity and testis is less than 2°C in monkey, man, dog and 7°C in goat. Intratesticular temperature is midway; between body temperature and the external temperature of scrotum. The thermoregulatory action does not begin until the animal approaches puberty and is subjected to testicular hormones. Thermoregulation is due the position of testicular artery and surrounding pampiniform venous plexus. In bovine mature testis 10-13cm long and 5 to 6.4 cm wide and weights around 500g. The total length of seminiferous tubules in a bull is 3 miles and each tubule is measuring around 300ì in diameter. 805 of testes of bulls are in tubules.

The nerve supply is entirely sympathetic. Vasoconstrictor nerves that control blood flow, the nerves of epididymis have both cholinergic and adrenergic types. Blood flow testis is diminished by fright due to adrenaline release. Spermatic artery is much convoluted around 140 to 226 cm long. Within testis because of non-pulsation and limited flow of blood, oxygen levels are lower and CO_2 levels are higher. Seminiferous tubules join to form tubual recti which lead to rete testis in mediastinum from efferent ducts, vasa efferent and forms epididymis. Testis appears by 25 mm embryo itself.

Testis: Testis is the singular and testes are the pleural terms while describing the testis. The testis is enclosed by peritoneum (tunica vaginalis), network of small blood vessels and delicate connective tissue (tunica vasculosa) and tunica albuginea comprising fibrous tissue, smooth muscles and nerve endings.

The testes enter the scrotum midway through foetal life in ruminants and shortly

before birth in horses. The testes of the dog pass into the inguinal canal on the 3rd or 4th 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 bucks and goats have pendulous sacs. The scrotal skin is thin and has a 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 animals. The musculature covering the scrotum, the tunica dartos is thickest in the distal part of the scrotum. The contraction of the dartos results in the elevation of the scrotum.

Examination of testis comprises of dissecting out testis, spermatic cord and epididymis. These should be examined for gross lesions. These organs are weighed and measured. Mid-saggital incision is made throughout the testis so that the mediastinum testis is exposed. After mid-saggital cut is made, the surface is examined, and each half should be cut transversely into slices of approximately 5 mm to 1cm. wide. The cut surface of normal testis bulges above the surface. If the testis does not bulge indicates severe degeneration seminiferous tubule occurred. The colour of testis varies among the species and also according to the age. The colour of the testis varies upon the amount of pigment present in the interstitial cells, and this pigment tends to increases with the age.

For routine histological examination, 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. A hard fixative such as Bouin's solution should be used for preserving the testicular tissue. Formalin fixation is very poor since it is a soft fixative. Periodic acid Schiff stain is useful for studying stages of spermatogenesis cycle. Masson's trichrome stain is used for differentiating connective tissue from Interstial cells. An elastic tissue is useful for studying the basement membrane of seminiferous tubules in case of degeneration. A reticulum stain outlines the cytoplasm of sustentacular cells and the cellular membrane of Interstial cells. Oil red O is useful for demonstrating lipid in the cytoplasm of interstitial cells and sustentacular 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 degenerated 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 Interstial cells.

Seminiferous tubules: The seminiferous tubules are small convoluted tubules, run parallel and terminate in epididymis. They are lined by cuboidal epithelium and are surrounded by elastic tissue. Two principle methods have been developed for the classification of the stages of seminiferous epithelium. One is based on the development of acrosome and the other on the germ cell association.

Basis on the acrosome development: Basis on spermiogenesiis this will be looked into the spermiogenesiis consist of four periods, namely Golgi, cap, acrosome and maturation phases. An acrosome cap appears on the nuclear surface to become head cap. During the last or maturation phase, the Periodic acid Schiff staining of the acrosomic system decreased gradually.

Classification bases on the germ cell maturation: Eight stages in the development of seminiferous epithelium.

Steps in the Formation of spermatozoa,

1. Elongation of spermatids nuclei.
2. Formation of spermatids bundles to the beginning of first maturation division of spermatocytes.
3. From the appearance of first maturation division to the end of second maturation division.
4. From the end of second maturation until the appearnace of dusty chromatin.
5. From the end of second maturation until the appearnace of dusty chromatin in young spermatic nuclei.
6. From the appearance of dusty chromatin in the nuclei of spermatids until the movement of spermatozoa bundles toward the lumen of seminiferous tubules.
7. From the start to the end of spermatozoa bundles towards the lumen.
8. From the completion of central movement of spermatozoa to the release into the lumen.

Testicular descent:

In almost all domestic animals, the testes lie in the scrotal sac after the birth of the animal. In the case of dogs the testes in the scrotum is observed after 8 to 10 days of birth. In five week old pig embryos, the testis is intra-abdominal and connected to the carnio-medial pole of the mesonpehros. The gubernaculums is a mesenchymal thickening that extends from the caudal pole of testis to a knob like expansion between the internal and external oblique muscles at the site of future inguinal canal. Peritoneum covers the gubernaculums located within the abdomen.

The peritoneum grows into the extra-abdominal part of the gubernaculums to initiate formation of the processes vaginalis. During testicular migration the total length of the gubernaculums, relative to crown-rump length, remains relatively constant, but the length and bulk of the extra-abdominal part increases considerably as 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 scrotum. Enlargement of the extra-abdominal part of gubernaculums is due largely to an increase of extra-cellular substance, a mucopolysaccharides component. The processes vaginalis follows the outgrowth of gubernaculum. The cranial part of

the gubernaculums enlarges, thus dilating the inguinal canal. The testes then rapidly move through the canal. As the gubernaculums degenerates, the testis moves into the scrotum. The gubernaculums draws the testis from its original position to the vagnial ring and possible out through the inguinal canal but not into the depth of scrotum. There is no organised connection between the tip of the gubernaculums and the scrotal floor. Inguinal passage of testes occurs at 100 to 105 days of gestation in cattle and approximately in swine, and before months of birth in horse.

Receptacles: The receptacles (transitional zone) are the connecting pieces between the terminal part of the seminiferous tubules and the tubuli recti. Ciliated cells are present into the rete testis but not in the receptacles. Receptacles are usually round in the testis of horses, dog and cat.

Tubuli recti: (rete tubules, straight seminiferous tubules): The tubuli recti connect the receptacles with the rete testis. In most species, the area located in the central portion of testis which are adjacent to the mediastinum testis, which contains the rete testis.

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 tunica albuginea. It contains rete tubules.

Rete testis: The rete testis consists of a series of interconnected wide channels lined with a simple cuboidal to columnar epithelium and resting on a thick basal lamina. Beneath the basal lamina dense bundles of collagen fibrils and large amount of blood vessels and nerve tissue are found. The rete testis is located in the central portion of the testes in most of the domestic animals.

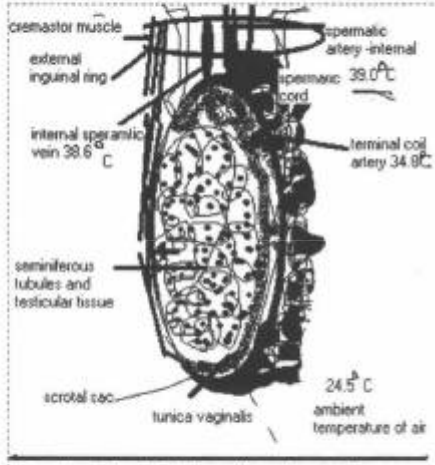
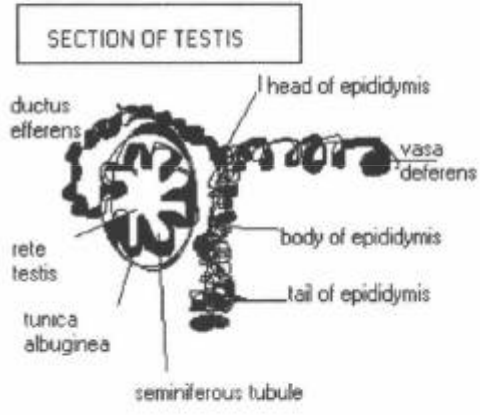
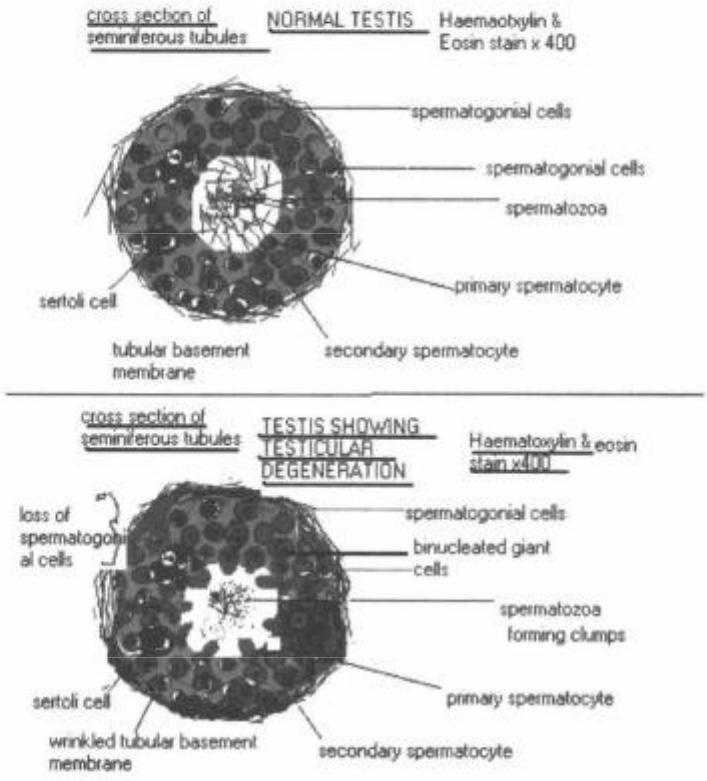


figure- showing the effect of pampiniform plexus on the modification of temperature of blood entering and leaving the scrotum and testes of rams.





Anomalies of development

Hypoplasia of the testis occurs in all species of domestic animals but has been most extensively studied in the bull.

Testicular hypoplasia due to hormonal anomalies. Sex chromosomal anomalies are common in humans. Eg. Klinefelter's syndrome. The syndrome has been identified in stallions, bulls, rams, dogsand rats. XXY-pattern of testicular disease. All cats with XXY chromosomal complement have hypoplastic testicles and are sterile. Testilces are small, seminiferous tubules although well formed, are lined only by Sertoli cells and no spermatogenesis is present. Leydig cells are usually present.

Cryptorchids: Incomplete descent of the testes is known as cryptorchids. Testicular descent, the process by which is gonad descends, from the dorsal abdominal wall into the scrotum occurs only within the mammalian species. Many mammals however retain the testes in the abdominal cavity. Formation of a scrotum and descent of the testis are regarded as late evolutionary developments. It varies from 1 to 105 in animals. Most cases are unilateral. The left testis is being more

retained than the right. Bilateral cryptorchids are sterile. Fertility varies. Rarely, retained testis may contain teratomas, but cryptorchid testicles have a high risk of developing other primary testicular neoplasms. The cryptorchid testis maybe acted at any point along the emigration path, such as the near kidney, in the inguinal canal or subcutaneously at the external inguinal ring. Marked fibrosis, especially of the tunics is a feature of cryptorchid testes in older animals. Affected testis is small and firm to hard and histologically resembles the severe form of hypoplasia. Intratubular concernments similar to those seen in testicular hypoplasia maybe present. Genetic tendency and cryptorchid is an inherited condition.

The pathogenesis of most cases of cryptorchidsm is unresolved, but the process is, in part, under hormonal control. Normal testicular descent requires both testosterone and Mullerian inhibiting hormone. Animals with testicles in which hormone production is abnormal or individuals in which normal hormone tissue sensitivity is lacking have a greatly increase change of having failure of testicular descent. This includes, among others, animals with sex chromosome abnormalities, individuals with androgen insensitivity, and dogs with persistent Mullerian duct syndrome.

Complete agenesis or lack of one or both testes occurs. Fusion of both testes has seen in boar. Testicular ectopic is an abnormal location of testis from the normal route of descent. They are located in the perineal or crura regions, in the abdominal or adjacent to prepuce, but away from the inguinal canal. Heterotopia of testicular tissue occur as multiple nodules which lack auxiliary structures. These are seen in pigs and measure upto 5 cm in diameter on the parietal or visceral peritoneum. Histologically the structures are those of testis.

Polyorchidism or the presence of supernumerary testicles has been observed in the horse, calf and pigs where three testes are seen attached to epididymides. They may be either in scrotal or abdominal.

Accessory adrenal cortical tissue in the testis or epididymis has been observed in stallion, ram, dog and cat. The masses are composed of irregular nodules of adrenal coartical cells.

Heterotopic Leydig cells are seen in cat in the tunica albuginea and stroma of the mediastinum testis.

Cystic rete testis is due congenital lack of communication between efferent duct and epididymis seen in cats.

Testicular degeneration

It is well recognized that the germinal epithelium is extremely sensitive to a great variety of adverse influences and that testicular degeneration or atrophy is the most frequent cause of reduced fertility in male animals. Within the seminiferous tubules, the diving primary spermatocytes especially then other differentiation germinal cells upto the spermatids stage are most susceptible to injury, whereas

the spermatogonia, or stem cells and the non-germinal Sertoli cells are comparatively resistant. Sertoli cells do not divide, the ratio of number of Sertoli cells to germinal cells, may sometimes be useful as a measure of the degree of testicular degeneration.

Grossly the testis undergoing degeneration may at first be enlarged by; oedema but is usually reduced in size. In early or rapidly producing regeneration the testis is off and flabby, lacks turgid and the cut surface bulges. Distinct wrinkling of the tunica albuginea may be apparent. The decrease in parenchyma is not parallel by decrease in stroma, and the end result of degeneration a small testis of firm consistency. Since the epididymis is usually less affected than the testis, it will ultimately appear to be disproptionately large. With continued degeneration and fibrosis, the testis becomes increasingly hard and variable demineralization may occur. The cut surface of such a testis has a coarse granular appearance.

Testicular degeneration maybe either unilateral or bilateral depending on the cause. It maybe focal or generalised. The histological changes vary with the severity and stage of degeneration. In early stages, there is failure of maturation of spermatozoa and degeneration of spermatids; Many spermatids are necrotic and others produce characteristic spermatidic multinuclear giant clells.the degenerative processes do not involve these uniformly, When the degenerations more advanced, the affected are more extensive degenerative changes appose in the precursor of spermatids, changes which are characterized by cytoplasmic vacuolation and nuclear pyknosis and with progression the tubule may be denuded to the basement membranes with loss ultimately of even resistant Sertoli cells. The tubules then collapse and there wave like hyaline thickening of the basement membrane.

Although increased basement membrane thickness is also a feature of testicular hypoplasia, the more pronounced shrinkage and collapse of tubules in testicular degeneration results in buckling of the basement membrane. This is particularly useful feature in the differentiation of hypoplasia and degeneration and this could be well differentiated by PAS staining. Apart form presence of giant cells, there is a granuloma formation is there characterized by the presence of lymphocytes and plasma cells indicative of interstitial orchitis. Osseous metaplasia sometimes occurs in tubules.

Causes:

1. Thermal degeneration, due to abnormal temperature surrounding the testis. This is common in cryptorchid or ectopic testis where testis temperature raises. High environmental temperature of ambient conditions.
2. Localised or systemic infections, that is epidiymitis or orchitis caused by brucella, periarthritis due to extensive peritonitis.
3. Systemic infections due to marked pyrexia as seen with babesiosis, anaplasmosis, trypanosomiasis.

4. Nutritional deficiencies or excesses include malnutrition and superimposed chronic diseases.
5. Vitamin A deficiency. This is due to decreased liberation of gonadotrophic hormones.
6. Zinc deficiency that is more common in ruminants.
7. Circulatory disturbances that is partial compete occlusion of testicular vessels like torsion of spermatic cord.
8. Obstructive lesions involving epididymis and malformation of efferent tubules.
9. Noxious chemicals metals and rare earth salts, alkylating agents including busuflan, lead acetate intra testicular injections, subcutaneous injection of cadmium chloride, oral administration of highly chlorinated naphthalene, dibromides, nitrofurnas, carbamate pesticides, anticancer drugs such as cyclophosphamide and chlorambucil contribute for the degenerative changes in the testis.
10. Mycotoxins, and products from locoweed seeds of plants.
11. Hypothyroidism and
12. Diabetes also responsible for causing degenerative changes in testis. Testicular calcinoisis occurs following degeneration and fibrosis is net result.
13. The two most widely accepted theories for testicular degeneration are tissue hypoxia and the lack of glucose substrate for tissue metabolism. Tissue hypoxia is increased with an increased testicular temperature; the metabolic rate is also increased and creates a demand of oxygen which cannot be met as the blood flow remains constant. Alternatively it is thought that the elevated temperature leads to an increased demand for glucose substrate which cannot be met and may inhibit the action of enzymes essential for the phosphorylation of glucose during it normal metabolism.

Orchitis may be interstitial (intratubular), intratubular or necrotising.

Interstitial orchitis, histologically characterized by mononuclear infiltrations of intratubular stroma with concurrent or subsequent fibrosis. Histologically in intratubular orchitis wherein solitary or multiple white yellow foci of up to about 1 cm are seen in sections. The tubule line is retained in the affected areas, but the seminiferous epithelium is obliterated and replaced centripetally by neutrophils and necrotic debris.

Necrotising orchitis is characterized with coagulative necrosis bordered by fibrosis and mononuclear infiltration.

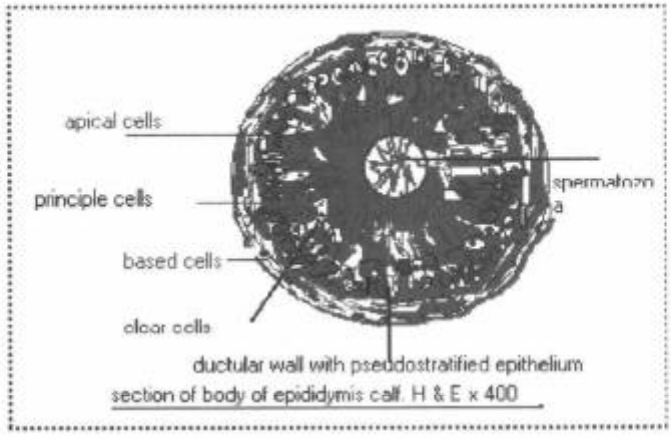
Abscessation and fistulation through the scrotum is seen. This is common with brucella infection of bulls. Tuberculous orchitis is also common in bulls wherein involved testis shows either lardaceous caseous and calcified foci. Other bacteria

that cause orchitis in bulls are streptococcal infections, staphylococcal infections, Actinomyces pyogens, Escherichia coli, Haemophilus spp, salmonella spp, acitnomyces bovis and Actinobacillus spp. and Nocardia. Chlamydial psittaci also cause orchitis in bulls. In boars Entero virus and Parvo virus infections also cause orchitis. In stallions *salmonella abortus equi* and strongylus *edentatus* cause infections.

Nodular orchitis occur is common in pox infections. *corynebacterium pseudotuberculosis* and *Actinomyces pyogens* cause orchitis in rams. In dogs orchitis is due *to E. coli infections, proteus vulgaris* infections, *brucella canis and pseudomonas pseudo mallei* also cause infections.

Epididymis

Anomalies of development: the epididymis, vas deferens, ampullla and the seminal vesicles are derived from the mesonephric duct; the tubuli recti, the rete testis, and the efferent ducts of the testis are derived from the mesonpehros by way of gonadal blastema, which migrates from the mesonpehros to the gonadal ridge. The separate origins for these excretory ducts may not be appropriate to all species but assist understanding of congenital obstruction in the excretory ducts. Obstruction of a duct leads to impaction with sperm, local dilatation of duct (spermatozoal) and extravasations of sperm to produce a spermatic granuloma. The condition appears to be inherited.



Segmental aplasia of the epididymis is segmented aplasia off mesonephric duct and therefore is unilateral. Segmental aplasia most frequently involves the body and tail of the epididymis and, concurrently the corresponding ampullla and seminal vesicles in about 1/3rd of cases. Histologically testicular changes in epididymial aplasia includes marked dialtation of the tubules, visible grossly, sperm morphology, and epithelial proliferation in the efferent ducts and the rete testis. Several congenital cystic conditions of the epididdymis, namely

paradidymis, blind efferent ductules, and aberrant ductules, are considered to result from cystic dilation of remnants of mesonephric tubules.

In paradidymis externus, isolated cysts upto several millimeters in diameter and of rounded to oblong shape are located in the spermatic cord just proximal to the head of epididymis. The cyst has no apparent connection with the epididymis. In paradidymis internus, similar isolate tubules are isolated entirely within the epiddymo stroma. Unlike paradidymis, blind efferent and aberrant ductules do retain communication with the testis or epididymial duct. Histologically paradidymis blind and aberrant ductules are line by ciliated epithelium, and cystic enlargement results from secretions.

Epdidymitis: Once initiated, the course of epdidymitis variable and the acute stage with oedematous enlargement may be followed by abscess formation, sometimes with perforation, peri orchitis and peritonitis and increasing fibrosis. Spermatic granuloma occurs after extravasion of spermatozoa.

Histologically affected epididymis ducts contain fibrin, neutrophils, and spermatozoa in various stages of disintegration, damaged epithelium, macropahges, and multinucleated giant cells many of which contain spermatozoa. Bull contracat epididymis-vaginitis (Epivag) due to viral infections. Associated lesions are abscess formation, tunic adnesions, ampullitis and seminal vesiculitis and testicular degeneration. Brucella ovis caused epididymis in rams. Actinobacillus seminitis and Staphylococcus aureus have been isolated from lesions from bucks.

Spermatozoal is defined as a cystic dilatation of the epididymial duct with the accumulation of sperm in the cyst. Most spermatocooels progress to development of spermatic grnaulomas.

Adenomysois of epididymis is a condition characterized by invasion of the muscular layers and surrounding stroma by the epithelium. Adenomysois occurs in older animals, particularly bulls and dogs and there is evidence to suggest that chronic estrogenic stimuli are involved.

Circulatory disturbances of spermatic cord: A varicocoele is a dilatation of a tortuosity of the veins of the pampiniform plexus and the ureteric veins. Varicocoele appear as dark red nodules, 1-3 cm or more in diameter, enclosed in fascia of the spermatic cord proximal to the testis. Dissociation of varicoele may reveal large organizing laminated thrombi. Torsion of the spermatic cord, mechanically permissible if there is a broad mesorchium occurs in dogs, pigs and occasionally horses. A normal descended testis is seldom involved in torsion.

Inflammation of spermatic cord: Funiculitis is the inflammation of spermatic cord. This follow due open castration. This may be necrotising as seen in pigs; this is chronic as see in chronic scirrhous cord of horses and cattle. Verminous grnaulomas cause by wandering larvae of strongylus species are occasionally observed in the spermatic cord and testes of horses.

Segmental aplasia of seminal vesicles and ampulla is seen in all species of domestic animals. Cystic dialtation of the lumina of occasional lobule occur in all species of domestic animals.

Inflammation of seminal vesicles: Seminal vesiculitis. Two forms of seminal vesiculitis in the bulls are recognized, a chronic interstitial form characterized by a considerable increased in size, excessive fibrosis, and firm consistency and loose of lobulation and a predominantly degenerative form characterized by a slight or no change in size, and only a slight increase in consistency. Histologicaly then chronic form is characterized by fibrosis and cellular infiltration of stroma with lymphocytes, plasma cells, histiocytes, neutrophils and occasional eosinophils. Corynebacterium pyogens appears to the most common isolate. Brucella abortus causes fibrinopurulent vasculitis. Mycoplasma bovigentialium causes seminal vasculitis in bovines. Chlamydia psittacosis has been isolated from the semen and epididymides of bulls.

Melanosis of bulbourethrla glands are observed in bulls and swine. Prostatic cysts in the dog are congenital or secondary to hyperplasia, neoplasia and inflammatory lesions. It has been suggested that such cyst arise from vestiges of the Mullerian duct, the uterus masculinus, but most reported cysts appear to have arisen from one or the other Prostatic lobes.

Inflammation of bulbourethal gland in the bull often accompanies seminal vesiculitis. Concretions may result form chronic inflammation.Prostatitis is common in dogs. It is often a disease of older dogs in which hyperplasia of prostate are present. The inflammatory changes contribute to the enlargement in significant % of cases. The infectious agents are Escherichia coli, proteus vulgaris, streptococci and staphylococci which invade via the prostaic urethra. Prostatitis is often acute with systemic signs of illness, these exhibit urinary tract signs like appearance of blood Pyuria, urethral discharges, inconsistency or dysuria. Hyperplasia and hypertrophy of prostate is observed occasionally in the bulls. Squamous metaplasia of the epithelium of the Prostatic gland in the male dog may occur spontaneous in association to neoplasia of testes, particularly Sertoli cell tumor or following the administration of estrogens. The metaplastic change may involve acini in all parts of the glands as well as Prostatic urethra uterus and masculinus and cats. Affected epithelium is converted to stratified squamous type from the surface of which squamous plates are shed into the lumen. Neutrophils and macrophages are numerous in the lumina.

Disease of penis and prepuce

The penis is subject to many abnormalities of size and firm, congenital absence, hypoplasia, hyperplasia, duplication, direction deviation in ruminants absence of sigmoid flexure. The neonatal penis is very slender and half to that of adult one. The sigmoid flexure is absent. It contains only small amount of erectile tissue. Its apex has not yet been separated from the sheath. The separation occurs in young-adults due to the action of testosterone.

Inflammation of the prepuce is called posthitis and that of glans penis balanitis. Usually both occur together as balano-posthitis. In the dog it is common condition. Causes may be trauma or bacteria. There are catarrhal exudates with infiltration of leukocytes into the degenerated epithelium. Mucosal lymph follicles are enlarged. In domestic animals balano-posthitis is associated with various organism including *Pseudomonas aerogenous, Corynebacterium pyogenes and Corynebacterium renale.* This is seen in bulls suffering from infectious pusutlar vulvo-vaginitis. Ovine ulcerative posthitis is also common in rams.

Phimosis is a condition in which the penis cannot be extended from the prepuce, due to inflammatory swelling.

Paraphimosis is the opposite condition which the extended penis is due to inflammatory enlargement cannot be withdrawn into the prepuce.

Priapism is the persistent erction of penis not associated with sexual excitement associated with spinal cord lesions, constipation and genitourinary tract infections. Persistent penile frenulum causes the penis erected to be incurved position.

Hypospadia wherein the urethra opens on the ventral surface of the penis. This is due to the failure of urethral folds to fuse.

Epispadia wherein urethra opens on the dorsal surface of the penis.

Uroliths

Uroliths: Calculi are formed in the urinary tract. Nephroliths that is formed in the kidney. Cystoliths are formed in the urinary bladder. The uroliths may be micrconcretions or micrconcretions. Small concretions (micro concretions) formed in these places may be carried by the urine into the ureters and urethra.

The disease caused by uroliths is among the most important urinary tract problems of domesticated animals. Several factors are important in predisposing to calculus formation, and several are important in precipitating disease. Calculogenesis is governed by certain factors like urinary pH, reduced water intake, in relation to the degree of urine concentration, deficiency of vitamin A and presence of infections in urinary tract.

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In these conditions, urine is often supersaturated with respect to the components of stone forming salts, and this super saturation of uroliths formation (nucleation). Saturation may be in the unstable region, where spontaneous precipitation occurs, or in the metastable region where precipitation occurs by epistaxis or heterogeneous nucleation. Thus a foreign body such as suture or a grass awn can act as a nidus for uroliths formation. Though horses suffer with crystalluria with supersaturated calcium carbonate solutions, low prevalence of calculi is seen in these species. Deficiency of inhibitors of crystallization may be important in calcium oxalate and calcium phosphate carcinogenesis.

In general calculi are important in cattle, sheep, dogs and cats and less important in horses and unimportant in pigs. In dogs, several breeds are predisposed to formation of calculi, namely Dachshunds, Dalmatians, Cocker spaniels, Pekingese, Basset hounds, Poodles, and Small terriers.

Type of calculi: Silica calculi, struvite calculi, oxalate calculi, uric acid and urate calculi, cystine calculi, clover stones, xanthine calculi, tetracycline and barium stones.

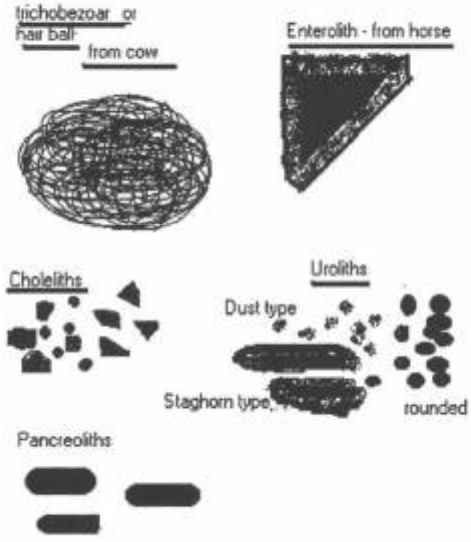
Urolithiasis has been associated with the use of hormones or their analogs for stimulating growth in feed lot lambs. Lambs which are fed diethyl-stilboestrol or have had implantation of this compound; may develop urinary obstructions in several days. In man renal calculi has been observed with parathyroid hyperactivity.

The size and shape of urinary calculi vary with the species of animal, place at which they are formed, and their composition. Urinary calculi are variable in size and shape. These may be lodged either in the cortex, medulla or in the pelvis of the kidney.

These calculi may be round to irregular in shape, white or brown or metalloid with luster. The author's observation in the bovines was that (stag horn) the calculi were single large size to that of multiple smaller ones. The larger ones were weighing around 8 gm and smaller ones to 0.117 gm. Multiple calculi were innumerable in number that is in hundreds. They are lodged either in the calyces, or in the renal pelvic fat or in the cystic cavities of the pelvic region.

The more common calculi in the horse containing calcium carbonate and phosphate and magnesium carbonate. In ruminants, calcium, magnesium, and aluminum salts of phosphoric acid compose the calculi. The present author observed that the chemical composition of renal calculi from Karnataka region of India was predominantly of calcium carbonate type. Reports from North America and Western Australia revealed that the stones found in beef cattle were made up of ammonium magnesium phosphate and in range herds where that of silica type.

The silica calculi of ruminants are hard, white to dark brown, radio-opaque and often laminated as much as 1 cm across. The bladder stones of silica calculi of



ruminants are spherical, ovoid or mulberry shaped and has smooth surfaces, but in the kidney they are angular and irregular.

Pure silica stones contain about 75% silica as silica dioxide. Mixed calculi contain some calcium oxalate or carbonates. Silica calculi contain about 20% organic matter. Most have a friable core, which is high in amorphous silica and low in organic matter; which separates it from the outer concentric lamination; which is high in silicon. Silica calculi are present in more than 50% of steers on cattle of Western Canada; fewer than 5% develop urethral obstruction.

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calculus formation could be reduced to sub clinical level by adding salt to the ration, thereby ensuing high water consumption.

Struvite calculi that are magnesium ammonium phosphate calculi (triple phosphate calculi) are important in dogs, cats and ruminants. In female dogs, these are more common perhaps the reproductive infections are common. Bacterial ureases from staphylococci and proteins induce super saturation of urine with triple phosphates by increasing urine pH and ammonium ions.

In cats, addition of 0.15 to 1.0% dry weight of magnesium induces struvite calculi formation in urinary bladder. In ruminants, struvite calculus develops in adult cattle when they have been fed with high grain rations. Calculi are gritty with high proportion of matrix. Inhibition of urethral growth but early castration predisposes to obstruction and increased water consumption, tends to prevent obstruction.

Diets high in phosphates can cause a very high incidence of calculi in sheep; calcium and phosphorous ratio of 1: 2 or wider appears to be the critical factor. Additional potassium tends to promote phosphate urolithiasis. Genetic tendency is also involved. Urolithiasis is more likely to occur in sheep that excrete phosphates in urine than that of faces.

Uric acid and urate calculi: These calculi are usually multiple, hard, concentrically laminated, yellow to brown and moderately radio dense. In the bladder, they are frequently spherical and less than 5mm across. Most contain ammonium urate with some uric acid and phosphate, in others sodium urate is the predominant salt.

Urate stones are common in Dalmatian dogs, but also occur in pigs and rarely in cats. Dalmatian excretes high levels of uric acid in their urine. Normally in all animals uric acid is converted to allantoin by the liver enzymes. In the Dalmatian, these enzymes are absent; hence uric acid is excreted in the urine.

Cystine calculi are small and irregular. Soft and friable, these are also waxy and yellow in colour. And on exposure to air and light it turns as green. Many cystine calculi consists of pure cystine, others may contain calcium oxalate, triple phosphates, brushite (calcium hydrogen phosphate dehydrate) and complex urates

Cystines stones occur in dog especially Dachshunds and rarely in cats. Cystine calculi occur in male dogs, but cytinuria is recorded in females. Blood cystine levels are normal.

Cystine precipitates in acid urine, but factors other than urinary pH probably are important in the genesis of cystine stones. Genetic factor have been attributed.

Xanthine calculi: Xanthine stone are yellow to brown red, often concentrically laminated, friable and irregularly shaped. They are radiolucent. Xanthine is a metabolite of purine and seldom appears in urine because normally it is degraded

by xanthine oxidase to uric acid. Xanthine calculi appear in sheep and calves and occasionally in dogs. A high incidence in sheep was circumstantially related to deficiency of molybdenum. When these are fed on these pastures. Molybdenum is a component of xanthine oxidase. Xanthine precipitates in acid urine. Calculi usually form in the collecting ducts and may cause hydronephrosis.

Other types of calculi: The tetracycline and barium stones are common in animals. Stones with high carbonate content are associated with alkaline urines and are seen in ruminants consuming high oxalate plants or clover dominated pastures.

Clover stones: These are present in sheep grazing oestrogenic pasture, particularly sub-terranean clover or injected or implanted with oestrogens. Three factors are operating for the formation of these calculi. One is the urethral obstruction by desquamated cells, and secretions of accessory glands originating in the urethral udder the influence of oestrogen.

The second type is so called clover stone, is usually found in the renal pelvis as a yellow, soft material, which leads eventually to fibrosis and shrinkage of kidney.

Thirdly sudden and serious mortalities occur in male grazing on subterranean clover during the period of rapid maturation. Urethral process becomes impacted with soft paste consisting of mainly calcium carbonate.

Oxalate Calculi: Oxalate calculi are hard, heavy, white or yellow, and typically covered with jagged spines, though some are smooth. They tend to be large and solitary in the bladder. Oxalate calculi occur as calcium oxalates. Hypercalciuria are involved in the development of calculi.

Oxalic acid is synthesized from glyoxylic acids and ascorbic acids and may be ingested in certain foods. Hyperuricosuria maybe involved in oxalate precipitation. Oxalate containing plants ingestion is not important, since oxalate is metabolized in the rumen.

Feeding a low calcium diet that is as low as 0.3% produced oxalate urolithiasis in steers; this is due to bone resumption that is hydroxyl praline liberation and oxalate synthesis.

Tumors of testis

Based on the histogenesis testicular neoplasms are classified into seminomas, interstitial cell tumors, teratomas and adenoma or carcinoma of the excretory duct. Multiple seminomas may co-exist with Sertoli or interstitial cell tumors. Coffin (1952) had divided the growth of tumors into four stages, a) pre-neoplastic atrophy of spermtogenic epithelium, focal diminution of spermatozoa, spermatocytes and total disappearance of these cells. Only few Sertoli cells are left with few spermatogonia along the basement membrane with densely staining nucleus and eosinophilic cytoplasm, b) replacement of spermatogonia cells, c) semi-round cells extend along the basement membrane by multiplication and

desquamation of existing epithelium lining the tubules. Eventually tumor cells multiply and fill the tubules before invading the interstitial tissue. According to Ewing (1949) in dogs, the tumors of testis arise from any foci whereas in man it originates only in the vicinity of rete.

Seminomas

This tumor arises from the seminiferous epithelium of the tubules of testis. Seminoma is fairly common in dogs. Seminomas occur more frequently in cryptorchids. Various theories of seminoma origin have been postulated in human beings and animals. Seminoma may arise from the seminiferous epithelium and not from teratoma elements. Occasional combination of teratoma and seminoma resulted in the coexistence of these two types of growths.

Grossly seminomas are white or grey tumors bulging from the testis. It is lobulated and may be demarcated from the healthy tissue by a fine septum. Areas of necrosis may be found in some places.

Histologically, the cells are arranged as sheets or island and separated by thin strands of connective tissue. Some cells may be in intra-tubular location. The neoplastic cells are large, rounded and uniform in size and shape. The cytoplasm is acidophilic and granular. The nucleus is large, round, central, hyper chromatic with coarse chromatin and a definite nuclear membrane and one or two nucleoli. No vacuoles are present in the cytoplasm of the cells unlike in Sertoli cell and Leydig cell tumors. Mitosis is very frequent. Seminoma is a highly malignant tumor in man.

In the intratubular type with infiltration, there is a breakdown of tubular structures with variable amount of infiltration into the interstitial tissue. In the suffice type tumor cells are arranged diffusely along a delicate stromal network separated by collagen. The evidence of any tubular origin is completely absent. Lymphocytes are abundant in the stromal and giant cell are frequently met with.

Malignant type resembles diffuse type and consists of large sheets of anapalstic cells divided into irregular lobules by relatively inconspicuous fibro vascular trabaculae. Lymphatic and venous circulation is prominent and this account for the metastatic growth. Though locally malignant, rarely metastatic foci occur in the lumbar and mediastinal lymph nodes. Presence of this tumor does not give rise to any symptoms, but only suspected due to enlarged growth.

Sertoli cell tumors

This is also known as sustentacular tumor. This tumor is common in dogs and arises from the sustentacular cells of testes. Sertoli cell tumor is usually unilateral, rarely may it be bilateral. The tumors are firm; usually discrete sometimes extends into the tunica albugenia and epididymis. The growth is smooth, nodular, enclosed in white glistening vasuclarised capsule. Tumor bulges on section. Cut surface is

white or light grey and shows irregularly lobulated dense fibrous bands, usually firm inconsistency. Small cysts unto 1 cm. in diameter and these contain a brown fluid.

Histologically, the cells form tubules and so the tumor is known as tubular adenoma. The cells that are intra-tubular normally, may break through the basement membrane and thus be found outside the tubules as masses of cells. The neoplastic cells are spindle shaped with a clear cytoplasm and an oval or oblong nucleus. In some places, polyhedral cells with rounded nuclei may be seen. The tumor cells have a characteristic palisade arrangement, their long axis being perpendicular to the basement membrane. Numerous mitotic figures may be present.

Clinical features:

a) Atrophy of the uninvolved testis.

b) Alopecia, bilateral symmetrical alopecia with dry coat and pruritis are seen on the ventral surface of the thorax, abdomen and shoulders. Skin is thin and pliable with dense melanin pigmentation of hairless parts. The retarded hair growth is due to the atrophy of the hair follicles and dryness is due to the atrophy of sebaceous glands. Hair becomes brittle and dry and can be pulled out easily. Histologically, skin is thrown into folds with thin epidermis. Hair roots have no internal structures.

c) Prostatic changes are pronounced. The prostate is enlarged; the epithelium is showing squamous metaplasia and cystic degeneration leading suppurative prostration.

d) **Gynecomastia**: Enlargement of the mammary glands especially last two pairs. Histologically, they show hyperplasia of the lactiferous ducts and in certain cases partial differentiation into acini and ducts.

e) Other changes: Animal becomes odoriferous and attracts other male dogs. Depression of libido, lethargy and pendulous penile sheath are observed. A few show feminine distribution of body fat. Since the oestrogen is converted into 17-ketosteroids and excreted in the urine, which gives a characteristic smell like that of a bitch in oestrous, other male dogs is attracted. Sertoli cell tumors are also seen in cocks, producing feminization.

Interstitial cell tumors

Tumors arising from the interstitial cells of testis or from cells of Leydig is called interstitial tumors. These are common in olddogs and in bulls. Grossly the tumors occur singly. Rarely multiple tumors may be seen. Histologically, the tumor consists of large cells, with large nuclei. The cells are larger than those of seminoma tumors as well Sertoli cell tumors. The cytoplasm of the cells is foamy and containing fat which is vacuolated in appearance in sections. The nuclei are round. Mitotic figures

are rare. There are large Leydig cells which are arranged, and supported by vascular stroma. Perivascular pallisading of cells is a feature. The neoplastic cells are arranged in masses, separated by fibrous tissue trabaculae. Metastasis is very rare.

Canine Venereal tumor

(Transmissible lymphosarcoma, venereal granuloma, canine condyloma, venereal lymphosarcoma, infectious sarcoma, infectious lymphosarcoma, Sticker tumor, histiocytoma)

A unique feature of canine transmissible venereal tumor is that it was the first tumor to have been recognized as transmissible as described by noted veterinarian Novinsky in 1876. Sticker's noted that this tumor during early 19th century and termed it as contagious. This occurs in sexually matured animals.

Incidence: The venereal tumor is found only in dogs and commonly in bitches. No other animals are affected. Bitches are more susceptible.

Sites: Since the tumor is transmitted by transplantation of tumor cells during coitus, it is found on the glans penis and on the prepuce in the male and in the vagina in the female. Rarely the scrotum and perineal regions may show the tumors. This tumor may also occur, occasionally, on the skin of other parts of the body. Ocular lesions occur as flesh coloured masses attached to the iris and protruding to the anterior chamber of the eye. The tumor cells can also spread by aberrant metastases in organs like liver and brain. The tumor spreads also by transcoelomic way.

Cutaneous tumors may vary in appearance depending upon the age of their development and are either solitary or multiple. Tumors are also common in lips. Extragenitial tumors, in the presence of primary tumor, can be considered as metastatic.

Nature or type of the cell: Morphologic, cytological, histochemical and tissue culture studies have concluded that the tumor cell is a mature and cells are usually of reticulo-endothelial origin. The remarkable similarity of Karyotype found in tumor samples, throughout the geographical locations is striking. The diploid number of chromosomes in a normal dog is 78 and normally these are acrocentric except for x and y. Canine transmissible venereal tumor cells have 19 metacentric or and 40 to 42 acrocentric chromosomes. CTVT generally have a chromosomal complement of 59±5. There are two morphological types of cells in culture namely, a spindle reticular type and the other one round cell type.

Transmission: The tumor can be transmitted from one animal to another not only by coitus, but by injecting the intact cells subcutaneously or rubbing them on a wound on the skin or a mucous membrane. Cell free filtrates have no effect. Mere deposition of the tumor cells on an intact mucous membrane cannot reproduce the tumor. There must be injury for the cells to develop. At the site of

implantation, the tissue of the host does not take part. The anapalstic cells alone proliferate. After sometime, the host develops immunity and so spontaneous regression of the tumor occurs and the animal is immune to further infection.

If removed surgically, the tumor does not recur. The tumor is transmissible to fox but not to other species. More virulent expression may be expected in canine populations.

Grossly the tumors may be solitary or multiple, small or large, sessile, pedunculated or may spread like a cauliflower. It is pink in colour and very soft. It may be ulcerated and blood stained discharges may be noticed. Tumor starts as small papule and cauliflower like lobulationsare seen in due course. Promiscus scavenging leads to exaggeration of this disease.

Histologically, sections reveal a very cellular tumor. Cells are of uniform in size and shape. The cells are round to polyhedral; having a finely granular cytoplasm and rarely the cytoplasm may be basophilic. The nucleus is large, round, central and hyperchromaitc. Numerous mitotic figures are present. The cells may be grouped in compact masses or sheets of rows. A fine connective tissue stroma is seen. Generous blood supply is present. In places where ulceration is present, inflammatory cells are found. Metastases are rare, Secondary tumors have been seen in the liver spleen and kidneys.

This may be confused with mastocytoma. In the mastocytoma characteristic granules are found and these could be stained by toludine blue. Mitotic figures in mast cells are few. While in venereal tumor there are more. Mast cell tumor occurs in old dogs while venereal tumor occurs in young ones.

Tumors of prostate

Hyperplasia of prostate is common among dogs; especially in old dogs and tumors are not so common. **Carcinomas** of prostrate have been reported in dogs. It may be nodular and white in colour. Grossly the tumor may be small or may occupy the whole of the pelvic cavity. Histologically, the tumor is an adenocarcinoma with acini lined by columnar cells with hyperchromatic nuclei. Polarity is not maintained and numerous mitotic figures may be noticed. The cells may project into the lumen of the acinus to form pappilliform ingrowths. In some places formation of cystic spaces may occur. Metastases occur rapidly and widely in various organs.

Haemangiosarcomas are observed in the bulbourethrla gland of goats.

Chapter 8

Diseases of Nervous System

Summary

Nervous tissue-nerve cell body -nerve cells types - nerve fibers -types -myelinated and non myelinated- neurons- types of neurons -neurosecretory neurons, conducting neurons. Schwann cell. Neurilemma cells- Endoneurium, Epineurium - Nissl substance - synaptic vesicles.

Embryology of nervous system; Glial cells-types of glial cells- Reaction to injury. Myelination -Schwann cell origin- Ependymal cells- Microglia- Axonal reaction- Wallerian degeneration- pia-arachnoids-Fiber tracts of spinal cord-Formation of Cerebrospinal fluid-Cerebrospinal fluid and blood brain barrier- Virchow-Robin space- Hydrocephalus

Secondary degeneration of nerves fibers -Wallerian degeneration- Encephalocystocoele (hydroencephalocoele)- Microencephaly - Sequential reactions consequent to the injury to a neuron (central nervous system)-Swelling of nerve cells. Necrosis- reaction to infectious agents-bacterial-parasitic and viral agents. Hog cholera-Ranikhet disease-Salt poisoning-Lead poisoning-. Nerve tumors in animals-Schwannoma- Astrocytomas-Epndymoma: neuroblastomas. Secondary or metastatic tumors of central nervous system:

Diseases of Nervous system

Nervous tissue

This is a highly specialized tissue for reception, discharge of stimuli and transmission. It is made up of nerve cells and their processes called the nerve fibers. Receptive processes are known as dendrons or dendrites and the discharging process known as axon. A nerve cell body or perikaryon with all it processes is called neuron. Besides these there are neuroglial cells which support the nerve cells. There are two types of nerve fibers called medullated and non-medullated. Medullated (myelinated) fibers are composed of three elements namely axis cylinder, myelin sheath or medullary sheath and neurilemma. The axis cylinder is central and its direct continuation of the protoplasm of the nerve cells. It remains covered by thin tubular sheath the axolemma, which is possibly the modified surface membrane of the corresponding nerve cell. The neurofibril of the nerve cells is continued into the axis cylinder, where they remain embedded in a clear liquid ground substance the axoplasm. So long as the nerve fiber remains

within grey matter, it remains uncovered but after entering white matter, it receives a quite covering called the myelin sheath or medullary sheath. This sheath is characteristic of myelinated fibers.

Neurons: Neurons are ectodermal in derivative. Neurons are divided into conducting and neurosecretory neurons. Conducting neurons are myelinated whereas neurosectory neurons are not myelinated. This is a highly specialized tissue for reception, discharge of stimuli and transmission. It is made up of nerve cells and their processes called the nerve fibers. Receptive processes are known as dendrons or dendrites and the discharging process known as axon. A nerve cell body or perikaryon with all it processes is called neuron. Besides these there are neuroglial cells which support the nerve cells. There are two types of nerve fibers called medullated and non-medullated. Medullated (myelinated) fibers are composed of three elements namely axis cylinder, myelin sheath or medullary sheath and neurilemma. The axis cylinder is central and its direct continuation of the protoplasm of the nerve cells. It remains covered by thin tubular sheath the axolemma, which is possibly the modified surface membrane of the corresponding nerve cell. The neurofibril of the nerve cells is continued into the axis cylinder, where they remain embedded in a clear liquid ground substance the axoplasm. So long as the nerve fiber remains within grey matter, it remains uncovered but after entering white matter, it receives a quite covering called the myelin sheath or medullary sheath. This sheath ischaracteristic of myelinated fibers. E.M studies indicate that myelin sheathes an integral part of the Schwann cell. It is composed of layer of mixed lipids arranged concentrically alternating with the layer of neruokeratogneic protein. The axon is first enveloped by the Schwann cell. Gradually this cell encircles the axon and forms many turns and thus the axon is surrounded by multilayered membrane- myelin sheath. Each layer of the membrane consists of the lipid molecules which extend radially a sandwich between tangentially arranged layers of proteins. Most nerve fibers which come out of and enter the CNS, somatic or autonomic, posses this sheath. The function of medullary sheath is to insulate the nerve fibers and thus to prevent the spread of the nerve impose to other adjacent fibers. All nerve fibers somatic or autonomic outside the central nervous system, receive another homogenous nucleated covering the neurilemma or sheath of Schwann. Myelinated nerve fibers which are found into brain and spinal cord differ from those of peripheral nerve fibers in that the neurilemma is not present. It is of ectodermal origin. Its functions are to protect the nerve fibers, to supplies nutrition partly and to play an essential role in the regeneration of damaged peripheral nerves. At regular intervals the peripheral nerve fibers is found to possess constriction of some 80- 200 ì apart known as node of Ranvier. These interruptions of myelin sheaths at these nodes permit sites for in exchange between axoplasm and extracellular fluid. At these nodes the medullary sheath is broken down and the outer neurilemma comes into contact with the central axis cylinder. Branching of the nerve fibers takes place at these nodes only. That portion the fiber which lies between two adjacent

nodes, is called the internode. Each internodes is found to posses a neurilemma cells with an oval nucleus just under the nerurolemma. These cells link up with each other and form the tube, i.e. neurilemma sheath. The myelin sheath in the internodes may show a variable number of oblique clefts that is myelin clefts or Schmidt-Lantermann, which divide the sheath into small segments that is segments of Lantermann or Schwann segment. Probably these clefts are artifacts being produce during histological preparation. Medullated fibers vary in size. The thickness is about 30ì or more in diameter, the intermediate ones 4-10ì, and the thinnest one 1-3ì. The role of propagation nerve impulse varies directly as the thickens of fibers.

The postganglionic fibers of the autonomic nervous system belong to this type. These are recomposed of two elements namely the central axis cylinder and the neurolemma. Non-myelinated nerve fibers differ from myelinated fibers in great reduction or absence of myelin sheath, the fiber being directly invested with neurilemma.

In the peripheral nerve trunks the fiber s are grouped into separated bundles, the individual nerve fibers are held together by looses connective tissue called the endoneurium, several nerve fibers are collected into the bundle and surrounded by and sheath the epineurium. Another sheath, epineurium encloses the whole nerve trunk. These sheaths and protect the nerve fibers and also support blood vessels and lymphatics to the nerve. As the nerve trunk branches each branch becomes covered by sheath called Henle's sheath, which propagation from the epineurium and perineurium. Neurons are ectodermal in derivative. Neurons are divided into conducting and neurosecretory neurons. Conducting neurons are myelinated whereas neurosecretory neurons are not.

Most of the materials within the axoplasm move slowly at rate of 10 to 200 mm/ day.

Neurons are multipolar, bipolar and unipolar. Most of the neurons are multipolar and posses number of branching dendrites that join the perikaryon at scattered points. In bipolar, the dendrites join in a common trunk before reaching perikaryon at a site remote from the origin of axon. In unipolar, the dendrite tree and axon first combine in single extensions of the perikaryon which later branches.

The typical neuron is an elongated cell that consists of a cell body containing, the nucleus and therefore known as perikaryon and various processes. Internal neuronal connections are known as synapses and these axosomatic, axodendritic and axoanonic.

The junction between one neuron and the next is called a synapse. It is composed of three major parts, the soma which is the main body of neuron, a single axon which extends from the soma into the peripheral nerve and the dendrites which are thin projections of soma that extends up to 1 mm into the surrounding areas

of the cord. The neuron has a cell body (peri-karyon) that is about 50îm wide, a large some what eccentrically placed nucleus, a prominent nucleolus and abundant Nissl substance. Many neurons contain neurotubules, neurofilaments, prominent Golgi apparatus, rough endoplasmic reticulum and synaptic specializations.

Morphologic change is seen in perikaryon, consisting of enlargement and rounding up of cell body, peripheral displacement of nucleus, enlargement of nucleolus and dispersion of Nissl substance, particularly in the centre of the cell (central chromatolysis).

Neuronal inclusions occur as a manifestation of ageing, where there is intracytoplasmic accumulation of complex lipids, proteins and carbohydrates (Liofuchsin) believed to be residual bodies derived from lysosomes. Viral diseases can lead to abnormal intranuclear inclusions as seen in Infectious canine hepatitis, distemper, intracytoplasmic inclusions as seen in rabies (Negribodies).

An average about 6000 small knobs called synaptic knobs lie on the surface of the dendrites and soma of the motor neuron, approximately 80 to 90% of them in the dendrites. These knobs are the terminal ends of nerve fibrils that originate in many of other neurons and usually not more than a few of the knobs are derived from any single previous neuron. Many of the sub-synoptic knobs are excitatory and secrete a substance that excites a neuron, while others are inhibitory and secrete substance that inhibits the neuron.

Neurons in other parts of the cord and brain differ markedly from the motor neuron in the size of the cell body, the length, size and number of dendrites, ranging length from almost none at all up to as long as one meter and the length and size of the axon and the number of synaptic knobs, which may range from only a few to more than hundred thousand. These in difference make neurons in different parts of the nervous system react differently to incoming signals and therefore perform different functions.

Firing of neurons: Electron microscopic picture of synoptic knob shows that they have varied anatomic forms, but most resemble small round or oval knobs and therefore frequently called terminal knobs, boutons, end feet or simply presynaptic terminals.

The synaptic knob separated from the neuronal soma by a synaptic cleft having width usually of 200 to 300 Å (angstroms). The knob has two internal structure important to the excitatory or inhibitory functions of the synapse; the synaptic vesicles and mitochondria. The synaptic vesicles contain a transmitter substance which when released into the synaptic cleft, excites or inhibits the neurons. Excites if the neuronal membranes contain excitatory receptors, inhibits if it contains inhibitory receptors. The mitochondria provide ATP which is required to synthesize new transmitter substances. The transmitter must be synthesized extreme rapidly because the amount stored in the vesicles is sufficient to last for only a few seconds to a few minutes of maximum activity.

When an action potential spreads over a presynaptic terminal, the membrane depolarization causes emptying of a small number of vesicles into the cleft, and the released transmitted in turn causes an immediate change of the permeability chacteristics of the sub synoptic neuronal membrane, which leads to excitation or inhibition of the neuron, depending on the type of receptor substance. The synaptic knobs have the capability of continually synthesizing new transmitter substances.

The transmitter substance is acetyl choline and is synthesized from acetyl Co.A and choline in the presence of the enzyme choline-acetyl transferases. When acetyl choline is released from the knob into the synaptic cleft, it is rapidly split again to acetate and choline by the enzyme cholinesterase that is adherent lot the outer surface of the knob. That the choline is actively transported back into the knob to be used once more for the synthesis of new acetyl choline. Thus the vesicles are used and used again. New vesicles and mitochondria are transported from the cell soma down the axon to the synaptic knob moving the axon at a velocity of about cm. per day, thus replenishing the supply in the knobs.

Action of transmitter substance on the post synaptic neuron: The membrane of the post synaptic neuron where a synaptic knob about is believed to contain specific receptor molecules that bind the transmitter substance. These receptors are probably proteins that in response to the binding, change their shapes or activities in such a way that they increase the membrane permeability to most ions when the membrane receptor is excitatory and increase the permeability mainly to chloride ions when the receptor is inhibitory.

Axons terminations are the presynaptic membranous elements, whereas membrane of adjacent cells are the post synaptic membrane elements. These are separated by intercellular space (synaptic clefts) that varies in width from 6-20 nano meters. The presynaptic position of axis cylinder expands into bulblike processes called end bulbs, boutons or boutonus terminal. The neuromuscular junction is a special type of synaptic relationship between neurons and striated muscle.

The common neurotransmitter substances are acetyl choline, dopamine, norepinephrine, γ-amino butyric acid, serotonin, histamine, glycine, glutamate. The neurotransmitters act between presynaptic neurons and post synaptic neuronal junctions.

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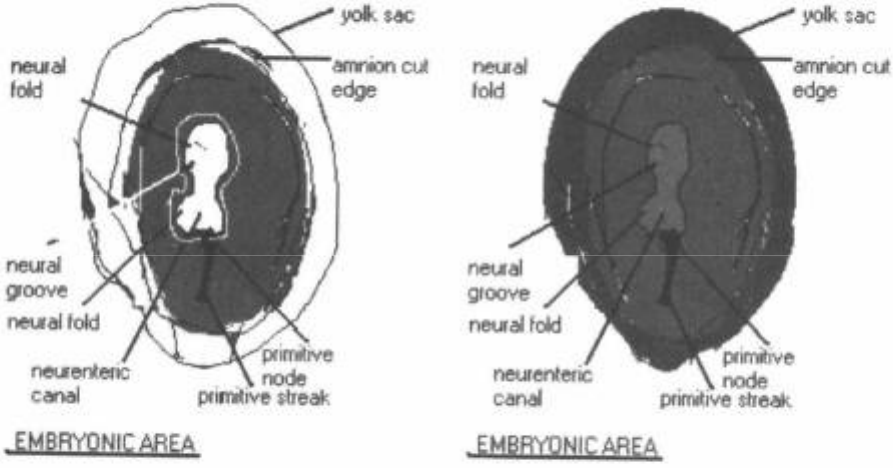
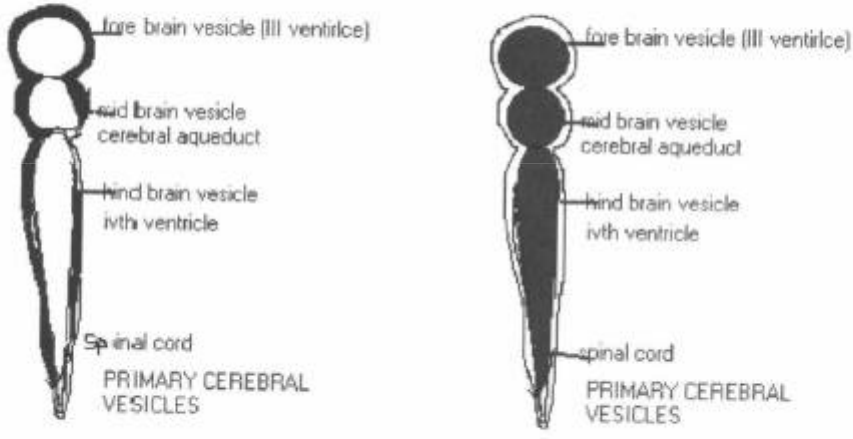
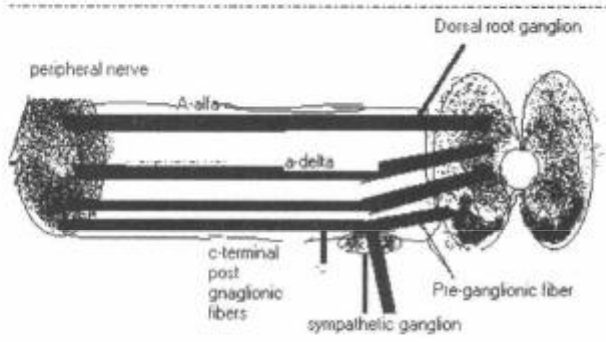
Th epineurium which encloses the entire nerve, the perineurium a multilayer concentric connective tissue sheath then encloses each vesicle and the endoneurium, which surrounds individual nerve fibers. The nerve microenvironment is regulated

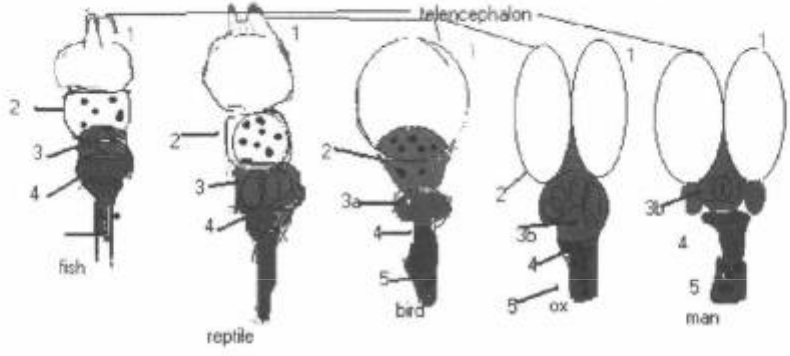
by the perineurium barrier formed by the tight junctions between perineurium cells, the blood nerve barrier and the nerve cerebrospinal fluid barrier. Endoneurial capillaries derived from vasa nervosum and their endothelial cells from tight junctions to establish the blood nerve barrier.

This barrier has been found to be relatively less competent within nerve roots, dorsal root ganglia and autonomic ganglia than along the rest of the nerve. The nerve-CSF barrier is formed by the tight junctions between the cells that form the outer layer of the arachnid membrane. These cells and cranial nerves and they leave the subarachnoid space. The motor and sensory nerve fibers which are separated within anterior and posterior roots intermingle within the mixed sensor-motor nerves that exist in the spinal cord.



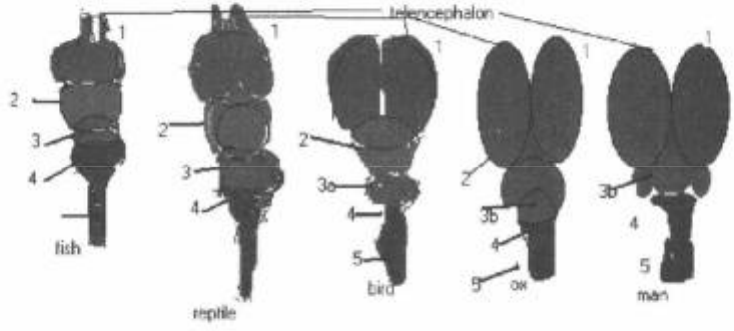






COMPARATIVE DEVELOPMENT OF BRAINS OF DIFFERENT ANIMALS

1-telen cephalon; 2-mesen cephalon; 3-meten cephalon; 4- myelen cephalon; 5- spinal cord
3a- archi cerebellum ; 3-b,neo cerebellum
procen cephalon (forebrain), mesen cephalon (mid-brain), and rhomben cephalon (hind brain)



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Embryology of nervous system

The embryonic area is that region of the developing embryo where the ectodermal and endodermal vesicles lay in apposition with the trace of primary mesoderm in-between them. The other cells in extra-embryonic area will form the various membranes and covering of the embryo and other extraembryonic structures.

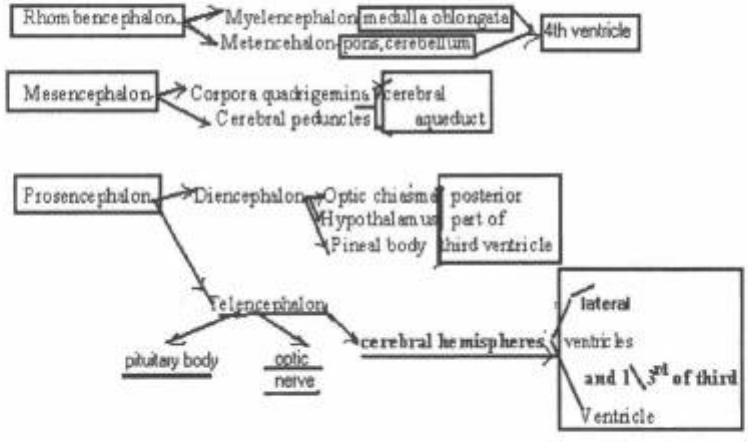
Cranially the cells of the head process blending with the endodermal cells break through them communicating temporarily with the endodermal vesicles. The canalized head process which pierces through the embryonic area is called the neurenteric canal, which ultimately obliterates, failing which a sinus may form communicating the intestine with the skin on the back and lumbar regional at later stage the cells of the head process intimately related to the endodermal cells become separated from the underlying endoderm and collect themselves ventral to the neural tube, in the form of a solid flexible column called the noto-chord. The cephalic end of the notochord reaches the anterior part of the mid brain where it ends like a hook over the future dorsum sellae of the sphenoid; caudally it extends throughout the future length of the vertebral column. The cylindrical rod of the notochord becomes surrounded on either side by a sheath of secondary mesoderm, from which the segments of the vertebral column are subsequently developed. The notochord is a temporary structure it remains as a pulpy centre in between the intervertebral fibro cartilage.

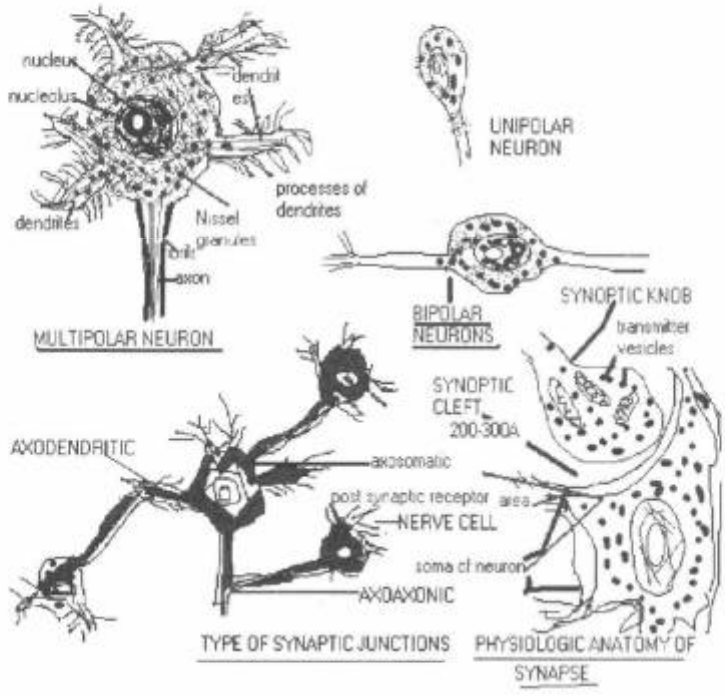
The embryonic area therefore consists of three layers, ectoderm, mesoderm and endoderm.

This area is at first circular, and then becomes oval and finally pear shaped, the narrow end being caudal. In the third week, when the embryonic area is about 1 mm there appears along the middle line of it caudal half a linear opaque area called the primitive streak due to proliferation and thickening of the underlying ectoderm. Its cephalic end present knob like thickening called the primitive knob. Anterior to the cephalic end of the streak another ectodermal thickening takes place called the medullary plate which extends caudally beyond the primitive node. A median longitudinal groove called the neural grove is produced by the longitudinal upholding of the ectodermal layer of the medullary plate on either side of the middle in the lateral margins of the neural groove and raised due to proliferation of the ectodermal cells and are called neural folds. the neural groove gradually depends and the edge of the neural folds of more and more raised and approach each other till they meet together dorsally in the middle line and convert the groove into a tube, the neural tube or the neural canal the fuse dorsal wall of the tube is connected with the ectoderm by a stalk of cells called the neural crest. From the neural tube and crest are developed mainly the brain including the retina and the optic nerve, the spinal cord, sympathetic system, chromaffin cells, and cerebral and spinal nerves with their ganglia. The anterior end of the neural tube widens and expands with two constrictions within, subdividing it into three primitive cerebral vesicles called, and fore-brain, mid brain and hind brain vesicles. The caudal end of the canal will form the spinal cord. The lining cells of the canal

form the nervous tissue and; the canal itself represents the ventricles of the brain and central canal of the spinal cord. The wall of the neural tube develops into the nervous structure of the brain and the spinal cord whereas the canal forms the ventricles of the brain and the central canal of the spinal cord continuous with each other.

The spinal cord is developed from the caudal narrow portion of the neural tube. The neural tube when first formed is thin walled and oval in shape on transverse section with a slit like narrow lumen-the central roof plate, the ventral wall, the floor plate, and the lateral boundaries are called the lateral walls. The single layer of columnar ectodermal cells forming the lateral wall proliferates rapidly so that these wall become thickened and they become transformed into a multinucleated mass of protoplasm without any cell diffentiation.The undifferentiated mass of protoplasm with nuclei is called syncitium. Soon a differentiation takes place in the syncitium of the lateral wall into three layers. The inner most layers are called the ependyma layers, which contains a single of columnar ciliated cells lining the canal of the neural tube. The intermediate layer is called the mantle layer. Which ultimately forms the grey columns of the spinal cord, in which the cells diffenrtiate two types of the spinal cord, the spongioblasts and the neuroblasts. The spongiblasts become transformed into the neuroglial cells, the surrounding condensed protoplasm forming their branching processes. The neuroblasts are transformed into the nerve cells. They are at first round or oval and then biome pear shaped, from the tapering end of which the axis cylinder process or the axon develops. At the broad end, are subsequently seen finer protoplasmic processes, called the dendritic processes or dendrons. The outer most layer of the lateral wall is called the marginal layer. It forms the white matter of the spinal cord. In it the nuclei disappear and the protoplasmic condense to form a reticulum through which the fibers of the ascending and descending fascicule of the spinal cord pass. The roof plate and the floor plate do not thicken, neither do they diffenrtiate into three layers as into the lateral walls but remain thin and are represented by single layer of ciliated ependyma cells.





Autonomic nervous system consists of two parts namely sympathetic and parasympathetic parts.

Glia is derived from neuroectoderm (macroglia- astrocytes, oligodendrocytes, ependyma) or from bone marrow (microglia). Glial cells act as supporting systems for the neurons and their dendritic and axonal processes; they also have primary role in wide range of normal functions and reaction to injury, including inflammation, repair, fluid balance and energy metabolism. The size and shape of the nucleus determines the type of glia. Cytoplasmic processes are not apparent with Haematoxylin and eosin but also with sliver impregnation preparations.

Oligodendrocytes have a denser, more homogenous chromatin in a rounder and smaller nucleus (8μ) and microglia have an elongated irregularly shaped nucleus (5 to 10μ) with clumped chromatin. Ependymal cells are columnar epithelial like cells with a ciliated microvillus border and facing the ventricular surface with pale vesiculated nucleus and have about 18μ at the albuminal end of the cells.

Fibrous astrocytes are present in white and gray water.This cell derives its name from the star shaped appearance imparted by multipolar, branching cytoplasmic processes that emanate from the cell body. Intracytoplasmic intermediate filaments are seen Ultrastructuraly, astrocytes surround the capillaries extend to the subpial and subependymal zones where they contribute to the barrier functions controlling

the flow of macromolecules between the blood, the CSF and brain. Astrocytes are also involved in repair and scar formation in the brain.

Glial cells reaction to injury that leads to nerve cell death or degeneration.

Gliosis: Astrocytes show hypertrophy and hyperplasia. Nucleus enlarges and becomes vesicular. Nucleolus is prominent. The previously scant cytoplasm stains to a bright pink, and from which emerge numerous star type ramifying processes (Gaemastocytic astrocytes). The astrocytes may be regarded as the interstitial cells of the CNS. They are present most of the spaces between and around the neuronal and oligodendroglial elements, and the perivascular and subpial zones. The protoplasmic astrocytes are located mainly within the cerebral gray matter and the fibrous astorcytes are located mainly within white matter tracts. All capillary blood vessels in the CNS are closely invested by the expanded ends of astrocytic processes, the so called end feet. A specialized population of astrocytes occurs in the Purkinje cells layer of cerebellum. These cells have long straight processes, which extend out through the molecular layer to the surface. These glial cells are found throughout the central nervous system in both gray and white matter. **Protoplasmic astrocytes** occur mainly in the gray matter. Astrocytes have round to oval nuclei (10ì wide) with evenly dispersed pale chromatin.

When lethal astrocytic injury occurs, the cytoplasm swells and becomes visible, faintly and the nucleus becomes eccentric and pyknotic. Disintegration of cytoplasm and nucleus follows rapidly. Disintegration of astrocytes brings about acidophilia of the cytoplasm, with some cells acquiring two or more nuclei. These plump reactive astrocytes called **gemistocytes**.

Proliferation of astroglial cells called **astrogliosis**. Reactive astrogliosis is expected. Following neuronal loss and in sustained cerebral or spinal oedema and is a future of many viral encephalitides.

Oligodendrocytes: Their cytoplasmic processes wrap around the axons of neurons in a manner analogous to Schwann cells of the peripheral nervous system. The oligodendrocytes are one of the close companion cells of the neurons in the CNS. One population of these cells occurs as satellites to nerve cell bodies and may proliferate in the event of injury to the neurons. The role of majority of oligodendrocytes is to provide and maintain the myelin sheath around the axon with a diameter greater than about 1ìm. They are accordingly located in the myelinated tracts among the fascicles of axon. Axon may survive for a long period without its myelin sheath; loss of axon provokes immediate disintegration and removal of the myelin sheath. This situation of axonal degeneration with secondary myelin loss is termed **Wallerian degeneration**.

Myelination in the peripheral nerves is the responsibility of the Schwann cells. Each peripheral internode is myelinated by a single cell and the myelinated axon is invested by a basal lamina tube of Schwann cell origin. The cell body of the

Schwann cell origin directly apposes the axon. Peripheral myelin is also chemically distinct from central myelin. Schwann cells proliferate rapidly and phagocytose damaged myelin and to remyelinated newly regenerated or previously demyelinated axons. Destruction Schwann cells will result in the disintegrating of the dependent myelin. Destruction axon will cause myelin degradation. In demyelinatng diseases the sheath is removed from the axons, leaving them naked over varying length and providing potential of serious slowing of impulse conduction.

In the CNS there is scope for remyelination. Regenerated myelin sheaths area thinner than original. Remyelinated internodes are shorter. In peripheral nervous system remyelination is more favorable.

Oligodendroglial plasma membrane's bilayer wound concentrically and spirally around the axon like a rolled up news paper. One oligodendrocytes myelinated several axonal internodes, that the myelin sheath is a part of the oligodendrocytes and that death of oligodendrocytes will result in the demise of all the myelin sheath segments supplied by that cell. Myelination occurs relatively late in the development of the CNS and the maturing oligodendrocytes invest the axons with myelin replacing an initial ensheathment of astrocytic processes.

Ependymal cells: Line ventricular system. These are closely related other cuboidal cells lining the choroid plexus.

Microglia is mesodermal derived cells whose primary function is to serve as a fixed macrophage system. These express many marker antigens common to many monocytes or macrophages of blood like CR3 and CD4. They respond to injury by proliferating, developing elongated nuclei that is rod cells. The form aggregates about small foci of tissue necrosis that is microglia nodules and congregated around dying particle of neurons (neuronophagia).

Ultastructural studies of microglia reveal extensive thin processes of cytoplasm and dense perikaryon cytoplasm, rough endoplasmic reticulum and Liofuchsin like granules. They are so frequent in gray matter of brain. They are most adjacent to blood vessels. They are considered to be of mesodermal origin and to form a tissue reserve of potential phagocytes. They may also derived from blood monocytes which also give rise to the rich population of leptomeniges and perivascular histiocytes, which can migrate into the neurophil when significant vascular damage has occurred. The simplest microglia reaction to tissue injury is hypertrophic reaction in which the nucleus becomes rounded and the cytoplasm visible as a narrow, often eccentric eosinophilic rim. Focal proliferation gives rise to nodules of 30 to 40 or more cells. These are reactions to viral infections. The most vigorous response of microglia is their transformation to macrophages when they assume the morphology of typical of cells engaged in phagocytosis. When ingested myelin debris, their cytoplasm becomes foamy as they load themselves with lipid vacuoles. Often the nucleus becomes pyknotic and they are referred to

as gitter cells, compound corpuscles or fat granule cells. The phagoyctic activity of microglia results in neuronophagia of myelin and in that way injured and dead numerous are removed.

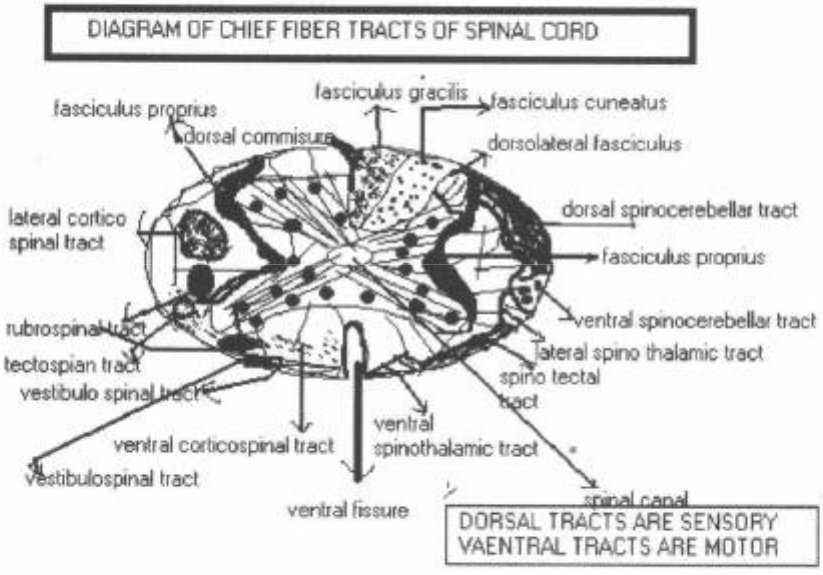
Axonal reaction: The first part of the axon is called the initial segment. It is the site of membrane. The ion channels critical for the initiation of a propagated action potential. The axoplasm contains mitochondria, endosome, intermediate filaments (neurofilaments), microtubules (neurotubules) and secretory vesicles or granules containing neurotransmitters appropriate for the particular cell. The axoplasm contains enzymes. Axons are sustained by their parent cell bodies and by the cells that invest them among their course. The axoplasm is devoid ribosomes, and axoplasmic proteins are provided by the soma. The role of neurotubules in transport mechanisms is critically important for the maintain of the axon. Axonal diameter is distinctly reduced at the nodes of Ranvier and these structures are probably the reason that paranodal swelling filled with transported vesicles and organelles. The neurofilaments are responsible for the maintenance of size of neuron. The larger axons are invested in segmental manner by myelin sheath, depicted in picture and interrupted at the nodes of Ranvier.

Degenerative changes in the axon are called axonopathies. These may start either in the proximal or distal portion. The classical changes in the distal part of the axon are called **Wallerian degeneration**. When the soma is uninjured there is potential for regeneration and in peripheral nerves this may be complete. Whenever there is injury to the distal part, which effectively transects axoplasmic flow. Within 24 hours the distal segment begins to degenerate fairly evenly along the length. Focal eosinophilic swellings occur, often containing accumulation of degenerated organelles, and then fragmentation becomes evidently 48 hours or so. There is rapid response by the Schwann cells as the myelin sheaths are made useless by the disintegration of the axon. Initially myelin retracts from the nodes and those forms into ellipsoids, where myelin is disintegrated. The myelin itself condenses into aggregates and fragments and together with remains axonal debris, becomes the target of invading macrophages. Prior to this, the complex myelin lipids are progressively transformed into simple neutral lipids over a period of 10 to 20 days. Macrophages enter the sheath and soon become filled with lipid droplets. The lipid laden cells may stay in the interstitium for many weeks. Some of the myelin debris is phagocytosed by Schwann cells and they begin to proliferate. As the debris is cleared away, proliferating Schwann cells from and along the former course of myelinated axons.

Similar Wallerian changes occur proximal to the site of injury over several Raniever nodes. If the conditions are favorable at the site of injury sprouts from axonal stump will find their wall along the Schwann cell bends and directed to their correct destinations. In most instances the growing axonal sprout advance at a rate of 2 to 4 mm/day. The new axon will be invested by the Schwann cell cytoplasm. The generated axon is myelinated by Schwann cells and the nodal

length is variable and shorter. Abortive regeneration can lead to a clump of axons, Schwann cells and fibrocytes at the injured site. Popularly called as amputation neruomas. This will happen after transecting of the severed end of the nerve fibers when they are separated to a great distance.

Brain and spinal cord are bound by a thin limiting membrane, the pia-arachnoids, whose few cell layers are intimately joined with the underlying soft parenchyma. The pia-arachnoids follow the convulsion on it surface into depth of sulci and over the summits of gyri. In the sulci, especially the pia arachnoids thicken slightly to form a matrix through which passes most of the blood and lymph vessels. Between the dura and the pia arachnoidal is the subdural space. Its surface is lined with flat mesenchyma or endothelial cells.



Fiber tracts of spinal cord

The white matter of the spinal cord is composed of nerve fibers. Those possessing similar functions, origins and terminations are grouped together in fairly definite bundles called tracts. Certain groups of nerve fibers located in the same general region of the cord but possessing different function are called fasciculi. They are mixed bundles of fibers. The tracts of the spinal cord are dividing into ascending and descending tracts. Some are short, connecting adjacent segments of the cord; others are longer, connecting more remote levels often cord; still others extend from the cord to the brain or from the brain to the cord. The tracts are usually designated by a compound word formed from the name of the places of origin and termination of the tract, the name of the place of origin coming first in the word. As they run up the cord, the ascending tracts gain fibers from successive

groups of nerve cells around which the dorsal root fibers terminate or from branches of the dorsal root fibers themselves and therefore become larger. As they travel down the cord, the descending tracts give off fibers that tend in relation to motor nerve cells in successive segments of the cord and therefore become smaller.

Formation of Cerebrospinal fluid

Cerebrospinal fluid is formed at a rate of approximately 800 ml each day which is 5 to 6 times as much as the total volume of the fluid in the entire cerebro spinal fluid. Most of the fluid originates as a secretion from the choroid plexus in each of the four ventricles, though most of it by far in the two lateral ventricles. Additional amounts of fluid are secreted by all the ependyma surfaces of the ventricle. The fluid passes into the third ventricle through the foramina of Monro, combines with the secreted in the third ventricle, and the passes along the aqueduct of Sylvius into the fourth ventricle where a small amount of additional fluid is added. It then passes out of the fourth ventricle through three small openings, tow lateral foramina of Luschika and a midline foramen of Magendie, entering the cisterna magna, a large fluid space that lies behind the medulla and beneath the cerebellum. The cisterna magna is continuous with the sub-arachnoids space that surrounds the entire brain and spinal cord, and the CSF flows upward through this space toward the cerebrum; but before it can reach the cerebrum it must first flow through the small tinctorial opening around the mesencephalon where the flow is sometimes stopped. From the cerebral subarachnoid spaces, the fluid flows into arachnoidal villi that project mainly into the large saggital venous sinus. Finally the fluid empties into the venous blood through the surfaces of these villi. The choroid plexus projects into the temporal horn of each lateral ventricle, the posterior portion of the third ventricle and the roof of the fourth ventricle.

Cerebrospinal fluid and blood brain barrier

The constituents of cerebro spinal fluid are not exactly the same as those of the extracellular fluid elsewhere in the body. Furthermore, many large molecular substances hardly pass at al from the blood into CSF or into the interstitial fluids of the brain even though these same substances pass readily into the usual interstitial fluids of the body. Therefore, it is said that barriers called the blood-cerebrospinal fluid barrier and the blood brain barrier, exits between the blood and the CSF .These barriers exist in the choroid plexus and in essentially all areas of the brain parenchyma except the hypothalamus, where substances diffuse with ease into the tissue spaces. The ease of diffusion is very important because the hypothalamus responds to many different changes in the body fluids, such as changes osmolality, glucose concentration and so forth; these responses provide the signals for feedback regulation of each of the factors.

In general, the blood CSF and blood brain barriers are highly permeable to water, CO_2, oxygen and most liquid soluble substances such as alcohol and most

anaesthetics; slightly permeable to the electrolytes, such as sodium, chloride and potassium and almost totally imperable to such substances like arsenic, sulfur and gold. The blood barrier is also called Virchow-Robin space by the pathologists. The cause of the low permeability of the blood CSF and blood brain barriers is the manner in which the endothelial cells of the capillaries are joined to each other. They are joined by so-called tight junctions. That is the membranes of the adjacent endothelial cells are almost fused with each other.

The surface of the ventricles is lined with a thin cuboidal epithelium called the ependyma, and the CSF on the outer surfaces of the brain is separated from the brain tissue by a thin membrane called the pia mater. Both the ependyma and the pia mater are extremely permeable so that almost all substances that enter the cerebro spinal fluid can also diffuse readily into the brain interstitial fluid. Or like wise substances in the interstitial fluid can diffuse in the other directions as well.

Low concentration of potassium ions occur in the interstitial fluid of brain. The blood-brain barrier also prevents such substances as acetyl choline, nor-epinephrine, dopamine and glycine from entering the brain from the blood even though their concentrations might become quite high in the circulating blood.

Hydrocephalus

Hydrocephalus results from the over production or abnormal accumulation of cerebrospinal fluid in and around the ventricles of the brain which makes them to dilate the ventricles (Internal hydrocephalus). Hydrocephalus may be congenital or acquired. It maybe either internal or external.

In simple hydrocephalus the clear fluid is a transudates or increased cerebro-spinal fluid; in inflammatory hydrocephalus the fluid is a turbid exudates containing much albumin. Simple hydrocephalus is generally chronic and inflammatory hydrocephalus is acute. Hydrocephalus maybe congenital or acquired.

Congenital internal hydrocephalus: This is frequent in calves and foals. It develops in utero or though based on foetal malformations, may only attain a complete development in the first week or months of postnatal life. As at this time the cranial bones are still not completely ossified and united with another the dilatation of the ventricles of that produces enormous expansion and enlargement of skull. (Microcephaly), a condition never observed in association with acquired hydrocephalus. The circumference of the calf may exceed a metre in this case. The skull is spherical and distended like a balloon or more pointed or flat and expands laterally. If still more extreme, the condition is incompatible with life. Hydrocephalus is a frequent cause of dystocia and death of young animal.

In extreme degree of hydrocephalus, the cerebral hemispheres, by virtue of extreme dilatation of lateral ventricles, reduce to flaccid sacs which sometime burst during parturition or tear when the skull is opened. A large quantity of CSF

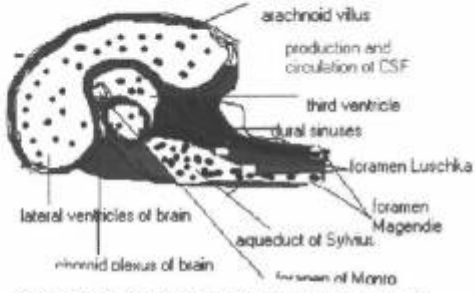
is secreted that is more than a litre wills come out. The third and 4th ventricle is also dieted. The brain substance is an anemic and shows evidence of pressure atrophy. In many cases, the brain substance is reduced to a translucent rind only a few mm thick. The convolutions are flattened out.The cerebellum is compressed and pushed backwards.

Secondary congenital hydrocephalous is associated with malformation of brain. Vitamin A deficiency is responsible to bring congenital hydrocephalus is calves and even more so in pigs.

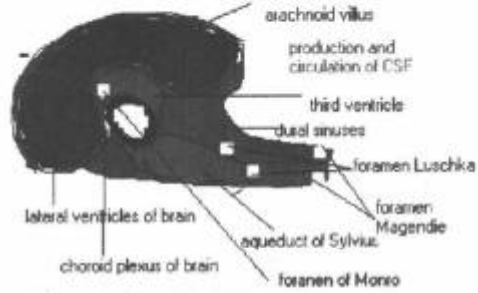
Acquired internal hydrocephalus develops in postnatal life, when growth of the skill has been completed, the sutures have become ossified and the cranial vault is rid and unyielding. The dilatation of the ventricle is never as extreme as in congenital hydrocephalus and proceeds at the expense of the brain substance.

Secondary acquired hydrocephalus maybe acute or chronic in cases of meningitis in which there is extension to the plexuses with swelling and obstruction of the inter=ventricular foramen or Lusaka's foramina (inflammatory hydrocephalus), it may also result from retention of CSF when out flow channel are obstructed or compressed buy tumors and inflammatory new formation, particularly meningeal tuberculosis, parasites such as coenurosis and hydatid cysts. It may also be due to compression dural plexus veins.

In hydromelia which corresponds to internal hydrocephalus, the central canal of spinal cord is dilated as a result of increased accumulation of CSF, with disappearance all of the gray substance. Syringomyelia is the cavities in the gray substance of spinal cord, unconnected with the central canal.



pathway of cerebrospinal fluid[CSF] flow from the choroid plexuses in the lateral ventricles to the arachnoid villi protruding into the dural sinuses



pathway of cerebrospinal fluid[CSF] flow from the choroid plexuses in the lateral ventricles to the arachnoid villi protruding into the dural sinuses

Cholesteatomas

Plexus cholesteatosis the result of deposition of crystalline cholesterol in tumor like chronic inflammatory areas. These bodies being generally termed as plexus cholesteatomas, they are found in 20 to 50% of old horses. They are situated in

the lateral plexuses of cerebellum, some what less frequently in those of lateral ventricles. Cholesterol constitutes about 30-50% of granulomas.

Massive cholesteatomas are produced by prolonged growth of pearl cholesteatomas over period of months and are found only in the plexuses of lateral ventricles on one or both sides. They are pea to hen egg size, elongated ovoid or ramiform, grayish yellow soft, flaccid tumor like neoformations with smooth, nodular or granular surfaces. Inflammatory cells and cholesterol like crystals and are present with these cholesteatomas.

Atrophy

Senile atrophy in animals: Meninges are thickened and there often deposits of bone and calcium in the durra water. This brain is reduced in weight. Convolutions are narrow, angular and wrinkled, while the sulci are deeper and wider. Sub arachnoids space and ventricles are enlarged as a result of loss of brain tissue and contain more fluid (senile meningeal hydrops and internal hydrocephalus). The ependyma is thickened. The adventitial space may gape so much that they are seen as small holes on the cut surface. Proliferation of glia renders the brain and spinal cord firmer than normal. The cord is thinner than usual.

Histologically there is shriveling (sclerosis) and disappearance of ganglionic cells and of purkinze cells in the cerebellum, particularly in dogs, reduction in size, and break down and disappearance of tigroid bodies, movement of nucleus to the periphery, increase of pigment, proliferation of glia and atrophy of myelin or the nerve fibers.

Thickened and tortuous nerve fibers in the cytoplasm of ganglion cells and asrtiosclerosis change are seen in aged humans. Senile dementia patient show loss of chromidial substance, loss of ascorbic acid in nerves and increase of mcuopolysaccharides in the cells of autonomic ganglia.

Pressure atrophy: There is a reduction in the capacity of cranium or spinal canal by tumors, inflammatory new growths (like tuberculosis lesions), exo-ostoses, collections of transudates or exudates.

Secondary degeneration of nerves fibers occurs due to pressure atrophy due to anemia and secondary there is nerve fiber degeneration of distal end (Wallerian degeneration).

Developmental disturbances

Malformations with defects in the skull: Complete absence of brain- anencephaly; Acrania is the total absence of cranial vault; Total absence of cranial vault and the skull is open- the condition's called total cranioschisis; When part of cranial vault has developed this condition is called partial cranioschisis, hemicranias or merocrania; Absence of spinal cord is called Amelia; Open vertebral canal is called total rachischisis; Encephalocoele results in cerebral hernia with resultant protrusion

of meninges and parts of brain through a defect in the cranial vault which is under the skin. The contents determine whether the condition is a menigocoele (hydromeningocole), containing only meninges and fluid;

Encepalocystocoele (hydroencephalocoele), containing part of the expanded brain sac covered with pia-encephalo cyst or menigocoele. Rachitic hernia of spinal cord: there may be total or partial fissure of the spinal column (rachischisis or diastematorachis) on the dorsal aspect (verterbalarches) or less frequently on the ventral aspect (bodies of vertebrae). These conditions are either known as **spina bifida.**

Microencephaly is the condition in which the brain is abnormally small. The hypoplastic brain lies in a closed but very small cranium (Microencephaly).

Anopthalima in these conditions, wherein eye ball is lacking and replaced by solid structures consisting of connective tissue, fat and cartilage. There is presence of pigment cells. The optic nerve, chiasma and optic tract are absent or defective.

Congenital aplasia or hypoplasia of optic nerve- hypoplastic changes of retina or the entire eye ball. Agenesis of corpus colosum-absence of cerebellum has been noted in calves, lambs, dogs and cats.

Porenephaly is a condition in which there are partial defects of individual parts of the brain which are seen as cystic spaces and deepest funnel shaped holes (pores) or clefts, often extending from the cortex into the ventricle, lined or covered with meninges and filled with clear or milky fluid.

Reduplications: There may be partial or complete reduplication of the brain and spinal cord. Defective formation or absence of myelin sheaths (hypomyelogenesis); occurs as a congenital malformation in calves and sheep. These show tremors and in-coordinated gait and hind limb ataxia and in some cases these animals are not able to stand.

Congenital Myoclonus of pigs (trembles) the disease has been observed in various breeds of pigs. It attacks new brown pigs and is characterized by clonic convulsive movements resulting in from excessive irritability of individual muscles or of the entire musculature. The tremor is leas marked in the head region. The signs may disappaaear after a few weeks the begin to thrive. In severe cases the pigs may die of inanition and unable to grasp the teats for feeding.

Pigmentations of brain: Melanins is present physiologically in the substantia nigra. Haematogenous pigmentation: Brown or red or brownish yellow foci containing blood pigment. Persist for long periods (haemosiderin or haematoidin) either free or in the macrophages and microglia cells persists for long period at the sites of heaemorrhages. Kernicterus: Icterus gravis neonatarum wherein there is intense yellow staining of nuclei in the ganglia of nervous system. The condition is seeming haemolytic icterus of foals of horse's and mules. Wear and tear pigments:

With increasing age, ganglion and glial cells contain increasing quantities of granular, yellow or brown iron free lipid pigment as a physiological l phenomenon. It is observed first into the pyramidal cells of cerebral cortex and ganglion cell of olivary nuclei and later in glial cells and adventitial cells.

Concussion and contusion of brain with or without fracture of skull may occur as a result of bows, violent impacts and falls. In some cases there are large heaemorrhages frequently as the side opposite to the point of impact. In concussion and contusion mechanical energy is transmitted to the brain substance, which then vibrates. If the energy of the brain is within the tolerance limits of the brain, reversible disturbances designated commotion is produced. When the vibration is more, it leads to irreversible morphological changes (contusion). Concussion or contusion occurs when smaller animals are slaughtered by stunning.

Necrobiosis

Primary degeneration or secondary or Wallerian degeneration. Should a nerve fiber be interrupted in any way whatsoever, the periphery and distal part separates from the ganglion cells or nerve cell body.

Degenerative changes in motor neurons of spinal cord occur in tetanus, here breaking down of Nissel body and extreme swelling of cytoplasm occurs. The intensity of degenerative changes does not correlated with the intensity of clinical symptoms.

In botulism there are degenerative changes in the neurons wherein neuronophagia, necrosis and haemorrges of focal glia proliferation and proliferation vascular endothelium is even. This is seen in horses, ruminants and birds.

In Anthrax toxin the nerve cell degeneration occurs with resultant apoplectic deaths.

In hepatic necrosis- due to toxins that persist as a result of failure of destruction or detoxification by liver cells, these cause degenerative changes in nerve cells.

In gross sickness of horses due magnesium deficiency the nerve cells of autonomic system present degenerative changes and necrosis of cells occur. Tigrolysis, accumulation of cytoplasm seen. Visceral changes like acute dilation of stomach and chronic dialtation of intestine also seen consequent to destruction of nerves.

In chronic parasitic diseases like fluke in ruminants, Echinococcus infection in ruminants as hydatid cysts, hepatic destruction, in Beri beri that is due to B-complex deficiency generative changes are seen in the nervous system especially in dogs and sheep.

In vitamin A deficiency especially in pig myelin sheath degeneration, wherein disappearance of axis cylinders of entire nerves, cochlear and vestibular nerve degeneration, degeneration of facial nerves and unilateral paralysis is seen in animals.

Hunger and hypoxemia also causes nerve cells degeneration resulting in Nissel substances disappearance and neuron changes.

Terms used in dealing with dysfunction of nerves

Coma: loss of consciousness. It results from the effect of various toxic agents upon the brain. There is complete loss of consciousness. In this the animal lies outstretched and motion less, its reflexes are gone; the pupils are dilated, respiration is slow and irregular, heart beat is weak and the skin is cool (lager mortis). It usually ends fatally.

Nervous depression: Due to pressure upon the brain such as due to sudden heaemorrhages resulting in concussion, a brain tumor or even collection of fluid within the ventricles. There is loss of feeling, sleepiness and muscular in-co-ordination. Even in encephalitis this may result.

Nervous excitement results from the inflammatory and congestion of the brain and in its coverings. There is delirium and mania and even convulsions. This is seen in rabies viral infection in dogs.

Spasm is in the increase activity of muscles.

Spasm may be tonic where it is continuous or clonic wherein intermittent contraction of muscles is observed.

Mild spasms are called as tremor which is confined to a group of muscles.

If the muscle spasms are widespread and involve the whole body, including the limbs, these are called convulsions. Common example is with distemper in dogs.

Paralysis is wherein both sensory and motor functions of muscles are lost.

Paralysis wherein motor function of muscles are only lost. Sensory function persists. Animals cannot withdraw the limb on pricking but exhibits the pupil or other pain reflexes.

Hemiplegia is the paralysis arising in the brain cortex and in the peripheral nerves and is unilateral.

Bilateral paralysis of posterior parts of the body and hind limbs are called paraplegia.

About spinal nerves

There are 12 cranial nerves. 1) Olfactory, 2.) Optic, 3.) occulomotor, 4) trochlear, 5) trigeminal, 6) abducent, 7) facial, 8) acoustic, 9) glossopharyngeal, 10) vagus, 11) spinal accessory, 12) hypoglossal.

Glial cells of brain:

Glial cells The common glial cells are astrocytes, oligodendrocytes, and microglia and ependyma cells.

The astrocytes are either fibrous type or protoplasmic type. Fibrous astrocytes are abundant in white matter and protoplasmic astrocytes in gray matter. These cells are responsible for repair of nervous tissue defects. Astrocytes show hyperplasia, hypertrophy.

Oligodendrocytes are the most numerous of Th neuroglial elements. Oligodendrocytes are intimately associated with the capillaries of the vascular bed. Oligodendoructes are therefore per neuronal, perivascular or interfasicular. Oligodendrocytes are responsible for myelination of nerve cell processes within the central nervous system.

Microglia cells are capable of pahgocytosis in response to minor injury.

Embryonic **Ependymal cells** are ciliated and these are cells of low cuboidal or of low columnar configuration. Ependymal cells contribute to the format of cerebrospinal fluid.

Once the neuron is destroyed it cannot be replaced.

Reaction of nervous tissue to injury

Nuclear margination: The neuronal nucleus is single centrally located normally and its margination indicates its nonspecific degeneration.

Chromatolysis: This is the first change observed in degenerating neuron. Dispersal of rough endoplasmic reticulum (Nissl granules) in the cytoplasm of neuron. Chromatolytic cells are swollen and rounded off. Nucleus becomes eccentric. Nissl granules clear from the central region of the cell body leading this zone with a smooth ground glass appearance. Reaction to injury occurs within 24 hours and becoming maximal into 1 to 3 weeks. Nucleus become extremely eccentric and develops prominent nucleolus. Nissl substance disperses; the cytoplasm becomes rich in free ribosomes, lysosomes and mitochondria. There is increase in the number of neurofilaments. All these changes reflex a shift in metabolic activity with a switch towards increased synthesis of structural cellular proteins and marked decline in synthesis of transmitters.

With completion of successful axonal regeneration chromatolysis stroma returns to normal, and packed with densely stained basophilic granules of Nissl substance.

The close to the cell body the axonal lesion, the more likely is the cell to die. Dying cells organelles are depleted and stainability is also less. The first part of axon is called initial segment and is essential for the propagation of action potential. The axoplasm contains mitochondria, endosome, intermediate filaments (neurofilaments), microtubules (neurotubules) and secretory vesicles or granules containing neurotransmitters. The axoplasm also contain soluble enzymes, Lysomal apparatus is limited to axon only.

Sequential reactions consequent to the injury to a neuron (central nervous system):

The neurons being highly specialized are easily susceptible to injury by hypoxia or toxic materials, evidenced by degenerative and necrotic changes. The following reactive change is noticed.

Shrinkage is characterized by cell becoming very irregular, nucleus pyknotic, clumps and condensation of Nissl substance and tortuousness of the processes.

Swelling of nerve cells. Cytoplasm stains very faintly and only the cell outline may be visible with fragmentation of the processes. It is a reversible condition and occurs in severe intoxication and systemic infections. Vacuolation of nerve cell is seen in toxic conditions and encephalitides. Chromatolysis where Nissl substance becomes fine and dispersed and totally disappears. The nucleus is eccentric. This change is seen injury to the axon. Neuronophagia occurs even the nerve cell dies, microglia and oligodendroglial invade the cells and remove it by phagocytosis. Satellitosis is seen wherein neurons are dying and degenerating. The microglia cells and astrocytes surrounds the area called as satellitosis. Microglia surrounds the dead neuron. Hypertrophied microglia with lipid material and devoured neuron are called gitter cells.

Thrombosis and embolism of cerebral arteries are rare in animals and may occur in the brain and spinal cord. Emboli may be detached vegetations from the cardiac valves or may arise from lesions of the lungs, left atrium or coronary artery, clumps of bacteria, tumor cells, parasites that are larva of Ascaris, bladder cysts of tapeworms and agglutinated RBCs.

Thrombus can arise from lesions cerebral vessels (atheromas) or can occur in diseases that damage the vascular endothelium, trauma causing fractures of the skulls, invasion of the vessel wall by neopalstic cells, abscesses and hog cholera. If collateral blood supply is inadequate infarction results. The infracted area is finally liquefied, a cyst being formed.

If the blood supply is not adequate to maintain the nutritive and oxygen requirements of the areas infarction occurs. The infracted area is pale or red depending upon the blood supply. Infarction ends up in liequefactive necrosis of the involved area.

Disturbances in circulation

Acute general active hyperemia is present when bacterial or vial agents are involved. Acute focal active hyperemia is seen in the vicinity of abscesses, tumors and infarcts. Chronic general passive hyperemia is seen where hyperemia due to lesion in the heart or lungs or an obstruction to the flow of blood from the brain such as thrombosis of both jugular veins.

Haemorrhaage: Petchiae are common in acute septicaemic diseases like anthrax, hameorrhagic septicemia, hog cholera, leptospirosis or infections by pyogenic organisms. These also occur after thrombosis or in degeneration of the vessel

walls or in general haemorrhagic diseases. Rupture of an artery will give rise to large areas of haemorrhages with clots causing apoplexy. Rupture may occur in injuries like automobile accidents, gun-shot wounds, diseases of wall of blood vessels (atheromas) with hypertension as in arteriosclerosis, chronic hepatitis, bursting of an aneurysm as in parasitic aneurysm in horses.

The first symptom in cerebral haemorrhage is shock, later passing on to coma and terminating in death. Animal that survive the first shock suffer from some degree of paralysis due to pressure on and damage to neurons. Haemorrhages may be found subdurally. These also may occur in the substance of the brain. When haemorrhages are found in the ventricles, the CSF may be blood tinged.

The blood clot in the brain first contracts separating the serum which is absorbed. The clot that remains is liquefied and cyst is formed with a clear fluid the apoplectic cyst. The capsule of the cyst is formed by the neuroglia. Hyperemia of the brain and meninges together with peticheal heaemorrhages and oedema are found in the following conditions namely electrocution, lightning stroke and sun stroke.

Oedema of brain: vasogenic in white matter and non-vasogenic or cytotoxic oedema-preferentially inn the gray matter of brain. Vasogenic oedema is due to break down or impairment of blood Brian barrier followed by leakage of serum into the perivascular parenchyma such as Virchow-Robin space, sub-arachnoidal spaces and spaces formed around neurons.

Oedema fluid in the white matter is extra-cellular and spreads within extracellular places. The fluid in the gray matter is intracellular Fluid escaped form vessels become entrapped within astrocytic processes and flows behind membranes. Grossly gyri are swollen and flattened. Cut surface is moist and shiny, parenchyma is softened.

Cyto-toxic oedema is the result of altered cell metabolism. Fluid accumulates within intracellular compartment of neurons, neuroglia and endothelial cells. Blood brain barrier remains intact. Edema is nonvasogenic.

Atrophy

Senile atrophy in animals: Meninges are thickened and there often deposits of bone and calcium in the durra water. This brain is reduced in weight. Convolutions are narrow, angular and wrinkled, while the sulci are deeper and wider. Sub arachnoids space and ventricles are enlarged as a result of loss of brain tissue and contain more fluid (senile meningeal hydrops and internal hydrocephalus). The ependyma is thickened. The adventitial space may gape so much that they are seen as small holes on the cut surface. Proliferation of glia renders the brain and spinal cord firmer than normal. The cord is thinner than usual.

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Secondary degeneration of nerves fibers occurs due to pressure atrophy due to anemia and secondary there is nerve fiber degeneration of distal end (Wallerian degeneration).

If a neuron dies surviving neurons with which it has synaptic connections may regress due to lack of activation, undergo atrophy and eventually die. This process is called tran-synpatic degeneration and it will progress along specific anatomic pathways. The mature neuron is a post mitotic cell.

Viruses that induce congenital anomalies of CNS

Virus	Anomalies
Blue tongue (orbi virus)	Hydraencephaly, porencphaly I sheep
Border disease	Hypomyelogenesis in sheep
Mucosal disease	Cerebellar hypoplasia in cattle, cats and ferrets
Feline pan leucopenia (Parvo virus)	Cerebellar hypoplasia in cats and ferrets
Hog cholera (pesti virus)	Cerebellar hypoplasia and Microencephaly, hypomyelogenesis
New castle disease	Microencephaly in chick embryo
Lymphocytic choriomeningitis	Cerebellar hypoplasia in rats
Mumps (reo virus)	Aque ductus stenosis, hydrocephalus in hamsters, mice, rats and ferrets

Necrosis

Simple or coagulative necrosis

This involves the neurons and glia. The causes are severe injury to the cells brought about by hypoxia, chemical poisons, bacterial toxins and viruses. Grossly there are no changes. Histologically the cells are swollen and become more globular in shape. The Nissl substance may eventually disappear, that is chromatolysis or tigrolysis. The cytoplasm stains more intensely with eosin and the nucleus shows pyknosis, karryorhexis or karyolysis. Around dead neurons satellitosis and these neurons are engulfed by neuronophagia.

Liquefactive necrosis

Because the brain is rich in lipids this is seen. In fact liequefactive necrosis is always common with brain.

Infarction is one of the common causes of **liequefactive necrosis**. It may also occur when the CNS is invaded by pyogenic bacteria. The lysosomal enzyme released from neutrophils induces liquefaction of myelin, neuroglia and other structures. This is known as **encephalomalacia**. Softening of gray matter is known as poliomalacia and that of white matter leukomalacia. Encephalomalacia is common in deficiency of vitamin E in young chicks (crazy chick disease), mouldy corn poisoning in horses, acute pancreatitis in all animals, antenatal copper deficiency in lambs (sway back), cobalt deficiency (enzootic marasamus), enterotoxaemia in lambs, mulberry disease in swine, vitamin B deficiency (Chastek paralysis) in fur bearing animals and claves and sheep and is called as cortical cerebral necrosis, blue tongue in sheep and distemper in dogs, toxoplasmosis, lead poisoning infarction due to an embolus consisting of tumor cells or parasites or pieces of a thrombus oar due to thrombosis of an artery and poisoning by mercurial salts. The lesions seen are thickening of blood vessels, endothelial hyperplasia and liquefaction brain substance. Around the area, there is proliferation of capillaries and the formation of a capsule by the cells of meninges. Astroglia proliferate and surround the area of encapsulation. The involved tissue undergoes liquefaction and a serous fluid is present.

Specific inflammation of brain and spinal cord

The blood vessels of the brain have some peculiarities. These are the arterioles and venules are very thin walled devoid of elastic and muscular tissue; veins do not have valves; the blood vessels acquire a meningeal sheath as they pass through the subarachnoid space and second outer sheath derived from the pia. So perivascular space is formed between these sheaths that are the space of **Virchow-Robin,** which is continuous with the perineural and interstitial space of CNS. It is in this space that the cells accumulate and give rise to **perivascular cuffing**. Depending on the nature of the pathogen the cells vary. In bacterial infections, neutrophils predominate while in viral, lymphocytes and in allergic encephalitis, macrophages are seen with salt poising in pigs, lymphocytes and plasma cells and eosinophils. In infections of the brain, inflammatory exudates collect in the space of Virchow-Robin space. The adventitial wall is the source of macrophages and the fibrous tissue elements that compose the capsule in abscesses that arise in some bacterial infections.

Rabies: It is an acute viral disease of domestic animals characterized by a very severe lymphocytic inflammation of nervous system. Here there is severe meningoencephalomyelitis. There is degeneration of neurons, astrogliotis, neuronophagia and satellitosis.

Pseduorabies: It is a viral infection cattle, pig, dogs and cats. Pigs rather show diffuse lymphocytic meningo-encephalomyelitis.

Hog cholera: There is diffuse lymphocytic meningoencephalomyelitis of brain.

Canine distemper;

There is typical diffuse lymphocytic meningoencephalomyelitis.

Infectious viral equine encephalomyelitis:

This is an acute viral disease of horses and mules and is characterized by lymphocytic meningoencephalomyelitis.

Avian encephalitis

In chicks this viral diseases cause lymphocytic encephalitis.

Ranikhet disease

This disease causes encephalomyelitis in chicks, and there is perivascular cuffing, satellitosis and extensive gliosis.

Listeriosis

In this perivascular cuffing with lymphocytes in large animal and monocytes as vascular cuffs in rabbits and gliosis is seen in CNS.

Parasitic encephalomyelitis

Myiais Larvae of the fly-hypoderm bovis migrate into the vertebral canal in cattle and invade even into the spinal cord and brain.

Larvae of oestrous ovis, the bots which stay normally in the nasal cavity of the sheep migrate into the brain and produce organic lesions.

Cestodes worm larvae that are tapeworm cysts are found in the central nervous system in domestic animals. The common tape worm cysts are Multiceps Multiceps, Taenia pisiformis and Taenia Echinococcus (hydatid cysts).

The larval stage of Multiceps Multiceps, a dog tapeworm is known as Coenuris cerbralis it causes a common disease of the central nervous system known as gid or sturdy. In goats Multiceps gaigalis produces Coenuris cerebralis like symptoms. This is also a dog tape worm and stay in the intestine of dogs. When the hexacanth embryos are swallowed by goats the bladder worms develop as cysts in brain.

Because the cyst contains a lot of water. It produces pressing lesions on the central nervous system. The symptoms depend on the bladder worms and are located either in the brain or spinal cord. In both the cases the cysts measure are more than 50 mm in diameter and contain around 500 scolices. As the cyst enlarges there is pressure atrophy of the surrounding nervous tissue. The convolutions maybe flattened and cortex becomes thickened. Even the cranial bones may subject to pressure atrophy. The chronic irritation produces lymphocytic meningitis,

encephalitis or myelitis. Death of the larva will result in calcification of cysts.

Cerebrospinal nematodiasis (KUMRI) in horses

This disease is caused by the larvae of Setaria digitata in horses. The nematode worm normally stays in the peritoneal cavity of cattle. The horse is an aberrant host. When the larvae migrate into the horse, these will settle in the spinal cord and damage it. This is exhibited by the weakness of loins and animals limp. Hence this form of neurofilariasis is called as kumri weak loin in Hindustani language.

Similarly *setaria cervi* stays in the peritoneal cavity of horses and the larval forms migrate into the cattle they cause similar disease in cattle, sheep and goat.

Grossly narrow tortuous streaks of heaemorrhages and malacic or softening zones are found in the spinal cord.

Histologically the lesions consist of central spaces where the parasite is surrounded by degenerated and necrotic tissue. Myelomalacia with haemorrhages in the spinal cord are the features.

Allergic encephalitis (Post-vaccinia encephalitis)

This occurs in dogs following vaccination. It occurs 3 weeks after vaccination and is characterized by lymphocytic meningoencephalitis. There is motor paralysis of one or more limbs, which may involve most of the body.

Pachymeningitis: Inflammation of the dura mater. This is usually secondary due to infection of the middle ear or adjacent bone. It may be suppurative or non-suppurative. In the suppurative variety local abscesses are found on the dura and the peri dural spaces. Chronic fibrosis develops when dura is thickened with local adhesions. Infection may spread to the arachnoid causing leptomeningitis.

Leptomeningitis: Inflammation of the pia-arachnoid and is in association with the inflammation of brain and is usually called as meningo-encephalitis. This may be suppurative or non-suppurative. The causes are extension from adjacent tissues as in viral encephalitis like, canine distemper, hog cholera and rabies. Mechanical injuries like fractures, bacterial infections from neighbouring areas in middle ear, nasal cavity and sinuses. The cause bacterial are Listeria, corynebacterium pyogenes, pseudomonas, coliforms, pasteurella, toxoplasma, mycobacterium tuberculosis, leptospira and Cryptococcus organisms. Haematogenous infections in septicaemic conditions like navel ill, enzootic pneumonia, colibacillosis, purulent pneumonia, metastasis from infections such as mastitis, metritis or peritonitis.

Parasitic cysts like Multiceps Multiceps and hydatid cysts in sheep

Haemorrhagic meningitis is seen in acute lead and copper poisoning.

Examination of spinal fluid collected from a lumbar puncture gives valuable information as to the measure of the infection.

Myelitis: Inflammation of the spinal cord. Usually Myelitis is found along with encephalitis when the condition is known as encephalomyelitis. Myelitis may be suppurative or non-suppurative. Fracture of spinal column and protrusion of intervertebral disc are the causes.

Grossly there is congestion of the pia, petchiae on and inside the spinal cord and in advanced cases softening of the nervous tissue.

Epilepsy

Epilepsy is a sudden brief (petit-mal) or prolonged (grand mal) loss of consciousness usually preceded by convulsions. Epilepsy is an inherited condition in Brown Swiss cattle and Cocker spaniels.

A true grand mal epileptic form seizure is manifested by an early period of alertness, followed by a state of tetany, which gives way after a few second to clonic convulsions with padding, opisthotonus, champing of jaws and salivation. The clonic convulsions are followed by a period of relaxation. The convulsions may spread from the initial area to the rest of the body. The animal is unconscious throughout the seizure. Evacuation of bladder oars bowel or both is common during the seizure. The animal may quickly regain its normal state after the seizure or dead or uncoordinated for a few minutes. The temperature may be elevated or normal. The pulse is frequent and respiration rate is increased. The blood, cerebrospinal fluid and urine are normal. The attacks always are recurrent and the animals are normal in the intervening periods.

Sway back or enzootic ataxia

The disease is seen new born lambs in certain parts of the world. The symptoms noticed are severe ataxia, locomotor disturbances, paralysis and inability to walk. Affected animals may be blind and so are unable to move. Death may also due to bronchopneumonia.

Sway back is attributed to a deficiency of copper. This is either due to copper deficiency, or grazing on lands with molybdenium rich grasses.

Histologically, a diffuse symmetric destruction of white matter in the cerebrum is noticed, which is liequefactive necrosis. There is destruction of descending myelinated tracts. Gitter cells are numerous in the areas. There is reduction in the cytochrome oxidase activity of neurons.

Salt poisoning

Salt Poisoning is a direct and immediate result of excessive ingestion of slat or it may be indirect and delayed, developing only after several days of excessive salt intake and restricted water intake. These won't occur in animals where copious amount of drinking water is provided.

Acute direct salt poisoning occurs chiefly in cattle, especially if they are very

thirsty when first give access to saline water. Poisoning may also occur in cattle if they are given free access to salt supplement after a prolonged period of salt restriction, such as occurs kin cattle grazing on mountain pastures. Clinical signs in cattle are referable to the alimentary tract and nervous system.

Apparent blindness and deafness initiate the clinical syndrome is indirect salt poisoning in swine. There is head pressing suggestive of increased intracranial pressure, arching, or pivoting and these signs usually lead to the convulsive syndromes. The convulsions are verifying characteristic in their pattern and in the regularity of the time intervals in which they recur. They begin as tremors of the snout and rapidly extend as clonic spasms of the neck muscles, with jerky opisthotonus which causes the pig to walk backward and sit down. The animal passes into lateral recumbence and generalised clone convulsions.

The specificity of the lesion is given by the abundance of eosinophils which are infiltrated into the menninges and Virchow-Robin spaces. Thus the eosinophilic meningo-encephalitis is a characteristic feature.

Mycotic leukoencephalomalacia

The neurological signs described in the spontaneous disease are related to the malacic injury. This has been reported in horses with the fungus *Fusarium moniliforme*. Even with aflatoxicosis in all domestic animals there are neurological signs with heaemorrhages in the brain.

Lead poisoning

Poisoning is common and fatal in cattle and less common but fatal in sheep; it is occasionally observed in horses and dogs and is rare in swine. The usual sources of led for cattle are paint and metallic lead in storage batteries. Licking pains also cause this poisoning. Lead arsenate, widely used as an orchard spray, is commonly responsible for poisoning of cattle and of sheep, but the signs and lesions refer largely to activity of the arsenate.

The acute poisoning kin cattle usually lead to deaths in 12 to 24 hours. Calve stagger, develop muscle tremors and rapidly become recumbent. Convulsions are intermittent until death and between convulsions there is opisthotonus, muscle tremors, champing of jaws and hyperesthesia to touch and sound. Adults show less tendency to early recumbence. In these there is frenzy, head pressing and apparent blindness, with death in convulsions. When the poisoning is less acute cattle may survive for 4 to 5 days. They are dull and apatethatic, apparently blind and without appetite. There maybe slaivaiton, intermittent grinding of teeth, and hyperesthesia, but dullness and immoblity predominate. Ruminal atony is fairly constant and ark foetid faces maybe passed terminally. Death occurs finally with convulsions.

Histologically in brain there is laminar necrosis of neurons. The capillaries and venules are congested, and there may be peticheal haemorrhages. There is some

endothelial swelling.

Nerve tumors in animals

Summary

Medullo-epitheliomas, gliomas, meduloblastomas, neuroblastomas, astrocytomas, gangliocytoma, oligodendroglioma, spongioblastoma, epndymoma, neoplasms of choroid plexus, meningioma, pinealoma, cranio-pharyngioma – malignant-melanoma – schwannoma-neurilemmoma, neurofibroma, gnalgioneuroma.

Nerve tissue tumors

Schwannoma: This is also known as neurilemmoma and originates from the cells of the sheath of Schwann of peripheral nerves. Among animals, these tumors are more common in the ox. These tumors are usually small in size, a few centimeters in diameter and are situated in the course of nerve fibers. Microscopically two distinct pattern of arrangement of cells are noticed. The first one is Anton type A and the other one is Anton type B.

Antonym type A: In this type the Schwann cells are elongated and spindle shaped with oval or cylindrical nuclei and the fibers from interlacing bundles. The cells are arranged parallel to each other. This palisade arrangement may take a whorl form also, when they are called Varocay bodies. Anton type B is the cells of varying shades and is arranged in a disorderly loose manner. Often intercellular vacuoles containing a watery fluid and stains blue with haematoxylin. In this type, fibers are not seen.

Meningioma

Meningiomas: These tumors are otherwise known as arachnoids- fibroblastomas arise from the arachnoid fibroblasts of the brain and spinal cord. Meningioma occurs singly and by expansion causes pressure on the brain. Grossly the tumor appears as white lobulated and encapsulated. Histologically, meningioma consists of spindle shaped cells of uniform in size and shape. They have elongated oval nuclei. The cells are arranged in whorls. Mitotic figures are seen in the following forms meningioma are observed, namely, epitheloid form, psammoma-form, fibrous form, ossified form, angiomatoid form and sarcomatous form.

Epitheloid form: In this type, cells resembling epithelial cells (polyhedral cells), are found in sheets or pseudo alveoli amidst vascular connective tissue.

Psammoma form; In this form of growth bluish calcified bodies, calico-spherules suggestive of grains of sand are dispersed in the substance of the tumor.

Fibrous form; In this variety dense fibro-collagenous tissue with or without whorl formation or sand grains is found.

Ossified form: In some part of the tumor, ossification with haematopoietic marrow may be seen.

Angiomatoid form: In these tumors, a rich supply of blood vessels is there and these blood vessels are thin walled.

Sarcomatous form: It is highly cellular and anapalstic without whorl formation.

Gliomas

These are the tumors of glial tissue. The normal glial cells in the brain are astroglial, microglia, oligodendroglial and Ependymal cells. Those arising from astrocytes are called as astrocytomas, while those from the oligodendroglial are oligodendroglioma. Gliomas are rare among animals and are common in humans especially aged persons.

Astrocytomas: Besides dog, the tumors occur in the fowl, cattle, cat and horse. Astrocytomas are mostly found in the cerebrum and cerebellum, though other parts of the brain may also be affected. In all animals except in the fowl, the tumor is single but in the fowl it is multiple due to multi-centric in origin. Grossly the tumors are soft and circumscribed. Some may imperceptibly merge with the brain tissue. In the fowl these tumors are multilocular and cystic, containing a mucoid substance. Due to presence of Liofuchsin in the astrocytes these appear as yellow in colour. Microscopically astrocytes are in two forms, namely fibrillar or protoplasmic. The structure of the astrocytomas varies according to type of cell predominating the lesion.

The cells may be enlarged and all forms of intermediary type are seen. These are pleomorphic, having giant nuclei and multinucleated giant cells are also seen. Sometimes the cells may be arranged radially around the blood vessels. In more malignant types, the cells are highly pleomorphic; show many mitotic forms and also a few giant cells. Such tumors are also known as glioblastoma multiform.

Oligodendroglioma: These are very rare in animals. Histologically the tumor cells have a faintly staining, indistinct cytoplasm containing small, regular, round and hyper chromatic nuclei.

Ependymoma: These are the tumors composed of Ependymal cells. They are present around the ventricles of the brain and line the central canal of the spinal cord and choroids plexus. These ependyma were reported from horses, cattle and dogs. They are present in the fourth ventricles. The tumors grossly show either, cystic appearance or solid or papillary appearance. Histologically the cells may be arranged in cords or may show a papillary pattern. The cells are cuboidal or columnar or oval shaped with indistinct cell membrane. Pseudo-rosettes consisting of the Ependymal cells arranged in a circular fashion with clear central spaces are frequently seen. Mitotic figures may be seen in more anapalstic type of tumors.

Neuroblastomas and gnalgioneuroma

Neuroblastomas are a tumor consisting of immature undifferentiated neuroblasts

while gnalgioneuroma denotes a tumor consisting of well differentiated nerve cells and fibers. The neuroblastomas can originate in the central nervous system, but the majority occurs in the adrenal medulla. Neuroblastomas are a rapidly growing and malignant one, while the gnalgioneuroma is benign one. All gradations between these two varieties may be encountered. These are extremely rare in animals and have been reported in cattle, horse, dog and fowl. Young animals are more often affected. The tumors found in the adrenal medulla are also called as sympatho-blastomas and these are present in the sympathetic ganglia of the abdominal and pelvic regions. The cervical and thoracic ganglia are affected. Grossly the tumors which are encapsulated vary in size. They may be white or grey in colour. They are fibrous in consistency. Histologically, the neuroblastomas are highly cellular and consist of undifferentiated small round cells. Large number of mitotic figures is present. There may be rosettes of cells around central core of nerve fibers. The gnalgioneuroma consists more mature nerve cells and their fibers. The cells show Nissl substance. Mitotic figures are common.

The primary brain tumors are usually single, and do not metastasize to distant organs; gliomas being the most common. Malignant tumors are known as glioblastoma or gliosarcomas. However, no gliomas metastasize to locations outside the cranial cavity or spinal cord. The glioblastoma multiform that is arising from the glia of astrocytes is having varied appearance hence the term glioblastoma *multiform* Oligodendroglioma also occur in dogs, but is rare. The tumor infiltrates and destroys adjacent tissue. Tumors involving Ependymal cells as already described called as ependymoma.

Pinealoma is a rare neoplasm derived from the pineal body. It has been reported in horses and rats.

Secondary or metastatic tumors of central nervous system: These secondary reach the brain by metastasis. They are mostly observed in the cerebral hemisphere, and are multiple, which indicates their metastatic nature. The majority of these metastatic tumors have their primary site in the lung. In the dog, the original tumor is usually located in the mammary gland. In cats and cattle, a malignant lymphoma is the most frequent of the secondary tumors, mostly located in the spinal cord. Melanomas and haemangiomas are also among the more frequent metastatic neoplasms.

Chapter 9

Diseases of Endocrine System

Summary

A hormone –definition-its action -anterior pituitary hormones: Growth hormone, adrenocorticotrophin, thyroid stimulating hormone, follicle stimulating hormone, lutensing hormone, prolactin and melanocyte stimulating hormone. Posterior pituitary hormones; Antidiuretic hormone (vasopressin) and oxytocin-Adrenocortical hormones especially cortisol and aldosterone-Thyroid hormones: thyroxin, triodothyronin and calcitonin-Pancreatic hormones: insulin and Glucagon—Ovarian hormones: oestrogens and progesterone—Testicular hormones: testosterone-Parathyroid hormones: parathormone—Placental hormones: Human chorionic gonadotrophins, oestrogens, progesterone, and human somatomammotropin... Development of hypohysis cerebri (pituitary body)): The pars tuberalis consists of dorsal projections of cells along the infundibular stalk.—Physiological functions of the anterior pituitary hormones: Growth hormone—Abnormalities of growth hormone secretion: Panhypopituitarism: Excessive secretion ofADH. Other causes of Acromegaly. Thyroid gland—thyroid hormone -Colloid goiter:-different types, Adrenocortical deficiencies and excess hormonal disease conditions- medullary tumors.

Endocrine Pathology

Endocrine glands are specialized organs that produce hormone necessary for haemostasis. These are ductless glands and release hormones into the circulation, thereby arose various activities in the body. They are vital to the life. These glands have widespread and specific influence on various processes connected with metabolism, growth and reproduction.

Control mechanisms that regulate hormone synthesis and secretion are complex, but in general each endocrine gland is regulated by feedback mechanism. Diseases of endocrine glands are due to over production or under production of hormones. This leads to diverse clinical and pathological sequences, depending on the hormones involved. Their effect is felt not only in the adult but also in the developing foetus. In fact sub-normal function of the foetal endocrine function especially in ruminants may disrupt normal foetal development and result in prolongation of gestation period which is common in Guernsey and Jersey cattle. Prolongation of gestation period in sheep is due to the ingestion of plants during gestation results in the malformation of the central nervous system, targeting the

adrenal cortex which fails to differentiate into three distinctive zones resulting in less corticoid secretion.

The type of hormone secreted by endocrine glands could be categorised broadly into four types namely polypeptide hormones, steroid hormones, catecholamine and idothryonines hormones.

Polypeptide hormones: These hormones are water soluble. Endocrine cells which produce polypeptide hormones, have well developed rough endoplasmic reticulum, the assembled hormone, and a prominent golgi apparatus that packages hormone into secretory granules for storage and transport. Secretory granules are present only in those endocrine cells which secrete polypeptides and catecholamines. They are not present in the steroid hormone secreting cells. Secretory granules provide a mechanism for the storage of substantial amounts of preformed active hormone within the cells. The primary site of action of polypeptide hormone is the plasma membrane of target cells. Receptor proteins for the hormone are present on the outer surface of the plasma membrane. The receptors perform two key functions. First they recognize the active hormone from among other proteins to which the cell is exposed. The concentration of hormone surrounding the cells is much lower than that of other proteins. The hormone binds to the receptor site and forms a reversible hormone receptor complex.

The second function of receptor protein is conveying the message of bound hormone from the outside to the inside of target cells. The magnitude of this transmembrane signal depends on the concentration of hormone to which the target cell is exposed, the receptor for the hormone and the concentration of receptor on the target cells.

Function of hormone at cellular level: There appear to be a single common intracellular pathology for many different polypeptide hormones. It begins with the activation of an enzyme, adenylate cyclase, in the plasma membrane of the target cell. Cyclic adeno monophosphate (Cyclic AMP) is formed intraceullary from ATP and activates cyclic AMP dependent protein kinase. Protein kinase in turn activate or inactivate a variety of enzymes by phosphorylating them, using ATP as a source phosphate. The intracellular pathway for each polypeptide hormone subsequently branches into a multiplicity of pathway leading to a variety of effects on any given target cell.

When the cell receives a signal for hormone secretion, secretory granules are directed to the periphery of endocrine cell, probably by contraction of microfilaments. The limiting membrane of granules then fuses with the plasma membrane of the cell. The hormone containing granular core is extruded into the extracellular perivascular space by pinisocytosis or exocytosis. The granular core is fragmented subsequently and the hormone is rapidly transported through capillary fenestrate into the circulation. Hormone synthesized in excess of

requirement is degraded by fusion of hormone containing granules with lysosome.

Endocrine cells which produce polypeptide hormones, have well developed rough endoplasmic reticulum that assembles hormone, and a prominent golgi apparatus that package hormone into secretory granules for storage and transport. Secretory granules are present only in these endocrine cells which secrete polypeptides and catecholamines. They are not present in the steroid hormone secreting cells. Secretory granules provide a mechanism for the storage of substantial amounts of preformed active hormone within the cells.

Steroid hormones: Steroid hormone secreting cells are characterized by large lipid bodies in the cytoplasm that contain cholesterol and other precursor molecules. The lipid bodies are in close proximity to an extensive tubular network of smooth endoplasmic reticulum and large mitochondria, which contain the hydroxylase and dehydrogenase systems. This enzyme system function to attach various side chains of the basic steroid nucleus. These hormones having a basic nucleus of three cyclo-hexane rings and one pentane ring account for 15% of mammalian hormones. The primary site of action is the nucleus of target cell. Receptors are proteins that bind the hormone in the cytoplasm, and nucleus of target cell. Steroid hormones are lipid soluble and transport through cell membrane. They have long half life in blood. They bind to high affinity specific binding proteins in plasma. After binding to cytoplasmic receptors, the hormone receptor complex is translocated to the nucleus where the hormones are bind to receptors in the nuclear chromatin. This results increased transcription of messenger RNA and in turn increased protein synthesis.

Catecholamine and idothryonines hormones: This chemical group of hormones is tyrosine derivatives. They account for 45% of mammalian hormones present in the blood. These hormones are epinephrine, no-epinephrine secreted by the medulla and sympathetic nerve endings and idothyronines (thyroxine-triodo thyronine) produced by follicular cells of the gland.

The action of catecholamine are similar to that of polypeptides, whereas to those of idothyronines are more closely resemble the steroid hormone.

Pathogenic mechanism of endocrine diseases: 1) Primary function of an endocrine gland : In this mechanism, hormone secretion is subnormal due to destruction of secretory cells by a disease process, due to failure of an endocrine gland to develop properly or due to the result of specific biochemical defect in the synthesis of pathway of hormone. Destruction of secreting cells may be due to viral infection as the destruction of β-cells of pancreas results in development of diabetes in humans or it may be due to immune mediated injury as in thyroid gland. Persistent lymphocytic choriomenigitis infection in mice of pituitary especially of Somatotrophs resulting in failure of growth hormone release. Lymphocytic choriomeningitis in virus in mice has been shown to persist in thyroid follicular epithelium and pancreatic islet β-cells which lead to hypothyroidism and diabetes mellitus

without any morphologic damage to the cells. Venezuelan equine encephalomyelitis virus infection in hamsters has been shown to be capable of interfering with the production of insulin. Hypo function of the pituitary due to the failure of or pharyngeal ectodermal differentiation resulting in lack of hormone secreting cells adenohypophysis in dogs resulting in pituitary dwarfism.

Secondary hypo function of an endocrine gland: A destructive lesion on one endocrine gland interferes with the secretion of a trophic hormone. A trophic hormone is one that influences the activity of a particular gland. As a result of reduced secretion of trophic hormone, hypo function of the target organ occurs. Thus destruction of cells in pituitary results in hypo function of adrenal cortex, thyroid and gonads.

Primary function of an endocrine gland: The glands secrete excess hormone, with resultant failure of utilization of hormone by the body, as well degradation, resultant hyper function.

Secondary hyper function of an endocrine gland: Trophic hormone is secreted in excess, resulting in the secretion of hormone by the respective glands. This trophic hormone leads to long term stimulation and hyper secretion of hormone by a target organ. Hyper secretion adrenocortico-trophic hormone results in hypertrophy and hyperplasia of secretory cells of the adrenal cortex, and an excess secretion of cortisol.

Control mechanism that regulates hormone synthesis and secretion are complex, but in general each endocrine gland is regulated by a feedback mechanism. Disease of endocrine glands is due to overproduction of or under production of hormones. This leads to diverse clinical or pathological sequences, depending on the hormone involved.

Diseases of Endocrine system

The endocrine system consists of a highly integrated set of glands. These endocrine glands are collections of specialized cells that synthesize, store and release their secretions (hormones) directly into the blood stream.

The functions of the body are regulated by two major controls system namely the nervous system and the endocrine system. The endocrine system is concerned principally with control of the different metabolic functions of the body such as controlling the rates of chemical reaction in the cells or the transport of substances through cell membranes or other aspects of cellular metabolism like growth and secretion. Some hormonal effects occur in seconds, while others require several days simply to start and then continue for weeks, months or even years. 50 or more hormones are elaborated by a variety of organs and tissues.

A hormone is chemical substances that is secreted into the body fluids by one cell or a group of cells and that exerts a physiological control affect another cells of

the body. Some are local hormones and others are general hormones. Example of local hormones are acetyl choline released at the parasympathetic and skeletal nerve endings, secretin released by the duodenal wall and transported in the blood to the pancreas to cause a watery secretion from pancreas. Cholecystokinin released into the small intestine and transported to the gall bladder to cause contraction and to the pancreas to cause enzyme secretion, and many others. The general hormones are secreted by specific endocrine glands and are transported in the blood to cause physiologic functions at distant points in the body. Examples are growth hormone from the adenohypophysis and thyroxin hormone form the thyroid gland. Control mechanisms that regulate hormone synthesis and secretions are complex, but in general each endocrine gland is regulated by feedback mechanism. This may be either through the circulating level of another hormone as that of anterior pituitary control, or level of circulating metabolites such as glucose or calcium for the release of insulin or parathormone respectively or blood pH and oxygen tension in the case of chemoreceptor organs.

The following general hormone shave proved to be major significance and are discussed in detail.

Anterior pituitary hormones: Growth hormone, adrenocorticotrophin, thyroid stimulating hormone, follicle stimulating hormone, lutensing hormone, prolactin and melanocyte stimulating hormone.

Posterior pituitary hormones; Antidiuretic hormone (vasopressin) and oxytocin

Adrenocortical hormones especially cortisol and aldosterone

Thyroid hormones: thyroxin, triodothyronin and calcitonin

Pancreatic hormones: insulin and Glucagon

Ovarian hormones: oestrogens and progesterone

Testicular hormones: testosterone

Parathyroid hormones: parathormone

Placental hormones: Human chorionic gonadotrophins, oestrogens, progesterone, and human somatomammotropin.

Chemically the hormones are of two types' protein derivatives or steroid hormones. Hormones of the pancreas and anterior pituitary are proteins, the hormones of the posterior pituitary are peptides and those of thyroid and adrenal medulla are of derivatives of amino acids. The steroids are secreted by the glands derived from the mesenchyma zone of the embryo, including the adrenal cortex, ovary and testis. Most hormones are present in the circulating body fluids and tissues in extremely minute quantities, some in concentrations as low as one millionth of an mg that is pictogram / ml.

Diseases of endocrine glands are either due to over or under production of

hormones. Persistent viral infections are emerging as another mechanism of altered function; such infections when occurring within endocrine cells can lead to hypo function. This has been demonstrated by persistent lymphocytic choriomenigitis virus (LCMV) infection in mice, where the virus replicates in Somatotrophs and interferes with transcription of growth hormone gene. LCMV in mice also persist in thyroid follicular epithelium and pancreatic islet β- cells. This lead to hypothyroidism and diabetes mellitus again without any morphologic damage to the cells. Similarly in cattle in foot and mouth disease virus infections destruction of pancreatic cells and temporarily islet cell dysfunction is noticed. Similarly in the same way in poultry in avian encephalomyelitis pancreas is affected. Venezuelan equine encephalomyelitis virus infections in hamsters have been shwon to be capable of interfering with the production of insulin.

Hormone resistance due to absence of cellular receptors or intracellular metabolism leads to a deficient state, this occurs in the presence of normalor usually elevated levels of circulating hormone coupled with hyperplasia of primary endocrine organ.

Development of hypohysis cerebri (pituitary body): Pituitary body is developed from two sources. Its anterior part is developed as a diverticulum of ectodermal lining of the roof of the stomodeum and its posterior part is developed from the diverticulum of the floor of the forebrain vesicle (diencephalons) which is also ectodermal in origin. Before the communication between the stomodeum and foregut is established, the anterior lobe develops as a hollow diverticulum arising from the ectodermal covering of the back part of the roof of the stomodeum which is called Rathke's pouch. After passing through the mesodermal tissue between the roof of the stomodeum and floor of the fore brain vesicle along a canal called cranio-pharyngeal canal, the pouch like diverticulum comes to lie in front of the downward growth from the floor of the fore brain. The anterior lobe is at fist a hollow vesicle with walls lined by epithelial cells, the cells in the anterior and lateral walls of this vesicle proliferate and form cell groups which are gradually separated from each other by strands of fibrous tissue from the surrounding mesoderm. These cell groups with the intervening stroma form the pars anterior of the hypohysis. They also proliferate in the upper part of the posterior lobe and surround the infundibulum like a collar lying underneath the tuber cinerium and form the tuberal part of the hypophysis.

The adenohypophysis consists of three portions, the pars distalis, pars tuberalis and pars intermedia. In many species the adenohypophysis completely surrounds the pars nervosa of the neurohypophyseal system. The pars distalis is the largest of three parts of the adenohypophysis and contains the populations of endocrine cells that secrete the pituitary trophic hormones. The secretory cells are supplied with abundant capillaries that have fenestrate in their peripheral cytoplasmic extensions and are supported by the cytoplasmic processes of stellate or follicular or sustentacular cells.

The pars tuberalis consists of dorsal projections of cells along the infundibular stalk. It functions primarily as a scaffold for the capillary network of the hypophyseal portal system during its course form the median eminence to the pars distalis. The pars intermedia form the junction between the pars distalis and pars nervosa. It lines the residual lumen of Rathke's pouch and contains two populations of cells. In the dog, one of these cell types synthesizes and secretes adreno-corticotrophichromone similar to corticotrophs in the pars distalis.

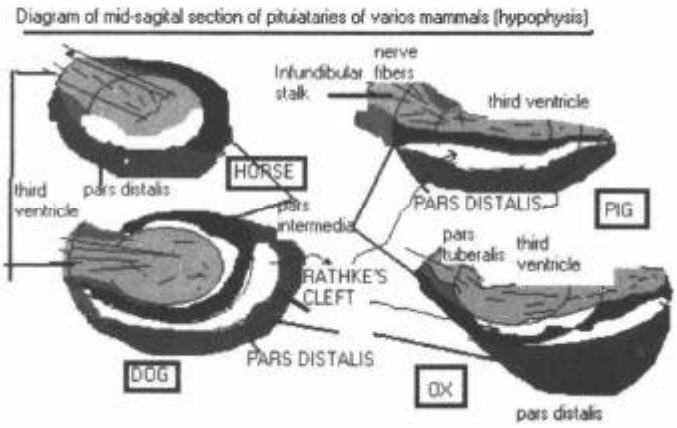
The posterior wall of the anterio lobe vesicle becomes thickened to form the intermediate part (pars intermedium) of the pituitary body which also consists of epithelial cells. The cavity of the anterior vesicle is thus reduced to a cleft lying between the pars anterior and pars intermedium of the hypophysis. The down growth from the fore brain is called infundibulum is at first hollow funnel shaped diverticulum from there floor of the plate of diencephalons. Afterwards its walls thickens and the distal portion becomes completely solid and form the posterior lobe of the hypophysis cerebri but the proximal portion which remains connected with the fore brain vesicle persist as a hollow recess called the infundibular recess of the third ventricle. The stalk of the Rathke's pouch ultimately disappears by the 9th week of foetal life but sometimes a minute canal is exist in the body of the sphenoid bone called craniopharyngeal canal marking the original site of the stalk of the buccal element of the gland. The posterior lobe being developed from the fore brain at first consists of nerve cells and neuralgia cells but later on it contains only neuroglial structure.

It should be noted that the pituitary body which influence the growth and control activities of the body, ovary, testis and uterus is of ectoderm in origin, having three different parts, via., buccal part from the roof of the primitive stomodeum, neural part from the floor of the third ventricle and the tuberal part form the proliferated cells at the root of the infundibulum stalk.

The neurohypophysis develops from the floor of the diencephalons which grows downward to make contact with the posterior wall of Rathke's pouch. Anterior pituitary secretes 6 important hormones and metabolically active substances. These hormones are follicular stimulating hormone, leutenising hormone, thyroid stimulating hormone, adrenocortico trophic hormone, growth hormone and prolactin (luteotropic hormone).

These are abbreviated as FSH, LH, TSH, ACTH, and GH, prolactin (luteotropic hormone or LTH).

The precursor molecule of ACTH is the propriomelanocortin (POMC) produces melanophore stimulating hormone α, β,γ; corticotrophin like intermediate peptide; β and γ lipotropin; α, β and γ endorphins. Although functionally distinct, these latter compounds and ACTH have functional overlap. A corresponding anterior pituitary cell exists for each hormone. Based on haematoxylin and eosin staining these cells have been recognized as acidphils, basophils and chromophobes. As



per immuno histochemical staining 5 cell types are identifiable in the pars distalis for 6 hormones (Gonadotrophs secretes both FSH and LH). A 6th cell type melanotroph is found in the pars intermedia. In the dog pars intermedia contains both melanotrophs and corticotorphs. Chromophobes are inactive basophils or acidophils. Cells of the posterir pituitary contain nerve fibers of axons and glial cells termed as pituicytes.

Hormones oxytocin and vasopressin which differ only by two amino acids are produced by large neurons located in the supraoptic and paraventricular nuclei. These hormones and their carrier proteins (neurphysins) are transported via unmyelinated axons through the suproptico-hypophyseal and paraventircular hypophyseal tracts to the posterior pituitary. Enroute, the hormones are produced to their final form, and are released from nerve terminals in the posterior pituitary. Actual hormones in tissue sections are seen as eosinophilic globules termed Herring bodies.

The adenohypophysis is in communication with the hypothalamus through two components, tubero-infundibular tract and the hypophyseal portal system. The releasing and inhibiting factors are produced in several hypothalamic nuclei by small neurons, which are located in the tuberal region and in the wall of the third ventricle. These factors are transported by way of axons to the infundibula. Here they leave the axons and enter the primary capillary bed of the portal system; they are transported to adenohypophysis to act on specific hormone secreting cells. It is the portal system that supplied bulk of blood supply to adenohypophysis.

All the major anterior pituitary hormones besides growth hormone exert their effects by stimulating target glands, the thyroid gland, the adrenal cortex, ovaries, the testicles and the mammary glands. The functions of each of these pituitary hormones are os intimately concerned with the functions of the respective target glands that except for growth hormone, does not function through a target gland but instead exerts an effect on all or almost all tissues of the body.

Table showing endocrine cells and hormones secreted by anterior pituitary

Cell type	Hormones	Cell characteristics	Primary hypothalamic hormones	Hormonal action
Somatotrophs (type 2 acidophil)	Somatotrophic hormone or growth hormone	H&E: Acidophilic granules, Pas-ve, Orange G+ve, E.M: Abundant dense granules size of 350 nm	Growth hormone releasing hormone, (somatomedin)growth hormone release inhibition hormone (somatostatin)	on post natal growth mediated through somatomedin from liver, chondrocytes, kidney, muscle and G.I, tract
Lactotrophs (type I acidophil)	Prolactin or lactogenic hormone	H&E: Acidophilic granules, PAS-ve, Azocarmine +ve, Erythrosine +ve. E.M: Sparse dense granules of 600-900 nm size	Chromotrophic	Essential for lactation
Gonadotrophs (δ-type 2 basophils)	Follicular stimulating hormone, Leutenising hormone	H&E. Basophilic PAS: +ve Aldehyde, fuchsins: -ve. E.M. dense granules: 200-250 nm in size	Leutenising hormone releasing factor	Stimulates granulosacells Stimulates theca cells and Leydig cells
Thyrotrophs (β-basophils or type1-basophils)	Thyroid stimulating hormone	H&E: Basophils PAS:+ve, Aldehyde fuchsins +ve, E.M: Dense granules of 150 nm size	Thyroid stimulating releasing hormone	Stimulates thyroid cells
Corticotorphs (type-3basophils)	1.Adrenocorticotrop hc hormone 2.γ-lipotropins 3. β-endorphins	H&E:Basophilic PAS: weakly +ve Aldehyde fuchsin:+ve EM: Variable dense granules of 200-400 nm size and cytoplasm have filaments	Corticotrophi releasing hormone	stimulates cortisol release by adrenal cortex lioplysis and MSH action opiate like effects
Melanophors	1)α-melanocyte stimulating hormone 2) CLIP 3)β-endorphin	H&E: Basophilic PAS: +ve	Melanotrphic releasing factor	Stimulates melanocyte proliferation, cortisol release and neural growth and regeneration Corticotrophin Opiate like effects

The releasing hormone peptides are GnRH, gonadotrophins (LH), releasing hormone (GnRH releases both LH and FSH), thyrotrophic releasing hormone (TRH). Corticotrophin releasing hormone (CRH), TRH has a prolactin releasing effect, a specific prolactin releasing hormone does not exist.

Physiological functions of the anterior pituitary hormones

Growth hormone is also called Somatotrophic hormone or somatotropin, is a small protein molecule containing 191 amino acids in a single chain and having a molecular weight of 22,005. It causes growth of all tissues of the body that are capable of growing. It promotes both increased size of cells and increased mitosis with development of increase number of cells. It causes growth of all tissues of the body that are capable of growing. It promotes both increased sizes of cells and incresed mitosis with development of increased number of cells. Once the epiphyses of long bones have united with the shafts, further growth of the bone cannot occur even though most other tissues of the body can continue to grow throughout life. Growth hormone does not have a direct effect on the growth of cartilage and bone, both of which must grow if the overall structure of the animal to increase. However growth hormone does indirectly stimulate their growth by causing several small proteins, called collectively as somatomedin, to be formed in the liver and perhaps in the muscle and kidneys as well; somatomedin in turn acts directly on the cartilage and bone to promote their growth. Somatomedin is required for deposition of chondroitinsulfate and collagen, both of which are necessary for growth of the cartilage and bone. Once the epiphysis of long bone shave united with the shafts, the bones cannot longer increase in length, but they can continue to increase in thickness. Therefore excess growth hormone after adolescence cannot cause further increase in height of a person but cause disproportionate growth of the membranous bones and excessive thickening of all bones.

Growth hormone effects by increasing rate of protein synthesis in all cells of the body. Growth hormone promotes increased mobilization of fatty acids from adipose tissue and increased use of the fatty acids for energy and decreased rate of glucose utilization throughout the body. Thus in effect growth hormone enhances the body protein uses up the fat stores and conserved the carbohydrate. It is probable that the increased rate of growth results mainly from the increase rate of protein synthesis.

Thus growth hormone in short brings about protein synthesis by interfering in portein breakdown, inhibiting conversion of amino acids into urea and accelerating protein synthesis from amino acids. Probably Somatotrophic hormone causes the release of glucagon, which in turn raises the glucose level of the blood by glycogenolysis in liver. It probably prevents the entry of glucose into the cell and also inhibits the action of hexokinase. STH is antagonistic to insulin and so is diabetogenic. This hormone has profound effect on lactation, which can induce and enhance lactation by STH administration.

In the tissues growth hormone enhances the conversion of fatty acids to acetyl CoA with subsequent utilization of this for energy. Occasionally fat mobilization under the influence of excessive amounts of growth hormone is so great that excessive quantities of aceto-acetic acid are formed by the liver and are released into the body fluids, thus causing ketosis. Growth hormone leads to moderately increased blood glucose concentration. This in turn stimulates the β-cells of the islets of Langerhans to secrete extra insulin. In addition to this effect, growth hormone has a moderate, direct, stimulatory effect on the beta cells as well. The combination of these two effects sometimes so greatly over stimulates insulin secretion by the beta cells that they literally burnout. When this occurs the person envelopes diabetes mellitus. At least three others can do the same. These are ACTH, TSH and prolactin. Cortisol then increases theblood glucose concentration by increasing the rate of gluconenogenesis. This effect, quantitatively is probably equally as diabetogenic as the effect of growth hormone.

Pituitary diabetes: Thus the increase in secretion of growth hormone or generalised increase in secretion of all the anterior pituitary hormones causes elevated blood glucose concentration; this condition is called pituitary diabetes and it differs from diabetes mellitus,which results from insulinlack, the following ways. First in pituitary diabetes the rate of glucose utilization by the cells is only moderately depressed, in comparison with almost not utilization in diabetes mellitus. Second the blood glucose concentration is relatively refractory to insulin that is decrease very little because inadequate insulin is already available in the body; the protein problem instead is the anti-insulin effect of growth hormone and other pituitary hormones that blocks insulin stimulation of glucose transport into the cells. Third mainly of the side effects that results from reduce carbohydrate metabolism diabetes mellitus are absent in pitutiary diabetes.

Growth hormone secretions controlled by through inhibitory hormone somatostatin or factors that control growth hormone releasing factors.

Abnormalities of growth hormone secretion: Panhypopituitarism: This term means decreased secretion of all the anterior pituitary hormones. The decrease in secretion may be congenital present from birth or it may occur suddenly or slowly at day time during the life of the individual.

Dwarfism: This is due deficiency of anterior pituitary secretion during childhood. The dwarf usually does not exhibit specific thyroid deficiency or adrenocortical deficiency for the entire body remains so small that only small quantities of thyroid stimulating and adrenocorticotrophic hormones are needed. Dwarf does not pass through puberty and never secretes a sufficient quantity of gonadotrophic hormones to develop adult sexual functions.

Symmond's disease (pituitary chachexia) or Sheehan's syndrome: This is found only in females, due to postpartum necrosis of the pituitary consequent on thrombosis following haemorrhage. Hence severe Hypopituitarism develops. The

characteristic are severe chachexia, loss of sexual function, weakness, low metabolic rate, loss of hair and pigmentation, mental apathy and drowsiness, microsplachnia and extreme dehydration and emaciation.

Since trophic hormones are not secreted, there is atrophy and fibrosis of the thyroid, adrenal, ovaries and parathyroids together with the symptoms and lesions consequent on the deficiency of the hormones secreted by these glands and structures.

Froehlich's syndrome-dystrophia adiposoa genitalis: This develops probably due to the pressure by a tumor or hydrocephalus and is mostly found in human females. This is characterized by obesity wherein there is disproportionate and excessive accumulation of fat on the abdomen, buttocks and thighs, while other parts are thinner; genital hypoplasia and decreased sexual function, mental retardation; thin skin and hair and reduced sweat secretion. In males it is feminizing with the characteristic distribution of fats in females.

Diseases due to hypo and hyper function of endocrine glands

Name of the endocrine gland	Hypo function-name of the disease	Hyper function-name of the disease
pituitary	Pituitary dwarfism	Gigantism in younger ones Acromegaly in adults
thyroid	goiter	Myxoedema
Adrenal cortex	Addison's disease	Cushing's syndrome, adrenal virilism (Hairsuitism)
Adrenal medulla	--	Increased blood pressure(essential hypertension)
parathyroid	—	Osteoporosis
Posterior pituitary	Pituitary dwarfism or infantilism, Symmond's disease or Sheehan's syndrome	Froehlich's syndrome or dystrophy adipose genitalia, Diabetes insipidus

Diabetes insipidus: Normally under the influence of the Antidiuretic hormone of the neurohypophysis 80% of water in glomerular filtrate is reabsorbed by the epithelium of Henle's loop and distal convoluted tubules. But if the secretion of the Antidiuretic hormone is interfered with due to failure of the hypothalamic-hypophyseal system, reabsorption of water from glomerular filtrate does not occur and large quantities of urine with low specific gravity are passed and this condition is known as diabetes insipidus. The causes are as follows.

ADH in moderate to high concentrations has a very potent effect of constricting of the arterioles and therefore of increasing the arterial pressure. Also one of the most powerful stimuli of all for increasing the secretion of ADH is severe loss of blood volume. As little as 10% loss of blood will promote a moderate increase in

ADH secretion and 20% are more blood loss can causes much as 50 to 100 times normal rates of secretion. The increased secretion is believed to result mainly from the low pressure caused in the atria of the heart by the low blood volume. The relaxation of the atrial stretch receptor supposedly elicits the increase in ADH secretion. However, the baroceptors of the carotid, aortic and pulmonary regions also participate in the control of ADH secretion.

Other factors that frequently increase in the output of ADH include trauma, pain, anxiety, and drugs such as morphine, nicotine, tranquilizers and some anesthetics. Thus ADH has vasopressive action.

Another hormone liberated by posterior pituitary is oxytocin. The hormone oxytocin in accordance with its name powerfully stimulates the pregnant uterus. especially towards the end of gestation. The oxytocin is carried by the blood to the breast where it because contraction of myoepithelial cells, which lie outside of and form a lattice work that surrounds the alveoli of the mammary glands. Thus this hormone is essential for milk let down or ejection in animals and mammals. Oxytocin promotes fertilization of the ovum by causing uterine propulsion of the male semen upward through the fallopian tubes.

Both oxytocin and ADH (vasopressin) are polypeptides containing nine amino acids. These two hormones are almost identical except that in vasopressin phenyl alanine and arginine replace iso leucine and leucine of the oxytocin molecule.

Primary or hypothalamic diabetes insipidus is the result of deficient secretion of ADH due to idiopathic in origin as seen in Bralleboro strain of rats and autosomal recessive trait results in failure to synthesize ADH and neurophysin.

Nephrogenic diabetes insipidus: Deficient in the renal tubular receptors for ADH. Affected individuals do not respond to the administration of ADH.

Excessive secretion ofADH: Elaboration of ADH by non-endocrine tumors. Secondary diabetes insipidus results from neoplastic destruction of pars nervosa or it hypothalamic connection due to adenomas of anterior pituitary due to inflammatory lesions and trauma to the posterior pituitary stalk or diseases leading to necrosis of neurons in hypothalamic nuclei. Lesions are also seen due to nematode larval migration and with glial cell tumors.

Somatotrophic neoplasms: Tumors related to this in humans are Acromegaly, and gigantism. They are composed of either acidophilic or chromophobe. In young animals it results in gigantism where extremely lengthened long bones are seen. In adults whose epiphysis has been closed, the bones grow heavily and thicker producing large hand, feet and skull. This is called Acromegaly (acro-extremity). Acromegaly with enlargement of skull, mandible, limbs and feet are common changes. Viscera are enlarged (splanchnomegaly or microsplachnia) and fibrous hyperplasia of skin and subcutaneous tissue is common. Nose, lips and ears become large. Kyphosis is also seen. Impotence in the male and amenorrhea in the human

females are common. These changes results in the production of somatomedin which stimulate formation of cartilage. Excessive STH secretion leads to diabetes mellitus. This is caused by interference with tissue glucose up take and insulin resistance. Hypoglycemia stimulates growth hormone release and hyperglycemia suppresses growth hormone release.

Other causes of Acromegaly in humans include release of growth hormone from extra pituitary tumors of pancreas, lung, ovary and breast. Excessive release of growth hormone is seen from hypothalamic tumors and other tumors of pancreatic islet cell tumors, adrenal adenomas, and pheochromocytoma.

Corticotrophin secreting tumors (adenomas) can arise in the pars intermedia of dogs. This tumor consists of many colloid filled acini or follicles, which are lined by tall ciliated often columnar epithelium. Solid arrays of chromophobic cells are scattered among the acini. Chromophobic cells having acidophilic cytoplasm without basophilic granules. This causes Cushing's disease. Larger tumor results in compression of the posterior pituitary and infundibular stalk leading to diabetes insipidus.

In horse adenomas of pars intermedia have been detected. Clinical symptoms are polyphagia, Hairsuitism, muscle wasting, hyperglycemia, Glycosuria, polyuria, polydyspia, progressive debilitation and increased incidence of bacterial and fungal infections.

Thyroid gland

The thyroid gland is an endocrine organ found in all vertebrates. In mammals it is usually bilobed gland located just caudal to the larynx, near the trachea. In some mammals the two lobes are connected by an isthmus that lays across the ventral aspect of the trachea.

The embryonic development of thyroid starts from the root of the tongue at the foramen caecum; the thyroid originates as a down growth of the epithelium which forms thyroglossal duct.

The lateral walls of the pharynx in embryo present a series of paired sacculations that bulge outwards towards the ectodermal grooves, five sets are formed but the last pair are rudimentary and merge in the fourth pair. Each pouch develops a dorsal and ventral wing. Each pouch, in its outward expansion, pushes a side the mesenchyme and come into contact with the overlying ectoderm fuses with it and forming a closing plate. The IST and 2nd pouches open into a broad lateral expansion of the pharynx. The 3rd and 4th grow outwards and communicate with the pharynx through narrow ducts.

The IST pouch retains its lumen and differentiates into the Eustachian tube and the tympanic cavity or the middle ear. The overlying ectodermal groove forms the external acoustic meatus and the drums of the ear. The 2nd pouch is greatly

reduced and becomes the fossa and covering epithelium of the palatine tonsil. The 3rd and 4th and 5th lose all the traces of lumen and give rise to ductless glands, thyroids, thymus and parathyroid.

The main mass of the thyroid gland develops from the floor of the pharynx, an endodermal packing mid plane about the level of the IST pharyngeal pouches in the thyroid diverticulum which soon becomes a solid mass attached to the pharynx by a narrow neck-the thyroglossal duct. This duct atrophies and the thyroid primordia is converted into a two lobed structure and settles to transverse position with a lobe on either side end of the trachea. Later on two bodies, the ultimobranehial bodies from the 5th pouch come into contact with the main mass and fuse it. Sometimes accessory thyroid maybe derived from the detached portion of the main primordia.

Parathyroid: The dorsal wings of 3rd and 4th pouches thicken to solid masses of cells and form Th primordia of the parathryoids. They are son set free from the pharynx and are drawn along the migrating thymic primordia which deposit them in the lobes of the thyroid.

The thyroid develops from the end of the duct, with the remainder degenerating before birth. Persistence of portions thyroglossal duct into an adulthood can give rise to thyroglossal cysts. Should the duct not descend an adequate distance, the thyroid may be placed abnormally high, when it is carried too far, the thyroid may occur within the mediastinum.

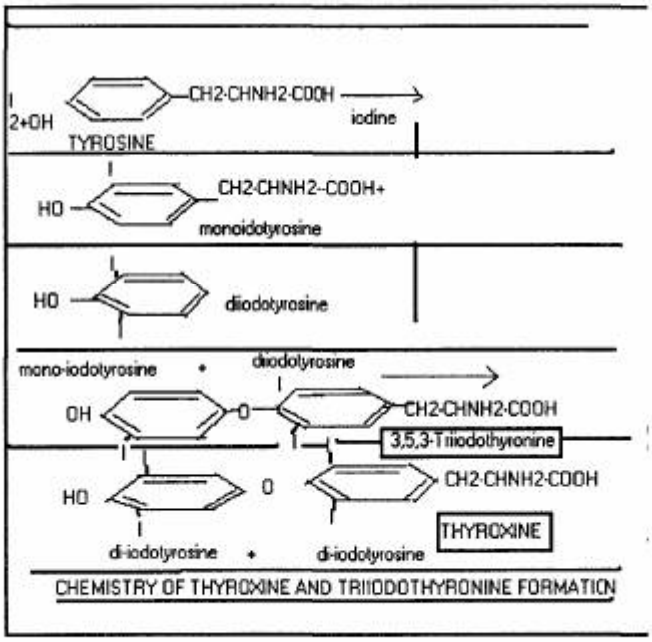
In addition to vascular, nervous and connective tissues, the thyroid has two types of endocrine cells. The preponderant epithelial cells are follicular cells that are arranged into acini or follicles, and which consists of cells arranged circumferentially around a central mass of colloid material.

The epithelial cells maybe tall columnar, cuboidal or flattened depending on their secretory activity. These follicular cells concentrate iodide from the circulating blood. In the course of several enzymatic reactions they form thyroglobulin, which stored as colloid and the subsequently secreted as thryoxine and triodothyronine.

Synthesis and release of thyroid hormone involve several steps.

1. Circulating iodide is trapped and transported against a gradient toward the follicular lumen.
2. Iodide is oxidized by iodide peroxidase to iodine.
3. All the microvillus border of follicular cell and colloid, iodine binds to the tyrosine residue of thyroglobulin (a glycoprotein synthesized by follicular cells). The result is the formation of bound monoidotyrosine and diodotyrosine within thyroglobulin.
4. These then undergo peroxidase dependent coupling, either as two molecules of Di-iodothryonine or one more of di-idothryonine or one molecule of mono idothyronine, the final form of circulating thyroid hormone.

5. Though the process of endocytosis of thyroglobulin and it proteolysis within phagolysosomes, T3 andT4 are released from the base of follicular cells into perifollicular capillaries and enter the circulation bound to thryoxine-binding globulin. T3 less firmly bound to protein than is T4 and is more readily available to tissues. The thyroid gland is the largest of the endocrine organs that function exclusively as an endocrine gland. The basic histological structure of the thyroid is unique for endocrine glands, consisting of follicles of varying size 20 to 250 ìm that contain colloid produced by follicular cells. The follicular cells are cuboidal to columnar and their secretory parity is directed toward the lumen of the follicles. An extensive network of capillaries provides the follicular cells with an abundant blood supply.



The synthesis of thyroid hormone is unique among endocrine glands because the final assembly of hormone occurs extracellularly within the follicular lumen. The assembly of thyroid hormone within the follicular lumen is made possible by unique protein (thyroglobulin) synthesized by follicular cells. Thyroglobulin is a high molecular weight glycoprotein synthesis in successive subunits on the ribosomes of the endoplasmic reticulum of follicular cells. The constituent amino acids that are tyrosine and other carbohydrates are derived from the circulation. The amino acid tyrosine an essential component of thyroid hormone is incorporated within the molecular structure of thyroglobulin. Iodine is bound to tyrosyl residue in thyroglobulin at the apical surface of follicular cells to form successively monoidotyrosine and di -diodotyrosine. These combine to form the two

biologically active idothryonines secret by the thyroid gland. Thryoxine is rapidly bound in plasma to albumin and three globulin fractions and triodothyronin is bound to albumin and one globulin fraction in dogs. TSH is conveyed to thyroid follicular cells where it binds to the basal aspect of the cell, activates adenyl cyclase, and increases the rate of biochemical reactions concerned with the biosynthesis and secretion of thyroid hormones. If the secretion of thyrotrophin is sustained thyroid follicular cells become more columnar and follicular lumina become smaller due to increased endocytosis of colloid.

Thryoxine and triodothyronin once released into the circulation act on many different target cells in the body. It is essential that thyroxin should prime each and every cell from any metabolic activity.

The subcellular mechanism of action of thyroid hormone resembles that for steroids, in that free hormone enter target cells and bind to cytosolic-binding protein. Free triodothyronin initially bind to receptors on the inner mitochondrial membrane to active mitochondrial energy metabolism and subsequently binds to nuclei receptors and increase transcription of the genetic message to facilitate new protein synthesis.

The function of thryoxine areas follows. It is to maintain a high rate of metabolism. The rate of metabolism is affected by the hormone acting at one or more points in the Kreb's citric acid cycle. Oxygen utilization is stimulated. Thryoxine because increased utilization carbohydrates increased catabolism of proteins and increased oxidation fats. There is loss of weight in hyperthyroid patients. Protein synthesis is enhanced, increased thryoxine stimulates the activity of central nervous system and so the animal is jumpy, nervous and irritable and hyperactive. Thryoxine cause hepatic glycogenolysis and so hyperglycemia and it also affect the normal reproductive functions. In hyperthyroidism and organ may not be produced and so thryoxine is required for libido. In the female the litter size maybe reduced, milk production is lowered and cysts form into ovary leading to sterility. Thryoxine raised the metabolic rate hence the temperature of the body is raised.

Hypothyroidism occurs in endemic areas where iodine deficiency is there. There is enlargement of the thyroid gland. This is called as goiter where there is Noninflamatory and nonneopalstic enlargement of thyroid all around the neck region. The condition found in young growing children is called cretinism. Cretinism may be sporadic or endemic. Sporadic cretinism occurs in young of healthy. Endemic cretinism occurs in areas where the incidence of goiter is common in a man and animals. In fact cattle and other animals where they are reared in endemic goiter animals are short, stumpy and may not grow. In India, it is common to find variety of breeds in hilly areas, where goiter is there short breeds of cattle. The height of the animal may not reach more than 3 feet. Common In punganur breed in Andhra Pradesh, Malanad giddas in Karnataka. These are cattle.

Symptoms in man: The cretin is dwarf, physically sexually and mentally. Growth is arrested, bone are brittle, abdominal muscles are flabby leading to pendulous abdomen, skin is dry and cold, lips and face are swollen, mouth is half open ways and the tongue is largest patient is extreme lethargic and have a vacant idiotic like and the gonad are ill developed. What was intended to be created in the image of God has become what has been called the untouchable of nature and of want of little iodine. Calves usually are either born dead or die within a day or two. Animals have Myxoedema and alopecia. The foetal placenta is retained. There is welling of the throat (goiter) and it may be so large that foetal dystocia may develop and it obstructs the pelvic cavity in parturition and passing of the foetus through birth canal. Growth of cranial, body and limb bones are arrested. Eruption of teeth and second dentine retarded. Deafness, idiocy and hypoplasia of the pituitary maybe noticed.

Hypothyroidism in adult is called Myxoedema. This seen in thryoidectomy patients, following an earlier ever hyperthyroidism atrophy and fibrosis of thyroid due to unknown etiology.

Clinically the patient is lethargic, heavy and has not inclination to move. She is cold and feels cold. The skin is dry and rough and hair is lost. The face is puffed and broad. The basal metabolic rate is low and heart rate is lower than normal (bradycardia). Serum cholesterol level is high. In the subcutaneous and other connective tissue there is an accumulation of mucoid or myxomatous substance, which gives the puffed up appearance of the face. Females are frigid and become sterile while males are impotent. The thyroid gland is atrophic and hard. In some place it is just a mass of fibrous tissue.

Hypothyroidism in cattle is manifested by sluggishness with agalactia, silent heat, retained placenta, stillbirths and a tendency to prurient endometritis. In hypothyroidism there is decrease in metabolic rate, oxygen utilization in the liver, kidney and muscles, cardiac output is lowered, blood pressure is lower, nervous function and myelination is affected, gut motility is interfered and animals appear sleepy, absorption of glucose, phagoyctic activity of leukocytes affected.

Grossly and histologically the changes are of goitrous.

Goiter is non-inflammatory and non-neopalstic enlargement of thyroid gland. Colloid goiter represents the involutionary phase of diffuse hyperpalstic goiter in young adult and adult animals. The marked hyperpalstic follicular cells continue to produce colloid, but endocytosis of colloid is decreased due to diminished pituitary TSH levels in response to the return of blood thryoxine and triodothyronin to normal. Both thyroid lobes are diffusely enlarged but more are translucent and lighter in colour than with hyperpalstic goiter.

Long term perturbations of the pituitary-thyroid axis by various xenobiotic or physiologic alterations like iodine deficiency are more likely to predispose the

lab animals to a higher incidence of proliferativelesions than in the case in human thyroid. Many drugs and chemicals are goitrogenic in that they disrupt one or more steps in the biosynthesis as and secretion of thyroid hormones, resulting in subnormal levels of T_3 andT_4, associated with compensatory increased secretion of TSH levels.

Histologically goiter could be divided as parenchymatous goiter, colloid goiter, nodular or adenomatous goiter and exophthalmia goiter. In the parenchymatous goiter is characterized by hyperpalstic changes in the thyroid. Grossly the thyroid gland is enlarged, meaty and firm. Histologically hypertrophy of the follicular epithelium is seen to start with. The cells become tall and plump and so encroach into the lumen that is either reducesd in size or even obliterated. Soon there is drop in colloids. Later there is hyperplasia of these cells and soon find a papillary projections into the lumen, completely filling it. There may be formation of new follicles, in the midst of new formed clusters of the epithelia cells. Histologically it may stimulate a papillary carcinoma but in the absence of anaplasia of the cells an invasion of the basement membrane this can be concluded that it is not of tumorous origin.

Colloid goiter: This is also called simple goiter. This is seen wherein animals are fed with low levels of iodine in soil and water, excessive demands of body to thyroxin needs as seen adolescence, pregnancy, disease conditions interfering with assimilation of iodine as like gastroenteric diseases of animal's indigestion goitrogenic substances like thiourcial and Soya beans.

Goitrogenic substances interfere in the synthesis of thryoxine; either they interfere with iodine intake by the gland or like sulfonamides.

Many drugs and chemicals are goitrogenic in that they disrupt one or more steps in the biosynthesis and secretion of thyroid hormone, resulting in sub normal levels of T_4 and T_2 associated with the compensatory increase secretion of pituitary TSH. The initial step in the biosynthesis of thyroid hormone is the up take of iodide from the circulation and transport against a gradient across follicular cells to lumen of the follicles. Perchloarate, thiocyanate inhibit iodide transport; a wide variety of chemical drugs and xenobiotic affect inhibit the organification thyroglobulin include thiourea, thiourcial propyl thiourcial carbimazole, aniline derivative, sulfonamides, para-aminslaycylic acid and antpyrines. Decrease in lysosomal protease activity, inhibition of colloid droplet formation and inhibition of TSH mediated increase in cyclic AMP Certain chemicals and irradiation appear to have a direct effect on the thyroid gland, resulting in genetic damage that leads to cell transformation and tumor formation.

Nodular thyroid hyperplasia is seen in old horses, cats and dogs, the affected lobes are moderately enlarged and irregular in contour. Nodular goiter in most is endocrinologically inactive and encountered in as an incidental lesion at autopsy.

On section the nodules are translucent and may contain cysts or vesicles filled with gelatinous colloid.

Histologically the picture is variable. All gradation may be found in different nodules, from the picture of a colloid goiter to that of hyperpalstic goiter. These nodules contain dilated acini and are filled with colloid and having flattened epithelium. In certain other placed papillary projection of the epithelium obliterating the lumen maybe found. Retrogressive changes leading to necrosis with subsequent softening and liquefaction are responsible for cyst formation (pseudo cysts). The connective tissue which is increased undergoes hyalinization. Calcification (calcareous goiter) and metaplasia in to bone (osseous goiter) of the connective tissue may also be encountered.

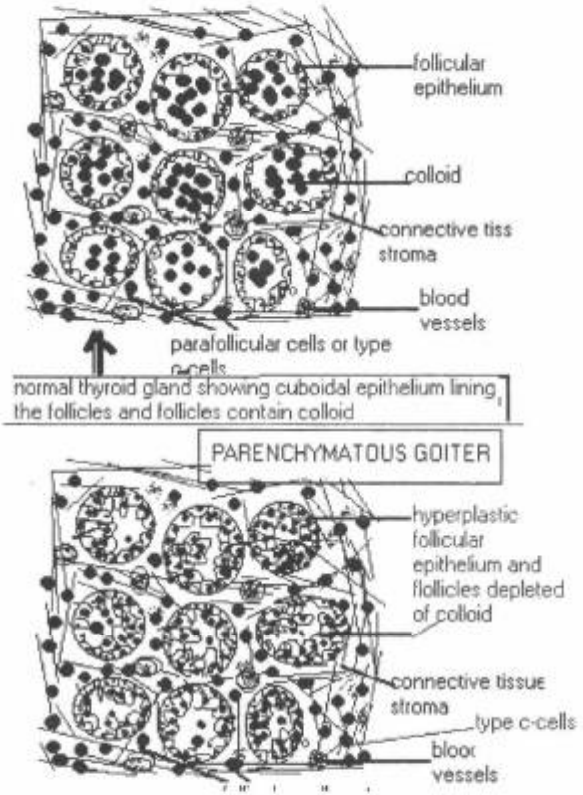
VI. Exophthalmia goiter: (Grave's disease), Bassedow's disease or primary thyrotoxicosis: this disorder of thyroid gland found in man is probably not seen in animals. Women are more often affected than men.

The exact cause of this condition is till obscure. Some kind of shock probably psychic, connected with sex is suggested being a causative. There is genetic predisposition of the condition. Lesions of the anterior pituitary are suggested by some. A long acting thyroid hormone (LATS), probably γ- globulin is responsible for this. This maybe an autoimmune thyroiditis. The theory is that the colloid is never come into contact with the blood in the life time. Whenever there is rupture of acini or with viruses and if the colloid have had the contact with blood, antibodies against this colloid liberates bring about the synthesis of LATS. The thyroid is infiltrated with lymphocytes and plasma cells around the disrupted colloid.

Clinically there may not be enlargement of the thyroid. The following are the characteristic symptoms. Protrusion of the eye ball called as exophthalmia, tachycardia, muscular tremors, high basal metabolic rate, weight loss and sweating.

Histologically the follicularepithelium is tall columnarand hyperpalstic. Papillary projections into the acini are often seen. Colloid is scanty in the acini and is thin and watery; vacuoles may be present in the colloid near the epithelium suggesting the resorption of the colloid by the cells. Throughout the stroma is found lymphocytic infiltration.

Grossly the gland is meaty, darker in colour and on section is not translucent but fleshy. Myocardial degeneration and fibrosis is seen. Muscular weakness and increased amount of fat and water in the eye and the extra-orbital muscles are swollen and firm. Retraction of the eye lids occurs so that the sclera is visible. These lesions are supposed to be due to the actin of an exopthalmus producing substance which is distinct from the thyroid stimulating hormone.



The most sensitive and accurate method for evaluation of thyroid function is measurement of blood thryoxine, T_4 and triodothyronin T_3 levels by radioimmunoassay. The normal blood levels of thryoxine in the dog are 1.5-3.6ig /dl and triodothyronin is 48-154 ng/dl.

Myxoedema may develop and produce a characteristic conical appearance in long standing or severe hypothyroidism. There is accumulation of much in the dermis and subcutis. This material bind considerable amounts of water and produces marked thickening of skin. This clear around the face and head where normal folds disappear. The eye lids appears as thick and drooping, thus contributing the sad facial expression. The skin feels thick and doughy, but the characteristic pitting observed with other types of oedema does not occurs with Myxoederma. Abnormalities of reproduction are common. Lack of libido and reduction in sperm count in males. The serum cholesterol level is elevated. Protein bound iodine levels are reduced. Atherosclerosis of coronary, cerebral and other vessels may develop in dogs. Corneal lipidosis is observable.

Tumors of thyroid: Adenomas. These are classified as follicular or papillary. Microfollicular adenomas consist of tumor cells arranged in miniature follicles with small amounts of colloid or in absence of colloid. Follicular adenocarcinoma is also seen in animals.

Tumors of the thyroid

The incidence of thyroid tumors follows closelythat of goiter and so it is prevalent among animals suffering from that condition. Therefore, it has a geographic distribution being found frequently in goiter belts. Tumors of the thyroid are common in human females between the age groups of 40 to 50, when they are in periods of menstrual cycles. It is rather difficult to differentiate hyperplasia of thyroid from adenoma. Actually, the nodular goiter described is an adenoma, according to some adenoma of the thyroid in horse, while adenocarcinoma is found mostly in aged dogs.

Grossly the adenoma is a small, rounded, well encapsulated tumor that is demarcated from the surrounding tissue. It is rather difficult to distinguish an adenoma from normal thyroid, but acing of the adenoma is smaller. The tumor is well demarcated from the rest of the gland and it may cause pressure atrophy of the normal tissue.

Histologically there may be formation of acini or the cells may be arranged as solid masses. The cells are low columnar or cuboidal and have an acidophilic granular cytoplasm and an oval hyper chromatic nucleus. Mitotic figures are common. Sometimes they form papillary projections into the lumen. Hemorrhages are seen. Connective tissue stoma is scanty. Metastases are common. These are seen in the lungs mostly. These lesions are found in other organs. Metastases may not resemble parent tissues.

Adenomas may produce hyperthyroidism and thyrotoxicosis. The adenomas are always fatal.

Thyroid C-cells and calcitonin: Calcitonin is secreted by thyroid -C cells in response to hypercalcemia which lowers plasma calcium. C-cells are distinctly from follicular cells, which secrete thryoxine and tri-idothyronines. They are situating within the follicular wall or between follicular cells or as small groups between follicles. They do not border the follicular colloid directly and the secretory material goes to the interfollicular capillaries.

Calcitonin is a large polypeptide with a molecular weight of approximately 3000 and having a chain of 32 amino acids.

The concentration calcium ions in plasma and extracellular fluids are the principal physiologic stimulus for the secretion of calcitonin by C-cells. Calcitonin is secreted continuously under conditions of normo calcemia, but the rate of secretion is increased greatly in response to elevation in blood calcium. Hyperplasia of C-

cells occurs in response to long term hypercalcemia. When the blood calcium is lowered the stimulus for calcium secretion is diminished, and numerous secretory granule accumulates in the cytoplasm C-cells. The storage of large amounts of preformed hormone in C-cells and rapid release in response to moderate elevations in blood calcium probably are a reflection of the physiologic role of calcitonin as an emergency hormone to protect against the development of hypercalcemia. Calcitonin secretion is increased in response to a high calcium meal. Gastrointestinal hormones may be important in triggering the early release of calcitonin to prevent the development of hypercalcemia following ingestion of a high calcium meal.

Calcitonin exerts its function by interacting with target cells primarily in bone and kidney. The action parathyroid hormone and calcitonin are antagonistic to be resorption but synergistic with deceasing the result of tubual reabsorption of phosphorus. The hypocalcaemia effects of calcitonin are primarily the result of decreased entry of calcium from the Skelton into plasma, due to a temporary inhibition of parathyroid hormone stimulated bone resorption. The hypophophetemia develops from a direct action of calcitonin, increasing the rate of movement of phosphate out of plasma into soft tissue and bone, and as well as from inhibition of bone resorption. The actin of calcitonin is not dependent on vitamin D since it acts both in vitamin D deficient animals and following the demonstration of large doses of Vitamin D. Specific structural alterations are produced by calcitonin in osteoclasts which have specific receptors for the hormone on their surface. The effect of parathyroid hormone on increasing bone resorption become manifest in the presence of calcitonin.

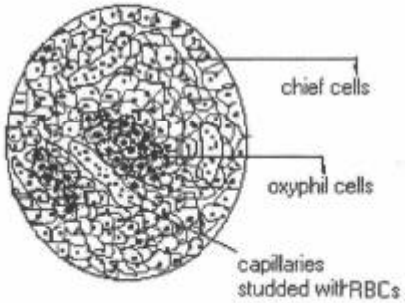
Both calcitonin and parathyroid hormone decrease renal tubular reabsorption of phosphate, leading to phosphaturia.

Parathyroid glands: Two pairs of parathyroid glands are present in all mammals and are located on the antero-lateral aspects of thyroids. In birds they are present near the thoracic inlet and in the connective encirclement of thyroids, near to the branchial plexuses branching on the veins. Unless looked for carefully, the parathyroid is usually missed being translucent and merging with the connective tissue. In size usually they are less than 100 mg.

Histologically the gland cells are of two types namely chief cells or water clear cells which are vacuolated and Oxyphil cells where they cytoplasm of which is granular and stains red with haematoxylin and eosin stains. The cells are arranged as islets or clusters in a vascular fibrous stroma.

The main function of the gland is mainly through its hormone, parathormone and is to maintain the calcium-phosphorus balance. This is brought about by influencing the renal excretion of phosphorus by depressing the renal absorption of phosphate, causing thereby phosphate diuresis and by regulation of the osteoclastic activity in the bone and demineralising the bone.

Parathyroid hormone is a small protein having a molecular weight of approximately 9500 and is composed of 84 amino acids.



Histologic structure of a parathyroid gland

Tumors of parathyroid

These occur in dogs suffering from chronic interstitial nephritis and in horses suffering from big head disease. In these cases, fibrosis of bones occurs. In man tumors of parathyroid causes rarefaction ofbone results in osteitis firbrosa cystica.

Parathyroid and related cysts: Small cysts are observed within the parenchyma or in the immediate vicinity of the gland, frequently in dogs and occasionally in other animals. Parathyroid cysts are usually multilouclated lined by cuboidal or columnar epithelium and contain a densely eosinophilic proteinaceous material. Chief cells adjacent to larger cysts may be moderatley compressed.

Parathyroid cysts appear to develop from persistence and dilatation of remnants of the duct that connects the parathyroid and thymic primordia during embryonic development.

Other cystic structures in the thyroid-parathyroid area include ultimo bronchial cysts and bronchial cysts. Bronchial cysts are located lateral to the parathyroid-thyroid area, often near the base of the ear, attached deeply to cervical structures. Salivary mucocoele are also present in this region.

Hyperparathyroidism is either of primary or secondary. Primary hyperparathyroidism is due to an adenoma; wherein excess parathormone is secreted. Changes like osteopathy, Nephrocalcinosis and urolithiasis are seen.

Secondary parathyroidism is found in adequate intake of calcium in the diet or imbalance of calcium and phosphorus ration, hypocalcaemia due to vitamin D deficiency, Steatorrhoea, chronic renal failure wherein phosphorus excretion is interfered with resultant retention of phosphorus and consequent activation parathormone and bone withdrawal of calcium resulting in osteodystrophia firbrosa.

Hyper-para thyroidism in dogs: Hyper-parathyroidism has been recognized in dogs where sub-normal amounts of parathyroid hormone are secreted is unable to interact normally with target cells. Lymphocytic parathryoiditis has also been recorded in dogs. Postparturiently hypocalcaemia is associated with functional disturbances in parathyroid. These disturbances are in turn related to the muscle paresis wherein due to loss of stabilising membrane bound calcium, nerve membranes become more permeable to ions and require a stimulus of lesser magnitude to depolarize.

Hyperparathyroidism occurs as a complication of chronic renal failure and is characterized by excessive production of parathyroid hormone in response to chronic hypocalcaemia. All four parathyroid glands undergo marked chief cell hyperplasia and the bone has a varying degree of generalised osteodystrophy firbrosa.

Parathyroid contains chief cells and in hypercalcemia conditions with cestrum diurnum plants, these chief cells will accumulate secretory granules after feeding and later to undergo involution and atrophy.

Neoplasms of parathyroid glands: Adenomas are common. Tumors of parathyroid chief cells are involved.

Hypercalcemia associated with neoplasms of nonparathryoid origin: Humoral hypercalcemia of malignancy or pseduohyperparthryoidsimis one form of cancer-associated hypercalcemia that is induced by the secretion of humoral factors which have effects distant to the site of neoplasms. The most consistent feature in this increased osteoclastic bone resorption distant to the site of the neoplasm.

Tumors derived from C cells of the thyroid gland are most frequently encountered in adult to aged bulls, certain strains of laboratory animal, rats and adult aged horses. C-cell adenomas appear as discrete, single or multiple gray to tan nodules in one or both thyroid lobes. Adenomas are smaller less than 3 cm in diameter and are separated from thyroid parenchyma by thin fibrous connective tissue capsule. Histologically expansive mass of cells greater in size than a colloid distend follicle. They are well circumscribed or partially encapsulated from adjacent cells follicles that are compressed to varying degrees. The neoplastic cells are well differentiated and have an abundant cytoplasm area that is lightly eosinophilic or clear. Multiple metastases to anterior cervical lymphnodes are common.

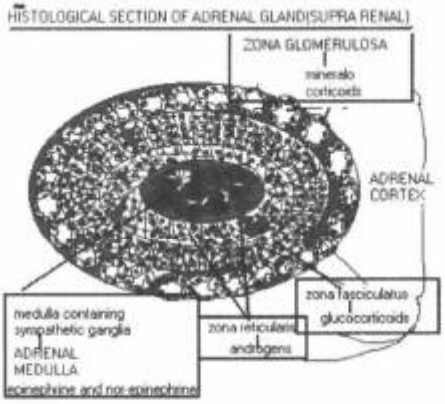
Adrenal gland

The adrenal glands, which lie at the superior poles of the two kidneys, are each composed of two distinct parts, the adrenal medulla and the adrenal cortex. The adrenal medulla is functionally related to the sympathetic nervous system, and it secretes the hormone epinephrine and nor-epinephrine in response to sympathetic stimulation.

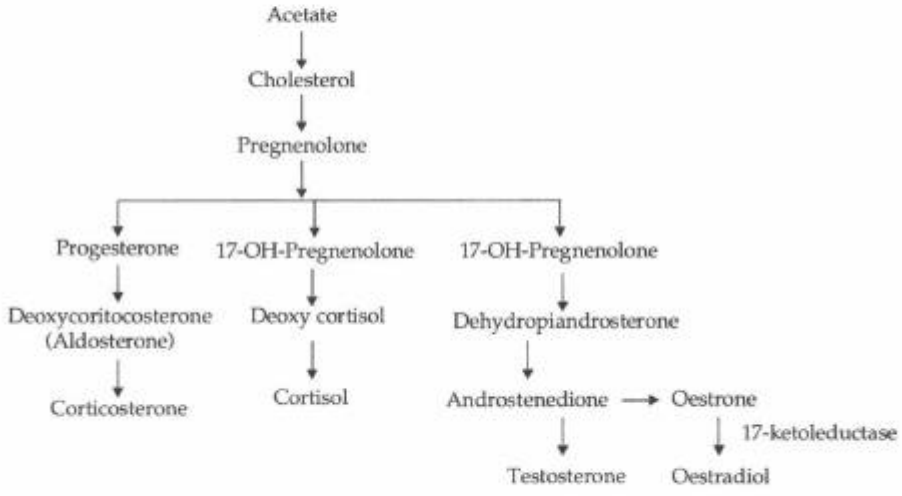
The adrenal cortex secretes an entirely different group of hormones called corticosteroids. These hormones are all synthesized from the steroid cholesterol, and they all have similar chemical formulas.

The Adreno cortical hormones do not all because exactly the same effects in the body. Two major types of hormones, the mineralocorticoids and the gluco-corticocids and secreted by the adrenal cortex. In addition to these, small amounts of sex hormones are secreted especially androgenic hormones which exhibit the same effects in the body as the male sex hormone testosterone.

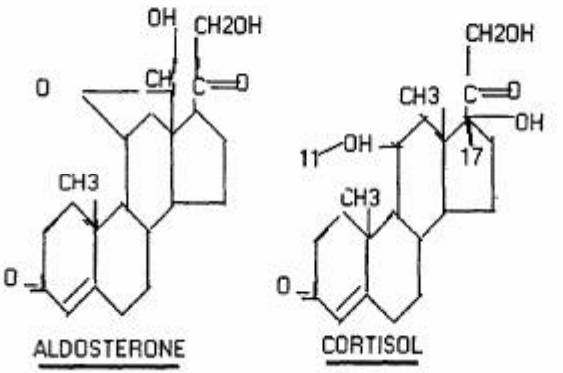
The mineralocorticoids have gained the name because they especially affect the electrolytes of the extracellular fluids, namely sodium and potassium in particular. The gluco-corticocids have gained this name because they exhibit an important effect in increasing blood glucose concentration.



Major steps in the synthesis of three principal adrenal steroids



TWO IMPORTANT CORTICOIDS SECRETED BY ADRENAL CORTEX



The adrenal glands of mammals consist of two distinct parts, which differ not only in morphology and function but also in origin. Because of their close structural relationships, the outer cortex and inner medulla of the adrenal gland usually have been considered parts of one organ. The adrenal cortex develops from coelomic epithelium cells that are of mesodermal origin. The chromaffin tissue and sympathetic ganglion cells of the adrenal medulla are derived from ectoderm of neural crest. It is not until relatively late in foetal development that a definitive relationship between the two primordia occurs.

The adrenal glands are richly vasuclarised, receiving arterial branches either directly from the aorta or from the phrenic, renal and lumbar arteries. In the capsule, the arteries form a vascular plexus, which eventually supplies the entire gland through separate channels to the capsule, cortex and medulla.

The adrenal cortex classically is subdivided into three layers or zones, although the demarcation between zones often is not distinct. The zona glomerulosa is composed of column of cells that have a sigmoid arrangement next to the capsule. It represents about 15% of the cortex and is responsible for the secretion of mineralocorticoids hormones. The secretory cells of zona fasciculate are arranged in long anastomosing cords separated by numerous capillaries. This middle zone which forms 70% of the cortex is composed of cells that contain abundant cytoplasmic lipid and are responsible for the secretion of gluco-cortiocids hormones. The zona reticular is accounts for the remaining 15% of the cortex. The secretory cells are arranged in small groups surrounded by capillaries. The inner layer is responsible for the secretion of sex steroids by the adrenal gland.

Mineralo-corticoids have their principal effects on in transport by epithelial cells, resulting in loss of potassium and conservation sodium. The most potent and important naturally occurring mineralcorticocids is aldosterone. The enzymes present in the epitheiali cells of renal tubules and sweat glands which control

mineral balance respond to Mineralo corticoids by conserving sodium and chloride and by wasting potassium. In the distal convoluted tubules of the mailman nephron, a cation exchange mechanism exists for the resorption of sodium from the glomeruli filtrate and secretion potassium into the lumen. These reactions are accelerated by mineralocorticoids but proceed at a smaller rate in their absence. A lack of secretion of mineralocorticoids may result in lethal retention of potassium and loss of sodium.

Gluco-corticocids hormones secreted by the adrenal cortex are concerned with the intermediary metabolism of glucose. Cortisol and lesser amounts of corticosterone are the most important naturally occurring gluco-cortiocids secreted by the adrenal glands. The action gluco-corticocids is gluconenogenesis resulting in sparing of glucose and a tendency to hyperglycemia and increased glucose production. They are responsible to cope up with flight or fight mechanisms. The acute effects of gluco-corticocids are observed within 15-30 minutes before the compensatory effects of insulin become prominent. There is decrease in glucose uptake in adipose tissue, skin, fibroblasts and lymphoid tissue followed shortly by increased catabolism in these tissue and muscle. This provides the amino acids for gluconenogenesis which increased mainly the liver. In addition gluco-corticocids decrease lipogenesis and increased lioplysis in adipose tissue, which results in release of glycerol and free fatty acids.

Gluco-corticoid also functions to suppress inflammatory and immunologic responses and thereby attenuate the associated tissue destruction and fibroblastic proliferation. Gluco-corticocids also decrease the initial inflammmatory reaction and its classic manifestation of hot, sweating and pain. The degree of hyperemia, extravasations, cellular migration and filtration at the site of injury consequent of inflammation is decreased. Capillary blood flow is decreased, and there is less endothelial swelling. In addition number of phagoyctic mechanisms is inhibited and clearance of particulate substances form the blood and lymph is impaired. There are diminished capacity lysosomes to interact with phagocytosed material and to release hydrolytic enzyme involved in intercellular digestion.

The rennin-angiotensin system is the major regulator of the aldosterone production by the glomerular zone of the adrenal cortex. Renin is an enzyme secreted by the Juxta-glomerular apparatus in the kidneys. These are present in the place of artery and distal tubules of the kidney where it touches the renal artery. The secretion that is rennin is liberated into the blood. Renin acts to cleave the plasma globulin angiotensingen to form angiotensin. The decapepitide is further hydrolyzed to form angiotensinogen II by converting enzyme. Angiotensin II is both a potent vasoconstrictor and a tropic hormone which stimulates the synthesis and secretion of aldosterone. It is a very labile peptide, which is quickly inactivated in plasma and tissues by an angiotensinases. Renin release and eventually aldosterone secretion are increased by conditions that compromises blood flow and pressure to the kidney, severe dehydration that results in decreased intravascular blood volume and sodium depletion.

ACTH secreted by the anterior hyophysis is the principal regulator of adrenal cortical growth and secretory activity particularly cells of zona fasciculate and reticular. Cortisol by adrenal cortex is secreted under the influence of ACTH. ACTH is one of many polypeptide hormone exerts its action on target cells through the mediation of 3-5-cyclic AMP. The tropic hormone attaches to receptors in the plasma membrane of secretory cells in the adrenal cortex, resulting in the activation of adenylate cyclase. This enzyme converts ATP to cyclic AMP, which accumulates in the cytoplasm of target cells in the adrenal cortex and certain extra adrenal tissues. Cyclic AMP serves as the intracellular mediator ofACTH action by stimulating certain key enzymes like protein kinase to initiate at the biochemical events leading to the biosynthesis of corticosteroid hormones. Control of the secretion ofACTH by the anterior pituitary gland is governed largely by the hypothalamus through the secretion of corticotrophin releasing factor. This peptide is secreted by neurons of the hypothalamus into capillaries which for the hypothermic pituitary portal system and cover it to corticotorphs of the pituitary. Corticotrophin releasing factors is though to act by situating Cyclic AMP formation within ACTH-secreting cells. Negative feedback control of ACTH secretion is exerted primarily by the circulating level of cortisol acting on secretory cells in the hypothalamus or anterior pituitary. When plasma cortisol levels are elevate d beyond the normal physiologic range, ACTH secretion is suppressed secretory cells in zona fasciculate and reticularis decrease the rate of synthesis and release of corticosteroid hormones and the adrenal cortex undergoes trophic atrophy. Conversely when cortisol levels are subnormal there is an increased release of ACTH for the pituitary gland in an attempt to increase cortisol secretion and return blood levels toward normal.

Diseases of adrenal cortex

Hypo function of adrenal cortex; Addison's disease:

The manifestation of Addison's disease may occur only if there isobilateral destruction of the glands. The causes are those conditions causing atrophy and destruction of adrenals. These most probably occur in generalised tuberculosis, amyloid infiltrations, and histoplasmosis infections, consequent to Hypopituitarism and due to secondary tumors.

The symptoms are general weakness, low blood pressure, and feeble heart beat, brown pigmentation of skin, vomiting and diarhoea, nausea, loss of appetite, slowed absorption, are noticed. Loss of water along with sodium leading to haemo concentration. Acidosis occurs due to loss of bicarbonates. Animals are weak and the ability of liver to convert amino acids to glycogen at usual rates.

These symptoms are due to absence of cortisol. The mineral and glucose metabolisms are deranged, leading to elevated potassium level and lowering of sodium, hypoglycemia, and hypotension. Higher blood urea and anemia. Pigmentation is due to increased melanin production as tyrosine is side tracked

to the skin when adrenaline is no longer synthesized from this amino acids by the destroyed adrenals. Another hypothesis is A CTH and Melanocyte stimulating hormone is similar in most respects chemically, as a result the actin on periphery also similarly. Hence high ACTHG levels cause increased formation of melanin giving rise to the bronzed coloration of the skin increased formation of melanin giving rise to the bronzed coloration of the skin. Atrophy of thyroid and heart is noticed.

Hyper function of adrenal cortex

Cushing's syndrome

This is due to excess of circulating hydrocortisone which again may be due to basophile adenoma of the anterior pituitary. Zona fasciculate is incresed and the adrenals are yellow in colour. Hyper cortical may be observed in case of tumors of non-endocrine tissue, like bronchial carcinoma, pancreatic carcinoma and thymomas.

The changes in the animals are painful adiposity of neck and trunk that is buffalo type of obesity. This is called moon face syndrome. Muscle wasting and weakness in animals are observed. In females and preadolescent males, hair is present in various parts of the body that is called Hairsuitism. Amenorrhea in females in human beings is observed. Osteoporosis and Kyphosis are observed. Peculiar striations on the abdominal wall and atrophy of the skin are seen.

Hypertension, hyperglycemia and diabetes are noticed. Sodium retention, polydypsia, polyuria, urine with low specific gravity excretion is seen. Suceptibility to infections are noticed, Pot bellied appearance is prominent. Thinning and atrophy of skin and dermatitis is noticed.

Hyalinization of the basophilic cells of the anterior pituitary together with disappearance of basophilic granules is common.

Adrenogenital syndrome

Adrenal virilism

This is commonly observed in human females. Little girl become little boy and little boy become men that is popular saying of famous pathologist, Boyd. In this condition there is an excess of androgens that is masculanising hormones. In the female foetus if the excess hormone occurs during the first week of intra uterine life, pseudo-haermaphroiditism results.

The clinical findings are rapid growth with great muscularity in children these are called infant Hercules, Hairsuitism, virilism, in girl enlargement of clitoris, Hairsuitism on chest, impotence in boys and testis are atrophied. In women amenorrhea, deep voice, Hairsuitism on face and body. The urinary excretion of 17-ketostoerids is increased and there may be deficiency of hydrocortisone, so hypoglycemia results.

Tumors of adrenal gland: Tumors of adrenal gland may arise from the cortex or medulla.

Adrenocortical tumors: These may be adenomas or carcinomas.

Adenomas of adrenal cortex are rare among animals and are reported in old dogs, horses, cattle, swine, sheep and goats. It was reported that incidence of adenomas of adrenals are high among castrated goats.

Grossly, it is difficult to distinguish the adenoma from hyperplasia of adrenal cortex. These tumors do not appear to produce any recognizable effects on animals unlike in man, in whom hyper-adrenalism is caused. In cows the voice changes to that of a bull. In man excretion of 17-ketosteroids and large quantities of estrogens are reported. A rare case of adeno-carcinoma of adrenal cortex has been reported in cattle.

Histologically, the cells are arranged as sheets or alveoli. The cells are anapalstic with hyperchromicity nucleus with vacuolated cytoplasm. Mitotic figures are frequent. Blood supply is plentiful and connective stroma is variable. Metastasis is not to widespread. Hemorrhages, calcification and ossification may be present. The neoplasm invades locally.

Tumors of adrenal medulla (pheochromocytoma or Chromaffinoma): This literally means a tumor that contains dark coloured cells. This is due to the affection of chromium salts on the cytoplasm and taking the colour. This tumor is supposed to arise from the cells that produce adrenaline. Pheochromocytoma is rare in animals and has been described in cattle, horses, sheep and dogs. Grossly the tumor may be unilateral or bilateral. Histologically, the tumor cells are large with central nuclei. They may contain lipid in their cytoplasm. Their cell boundaries aren't always distinct. This cell may line blood spaces. Mitotic figures are few. Metastasis occurs by blood stream and into the regional lymph nodes, liver and lungs. In animals excessive adrenaline liberation leads to such symptoms as tachycardia, hypertension, and hypertrophy of the heart, hyperglycemia and glycosuria as seen in that of men.

Neuroblastomas arise from primitive neuroectodermal cells often in younger animals and form a large intra-abdominal mass. Gnalgioneuroma are usually well differentiated small tumors that have multipolar ganglion cells and neurofibril. In cattle they are often pigmented with melanin. Neuroblastomas are differentiated from pheochromocytoma by being composed of small tumor cells, with hyperchromasia nuclei and scant amount of cytoplasm. The often resemble lymphocytes and tend to form pseudo rosettes. Neurofibril remyelinated nerve fibers can be demonstrated in neuroblastomas.

Gnalgioneuroma are benign tumors in the medulla composed of multipolar ganglion cells and neurofibril with prominent fibrous connective tissue stroma. They surround adrenal cortex and severely compress it. Neoplastic cells in

medullary tumor occasionally may differentiate in two directions, resulting in adjacent pheochromocytoma and gananglioneuromas in the same adrenal gland.

Metastatic tumors of adrenal medulla:

Secondary foci of neoplastic growth in the adrenal glands are common in case of disseminated neoplasia and originate primarily as emboli. The metastases are usually bilateral and the medulla is an early site of tumor growth. Direct invasion of adrenal glands may occur from primary or secondary tumors of contiguous structures.

Involvement of adrenal gland by lympho sarcomas and mammary carcinomas are common and extensive and both adrenals likely to be affected. Tumor emboli lodge in sinusoids of adrenal medulla and may grow to an extent that they compress the surrounding adrenal cortex.

The Pineal Gland

This is tiny gland placed above the posterior extremity of the third ventricle. In structure it is composed epithelial cells in loose connective stroma.

The pineal gland secretes a hormone, melatonin. Serotonin which's found is the gland's transformed into melatonin by the action of enzyme hydroxy indole-o-methyl-transferase which's found large quantities only in the pineal gland. Melatonin antagonizes the action of melanocyte stimulating hormone of the posterior pituitary.

Melatonin acts on the brain to depress the rate of gonadal maturation and to interfere with subsequent gonadal function and cyclicity. Pineal hyper function is associated with delayed puberty and hypofunction with precocious puberty. In man complete destruction of pineal gland causes chachexia, trophic disturbance, adiposity, premature developmental genital organs, premature spermatogenesis and growth of interstitial cells. Melatonin inhibits thyroid secretion rate and this secretion of adrenal steroids.

Three types of tumors arise from the pineal gland. 1.pinealomas: these consist of islands of large epithelial cells, with acidophilic cytoplasm and enclosed fibrous stroma. Among the large cells are scattered small cells believed to be lymphocytes and these tumors have been described in goat, horse, and dogs fox and cows. 2. Gliomas comprising of glial cells. 3. Teratoma form the totipotential cells.

Aortic body tumors

(Heart Base tumors)

Normally the adventetia of the aorta and the carotid arteries contain a cluster of chemoreceptors (aortic body and carotid body) that function as chemoreceptors, which are sensitive to the carbon-di-oxide and oxygen tension and the ^{pH} of the blood. Respiration and circulation are thus regulated by these. Sometimes these

chemoreceptors become tumorous. The tumors are located at the base of the heart, between the aorta and pulmonary artery or sometimes encircling both, hence the name heart base tumor. The carotid body tumor is found in the bifurcation of the carotid arteries. Histologically the tumors are reddish brown in colour and firm in consistency. They are encapsulated. Histologically tumor cells are polyhedral in shape. Cytoplasm is vacuolated or granular and acidophilic with a spherical nucleus. Connective tissue strands divide the tumor into lobules. The cells are highly invasive infiltrating into the media of blood vessels and into lymphatics. No endocrine function is associated with this tumor.

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Chapter 10

Musculoskeletal System

Summary

Diseases of muscle and Tendons, Embryology of striated muscles: The structure of muscle cell or muscle fiber, Molecular mechanism of muscle contraction: Diseases of muscles in domestic animals, Atrophy of muscle, Disuse atrophy. Hypertrophy Regeneration and repair of muscles

Myositis: Chronic myositis: Parasitic myositis: Sarcosporidiosis (Sarcocysts). White muscle disease or stiff lamb disease: Muscular dystrophy (Wallerian degeneration). (Zenker's degeneration). Physical injuries of muscle: traumatic injuries of muscles are common and may be the result of external trauma. Tumors of muscle tissue: **Myomas:** Rhabdomyoma

Diseases of muscle and Tendons

Embryology of striated muscles: Development of striated muscle in the embryo is from mesodermal somites, which give rise to myotomes. With each myotome, which corresponds roughly to a vertebral body segment, with its spinal nerve, the individual muscles develop by a process of aggregation and migration of presumptive myoblastic cells. It is very likely that the undifferentiated mesodermal cells will be committed to muscle density some time before significant structural changes is visible, and the earliest detectable modification to presumptive myoblasts is across essential rounding of the spindle shaped cells. There are myofibers and satellite cells at this stage. The first clear sign of differentiation is the migration of presumptive myoblasts, destined to become myofibers, into the region where future muscles will appear; this occurs before any nerve influence is exerted. The direct connection of the nerve to the myotomes determines the subsequent route of innervations, but because migration has occurred, the muscle may receive nerve sprouts (as it has received myoblasts group components) from more than one myotomes.

The second phase of muscle development is incompletely separated from the first and subsequent phases. It begins with the early development of sarco plasmic components such as myofibrils, which identify the cells as muscles. The commitment to my genesis is mutually exclusive with cell replication and with possible rear exceptions, committed; myoblasts are post mitotic. Myoblasts begin to fuse into elongated multinucleated cells about the time myogenesis begins.

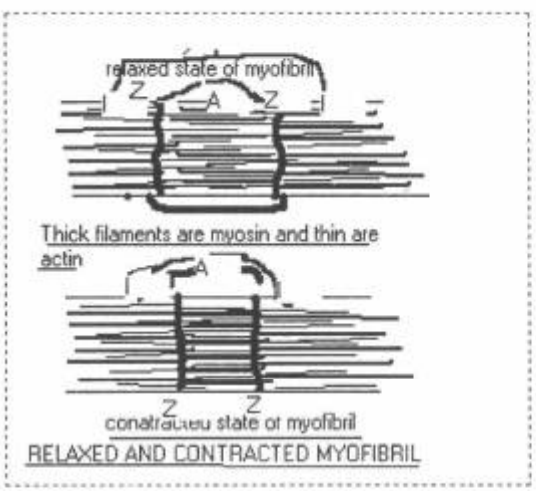
Subsequent development of the myotube allows it to become well developed muscle fibers and consists of stepwise construction of actin and myosin filaments, the formation of the Z band into which the thin actin filaments insert, and the evolution of the tubular systems. The last of these steps the invagination of the tubular T-system from caveolae or other small regular recesses on the outer sarco plasmic membrane, provides an elaborate system of tubules, which run parallel to the Z bands and make contact with all developing myofibrillar units.

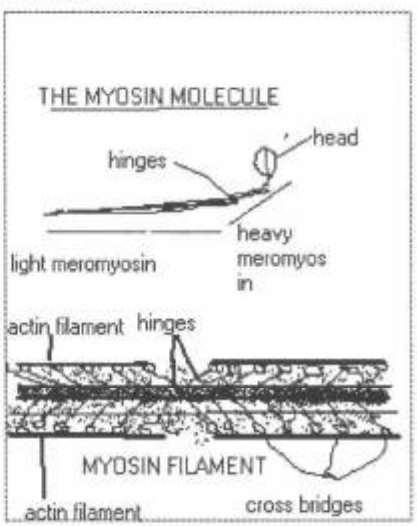
The fourth phase of development is one in which the evolving fiber grows, increase the number of myofibrils and nuclei, and moves the latter to the subsacrolemmal position. During the final phase of development, the development of basal lamina and an additional sheath of the collagen, fibroblasts, and capillaries invest each developing myotube as orientation of the fiber into its final position of tension takes place. Development of fiber sup to this pint, just after the end of the first trimester, is independent of any neural connection, but subsequent fiber enlargement and the considerable increase in the number of fibers which occurs during the immediate prenatal and postnatal periods is dependent on a functional neural connection. Waves of muscle fibers development takes place by early postnatal life. Temple fiber budding takes place by multiplying 6 fibers for each one fiber. During the period when templating is occurring, new fibers rapidly become innervated and do not later change neural connection. A single motor nerve axon serves two types of muscle fiber. Muscle structure is arranged around muscle fibers. Muscle fibers are variable in size depending on age, exercise, nutritional status, position and function of the muscle in question and on species.

The structure of muscle cell or muscle fiber is quite well defined. The outer component is a thin, amorphous, but apparently quite tough, basal lamina consisting of three layers which, on most muscle cell surfaces seems to be thrown into gentle folds. Within the basal lamina are two separate cell populations with very similar nuclei, the multinucleate myofibers and the small more numerous satellite cells, which play an important role in fiber repair and regeneration. The nuclei of both cell types are oriented to the long axis of muscle fibers and are distributed to the long axis of them and are distributed regularly in a spiral manner. In normal muscle less than 3% of the nuclei of the multinucleate myofibers cells are displaced internally, but the number tends to be higher adjacent to points where muscle and tendons interdigitated, or where muscle and bone meet through a short ligament or tendon. Nuclei are slender, oval, have evenly distributed chromatin and single, small nucleoli. The satellite cells consists of a simple cell membrane thrown around the nucleus, minimum of cytoplasm with mitochondria, and a scant tubular system, all of which lie in a shallow indentation on the myofibers surface within the basal lamina. Satellite cells constitute 1-30% of the visible nuclei associated with muscle fiber. The higher the satellite cells, the younger are the animal and in old age less number of cells is present. A modest concentration of them occurs adjacent to motor end plates.

Satellite nuclei are the only ones in muscle capable of mitotic division in postnatal life, and each times these cells divided in growing muscle, they contribute one myocytic nucleus and a minute amount of cytoplasm to the growing pool of nuclei in the enlarging multinucleate, myofibers cell. The other daughter cells remains as part of the satellite cell pool outside the myocytic and retain amitotic capabilities.

The most distinctive characteristic of skeletal muscle cells is the presence of striated myofibers approximately 0.5 to 1.0 ìm in diameter, consisting of thousands of regular in size and regularly oriented myofilaments.





Molecular mechanism of muscle contraction: Figure shows the relaxed state of sarcomere and the contracted state. By this one can appreciates in the relaxes state, the ends of the actin filaments derived from two successive Z membranes barley overlap each other while at the same time completely overlapping the myosin filaments. On the other hand, in the contracted state these actin filaments have been pulled inward among the myosin filaments so that they do not overlap each other to major extent. Also the Z membranes have been pulled altogether so tightly that the ends of myosin filaments actually buckle during very intense contraction. Thus muscle contraction occurs by sliding filament mechanism there are certain attractive forces exists with a resultant interaction of the cross bridges of the myosin filaments with the actin filaments. Under resting conditions, the attractive forces between the actin and myosin filaments are inhibited, but when the action potential travels over the muscle fiber membrane, this causes the release of large quantities of calcium ions into the sarcoplasms surrounding the myofibrils. These calcium ions activate the attractive forces between the filaments and contraction begins. But energy is also needed for the contractile process to proceed. This energy is derived from the high energy bonds of ATP, which is degraded to ADP to give the energy required.

The myosin filament is composed of approximately 200 myosin molecules, each having a molecular weight of 4, 90,000. The myosin molecule is composed of two parts namely light meromyosin and heavy meromyosin. The light meromyosin consists of two peptide strands wound around each other in helix. The heavy meromyosin in turn consist of two parts namely the first a double helix similar to that of the light meromyosin and second a head attached to the end of the double helix. The head itself is composed of two globular protein masses. Myosin molecules are flexible at two points. The junction between the light meromyosin and the heavy meromyosin and between the body of the heavy meromyosin and head. These two areas are called hinges. The total length of myosin filament is 1.6i and the 200 myosin molecules allow the formation of 100 pairs of cross bridges that is 50 pairs on each of the myosin filament.

The actin filament consists of three different components namely actin, tropomyosin and troponin. The back bone of the actin filament is a double stranded F-actin protein molecule. The two strands are wound in a helix in the same manner as the myosin molecule, but with a complete revolution every 70 nanometers. The actin filaments also contain two additional protein strands that are polymers of tropomyosin molecules, each molecule having a molecular weight of 70,000 and extending length of 40 nanometers. It is believed that each tropomyosin strand is loosely attached to an F-actin strand and that in the resting state it physically covers the active site of the actin strands that interaction cannot occur between the actin and myosin to cause contraction.

The skeletal muscle fiber is so large that action potentials spreading along the membrane cause almost no current flow deep within the fiber. Yet to cause contraction these electrical currents must penetrate to the vicinity of all the separate myofibrils. This is achieved by transmission of the action potential along transverse tubules that penetrate all the way through the muscle fibers from one side to the other. The tubules action potential inturn cause the sarcoplasm reticulum to release calcium ions intermediate vicinity of all the myofibrils, and it is these calcium ions that in turn cause contraction. Therefore when an action potential spreads over a muscle fiber membrane, it spreads along the T tubules to the deep interior of the muscle fiber as well. The action potential currents surrounding these transverse tubules then elicit the muscle contraction.

The amount of ATP that is present in the muscle fiber is sufficient to maintain full contraction for less than 1 second. When ATP is broken down to ADP, the ATP is rephosphorylated to form a new ATP within a fraction of a second. The first source of energy that is used to reconstitute the ATP is the substance creatine phosphate, which carries a high energy phosphate bond similar to those of ATP. The high energy phosphate bond of the creatine phosphate is cleaved and the released energy cause bonding of a new phosphate ion to ADP to reconstitute the ATP.

The next source of energy used to reconstitute both the creatine phosphate and the ATP is energy released from the food stuffs, from carbohydrates, fats and proteins. Most of this energy is released in the course of oxidation of these food stuffs. The oxidative release of energy takes place almost entirely in the mitochondria, which utilizes thereleased energy to from a new ATP. The ultimate source of energy for muscle contraction is the basic food substances and oxygen.

Muscle contraction is under the control of nerves. Each motor neuron that leaves the spinal cord usually innervates many different muscle fibers, the number depending on the type of muscle. All the muscle fibers innervated by a single motor nerve fiber are called a motor unit. In general small muscles that reach rapidly and whose control is exact have few a muscle fibers as few as 3 to 2 in some of the laryngeal muscles and in each motor unit and have a large number of nerve fibers going to each msucle. On the other hand the large muscle which do not require very fine degree of controls, such as the gastrocnemius muscle may have several hundred muscle fibers in a motor unit. Usually 150 muscle fibers are serving by single motor unit.

Muscle fibers could be considered as two types. Type I fiber rich in oxidative enzymes and showing slow twitch, red color and the type II fibers rich in glycogen show a fast twitch and is pale in colour. Muscles used repetitively but slowly and persistently should have high levels of type I fibers, while those used for short burst of activity should have high levels of type II fibers.

Sensory muscle spindles are found in all skeletal muscles in and anchored to the perimysial connective tissue and associated with small nerve radical which contains 6-20 large sensory nerve fibers. There are more numerous in some muscles than in others. Spindles are about 0.5 to 3 mm long and 200 to 500μ wide. The central space enclosed within the fibrous multilayered outer sheath is continuous with lymphatic space and contains 2-20 specialized small intrafusal muscular fibers.

Motor end plates are the sites of synaptic transmission of acetyl choline from nerve ends to muscle receptors, at which sites a surface membrane conducted, polarizing impulse is initiated. The end plate is contained within the endomysium and extension of the emdomysial connective tissue ensheathed the bare terminal axon for a short distance until it myelin sheath is reached. One end palate in each muscle fiber is a normal one. One motor neuron gives rise to an extremely variable number of terminal axons with one end plate each, the number being inversely proportional to the fineness of motor movement required of the muscle, and is directly proportional to the relative diameter of themselves fibers. Thus in the extrinsic ocular muscle the axon and end plate ratio is as low as 1:10 on same, round muscle fibers whereas in the gastroenemius muscle fibers it is around 1: 2000.

Diseases of muscles in domestic animals

Atrophy of muscle is broadly defined as reduction in size. It means reduction in muscle fiber diameter or cross sectional area reduction. Atrophy occurs due to denervation or neurogenic atrophy. Denervation atrophy is always accompanied by muscle paralysis. Examples are crycoartenoides muscles that are seen in laryngeal hemiplegia consequent to the injury to left recurrent laryngeal nerve. Injury to supraspinatus nerve by the pressure of a poorly fitting collar in a work horse. Radial or branchial paralysis due to trauma in dogs. Local spina osteomyelitis, disc protrusion, chronic meningitis, metastatic tumors all produces atrophy of muscles.

Disuse atrophy is the result of either reduced stimulatory or reduced movement of a normally innervated muscle or of an absence of a normal muscle tension.

Atrophy due to malnutrition or chachexia where animals starve are not able to supply adequate nutrients in feed. Of the contractile substance of muscles 1 to 5% is dismantled for each day. This is due to supply of protein from muscles to the body. A monogastric animal like the dog probably begins a net withdrawal for muscle after 24 hours after starvation, whereas ruminants reach the same point 2 days later, but calves and lambs reach it shortly. Back and thigh muscles are first to undergo atrophy.

Hypertrophy of muscle fibers is physiologic and desirable. Race horses and grey hounds have many more fibers in strategic places than do non racing animals.

Arthrogryposis literally means crooked joint. The syndrome can result from prenatal joint fixation by myofibroblasts around joints and coincident contracture of the tend muscle linkages around those joint.

Regeneration and repair of muscles

The ability of muscle to repair itself is remarkable considering its high specialization and the great length and great vulnerability of individual fibers. The ability to rapidly repair the damage segment of a fiber, without apparently complication to the rest of the fiber, is without parallel in other cells of the body. A muscle cell consists of single large multinuclear myofibers and large population of uni-nuclear satellite cells, coexisting within the tough basal lamina. As the major participants in the regenerative sequence are macrophages of the blood; the satellite cells because only they, within the fiber, have retained the capability for mitotic division and the basal lamina which acts a very efficient gate keeper. The integrity of the basal lamina determines from the very beginning whether the outcome will be regenerative repair, fibrous replacement or a mixture of the two. An intact basal lamina effectively keeps my nuclei, satellite nuclei, and myoblastic cells inside. It is equally efficient in keeping fibroblastic cells out, but allows phagoyctic cells easy entry and exit. If damage to the fiber is segmental and such that only the myofibrils and the sarcoplasm along with it is subcellualr component have been

injured, the first visible events consist of progressive mineralisation, and an early rounding up of satellite cells as they prepare to undergo mitotic division. Daughter cells become apparent in hours as they leave their former sublaminal site. At about 12 hours, macrophages appear and they may be accompanied by neutrophils I a short lived wave. Both of these cell types receive free access to the mineralised contents of damage fiber. Macrophages dissolve and remove the debris; neutrophils disappear unless infection complicates the process. Once removal sarcoplasmic debris is underway, and some space has been created within the collapsing sarcolemma, some of the proliferating satellite cells enter the myofibers. These are now myoblasts, which mix freely with the remaining myonuclei.

Myoblasts increase in number until a critial myoblastic mass is reached. Only then do myoblasts begin to fuse, and this triggers the next sequence of events. 5 or 6 days after degeneration occurred; fusion of myoblasts has produced unpolarised myotube giant cells, which begin to send out cytoplasmic processes as their nuclei divide. Some processes make contact with remaining viable segments of the original fiber within the basal lamina, and perhaps even within the original fiber within the basal laminae and perhaps even within original myofibers cell membrane. They make effective union either as a side to side, cell to cell splice or more likely they dissolve a cell membrane and unite the cytosol into a single myofibers free pole of the myotube giant cell then becomes a polarized regenerative probe, which grows within the cleared and collapsed sarcolemmal sheath. Other myotube cells may not make contact for some time, and remain as unpolarised giant cell until an adjacent myotube processes contact them. A growing myotube cell with its basophilic cytoplasm and central row of nuclei can grow for relatively long distances as long as the outer sheath is intact and no fibrous obstruction intrudes. Outside the sheath, a regenerating fiber can grow competitively with fibrous tissue for only 2-5 mm.

When contact has been made with the next viable segment of the original fiber at about 10 to 14 days, changes in the fiber consist mostly of production of new sarcomere in the enlarging fiber. The new fiber has to find growing space between existing fibers but seems able to do this efficiently. As myofibrils, sarcoplasm, and organelles are added, the fibers become less basophilic, and at about 15 to 17 days, the nuclei migrate from their core position to lie just under the new cell membrane. Only in the most ideal of circumstances are all the parts restored to the regeneration state by the efficient regeneration described. At the very least, two basal laminae, one inside proliferating satellite cell/myoblasts which do not enter the original cell or any myotube processes which escape from it may produce a second fiber oar a second branch of a fiber within the original basal lamina. Branched and split fibers, two or three small fibers replacing one large one over a segment and bridge between two or more parts of one original fiber, often occur in repaired muscle. The longer and the more numerous are the gaps are the more potential is there in the potential of repair. If nuclei are viable and basal

lamina persists healing is perfect.

Thus nutritional, exertional and toxic myopathies repair reasonably well. Primary dystrophies repair well but degenerate again. Ischemic damage repairs badly because satellite cells and their nuclei and endomysium cells have been killed. Limited oxygen debt may give repair quickly.

The reduced regenerative capability that develops with maturity may be related to low numbers of satellite cells/ myoblasts as the proportioned satellite cells to the total nuclear population in the fiber drops with age.

Myositis is the inflammation of the muscle. This may be acute or chronic.

The routes of infection and causes are trauma, by direct extension from lesions of neighbouring arthritis, osteitis or periosteitis; in pyemia, haematogenously; in parasitic infection.

Acute myositis is usually non-suppurative. Most of the clostridial organisms in animals cause acute non-suppurative myositis, one example is black quarter caused by clostridium chauvoei. In this condition, the organisms cause inflammation and necrosis of muscles with production of gas. The muscle fibers are torn by the gas bubbles. Local heaemorrhages are present and the area is black due to formation of black sulfide. Regional lymph nodes are congested and edematous. Serous contained blood filled serosanguinous fluid.

Histologically there is necrosis of muscles with mononuclear and clumps of anaerobes.

Suppurative myositis: Haematogenous infection may occur from other foci like strangles and glanders in horses. Infections also occur through lacerating and penetrating wounds or by extension from adjoining areas.

Histologically there are degenerative changes in muscles and sometimes they undergo liquefaction with abundant neutrophilic infiltration.

Sequleae: As there is loss of muscle tissue, healing is by means of fibrous tissue proliferation and scar formation. If severe septicemia may result.

Chronic myositis: Infections by Actinomycosis and actinobacillosis affect muscles also. The muscles of the tongue, cheek and throat are affected. The lesions are chronic suppurative myositis wherein sulfur granules are noticed in the mass of inflammatory granulation tissue. There is infiltration of large number of lymphocytes, neutrophils and plasma cells. There is necrosis and degenerative changes in the muscle fibers.

Parasitic myositis: These following parasites affect the muscles of domestic animals. Sarcosporidiosis (Sarcocysts) are present in the skeletal and cardiac muscles of species of domestic animals. Heavy infection lead to lameness, weakness, paralysis, emaciation and fatalities in few instances in animals are observed.

Parasitized muscle fibers are destroyed by the parasite and the adjacent fibers undergo pressure atrophy. Histologically, sarocystis organism is rarely accompanied by an acute inflammatory reaction and schizonts in endothelium because little or no evidence of endothelial cell destruction. As the organisms enter the muscle a wide range of changes may be encountered. Usually there is no muscle fiber degeneration, but there may be thin, linear collections of lymphocytes, between fibers in the region. Sometimes the muscle fiber undergoes segmental hyaline change in the regional invading parasite, and rarely extensive floccular degeneration of muscle fibers occurs. Generally less number of Sarcocysts produces less reaction.

Toxoplasma gondii infections, particularly in puppies and kittens and in other species of domestic animals produce disease in immunosuppressive conditions. Massive involvement of skeletal muscle fibers will be there. In muscle fibers both tachyzoites and thin walled cysts (bradyzoites) may be present, but the former are generally transient and hard to find and the latter are infrequent. Cysts inside the muscle fibers are spherical and non-reactive.

Cysticercus cellulosae: This is the bladder of Taenia solium, tape worms of man. Adult worms are present in the intestine of man. Eggs are passed into the faeces and pigs get the infection from infected faeces. Pigs on grazing the infected faeces, the hexacanth embryos present in the eggs penetrate the intestines, pass through the circulation and are deposited in the muscles of shoulder, neck, diaphragm, tongue, intercoastal, abdominal and cardiac muscles of pigs (measly pork). Heavy infection may result in anemia and cachexia. The bladder worms which are there in the muscles of pigs will be taken by human on ingestion of pork and develop as adult parasites in the intestine of man.

Cysticercus bovis is the intermediate stage of tape worm Taenia saginata which is present in the intestine of man. The eggs are passed in the faeces. On ingestion of hexacanth embryo containing eggs, by the cattle and buffaloes, the embryos come out of the egg in the intestine of bovines, and penetrate the gastric mucosa reach the various parts of the muscle through circulation. This is popularly called as **measly beef.** All muscles are affected but especially those of tongue, mastication and heart are most affected. Human beings get infection by eating the infected measly beef. The bladder worms reach the gut of man and become there the adult parasites.

Cysticercus ovis is the intermediate stage of dog tape worm Taenia ovis and is found in the muscle of sheep.

Eosinophilic myositis of cattle and sheep: These are usually discovered in skeletal muscle and myocardium of animals slaughtered for human consumption. This reaction may be due to allergic reaction consequent to the rupture of parasites. There are reports of traumatic muscle rupture in cattle in initiating an eosinophilic response. A heat stable eosinophil-chemotactic substance has been isolated from

affected bovine muscles in which eosinophilic myositis lesions are present. The gross lesions in muscles are green focal stripes or patches which fade to of white when exposed to air. Histologically both acute reaction and chronic reaction characterized by Eosinophilic myositis in sheep tends to occur in young animal younger than 2 years. Lesions are comparable in distribution and type to those in cattle, although the frequency of granulomatous type of change may be higher. Fibrosis reaction exit side by side.

Myositis by Hepatazoon canis is also seen, where dogs show fever, anorexia, general body pain and gait abnormalities and may show respiratory signs. The organism in gametocyte form may be present in neutrophils, and muscle biopsy may demonstrate the cysts, or the typical pyogranulomatous reaction to the release of merozoites or the schizonts themselves.

White muscle disease or stiff lamb disease

Muscular dystrophy is a term used where skeletal muscle diseases are characterized by progressive degenerative changes leading to a loss of muscle fibers.

The causes are vitamin E deficiency, selenium deficiency, vitamin B deficiency, deficiency of choline and even vitamin A deficiency wherein muscle necrosis and extensive degenerative changes are seen. Extensive degenerative changes are seen in the muscles of animals (Wallerian degeneration). It is found that thiamine deficiency produces cardiac necrosis. Deficiency occurs since ruminants when the ruminal flora is not active to synthesize the vitamin. Cobalt deficiency also lead to B-complex deficiency especially vitamin B12.

The disease occurs in calves and lambs and can be produced in rabbits and guinea-pigs.

Vitamin E and selenium containing enzymes are required in many cells as physiologic antagonists to a group of chemically varied substances known as free radicals. Free radicals are molecules with an odd number of electrons and they can be either organic or inorganic. Some free radicals are products of normal metabolic function, and several participate minor are products of oxidative metbolism. They may also be produced outside the cell as products of tissue radiation, drug reactions, and inflmmation. One of the major sources of free radicals is the cell detoxification process, which renders materials less harmful by converting them to epoxides. Many intracellular and extracellular free radicals contain oxygen, and are involved in electron transfer reactions. They are highly active and this is responsible for their rapid alteration (instability) which occurs in oxidation- reduction reactions within a wide range of celular structures and enzyme systems. Free radicals may initiate cell injury by causing peroxidation of membrane lipids and by causing physicochemical damage to protein molecules, including those of mitochondria, endoplasmic reticulum and cytosol. Protection

against the effects of free radicals is provided partly by the constant presence of small scavenge molecule like tocopherols, ascorbate and beta carotene which quench free radicals should they accumulate; both radicals and scavengers are consumed in the process. Protectionism also provided in part by selenium containing enzyme of glutathione peroxidase or glutathione reductase system.

In the absence of sufficient protection, cellular membranes are modified by free radicals and the ability of those membranes to maintain essential differential gradient for one or more ions is diminished or lost. As a result mitochondrial accumulate calcium and there is depletion of energy system.

Clinically three types of forms have been detected.

Stiff type: The head is carried low and has a drooping posture. Animal experiences difficulty in raising and walking. While walking the gait is stiff. The weight bearing and active muscles like hind quarters and diaphragm, heart and intercoastal muscles are affected and in lambs this is the form encountered. Animals lie in recumbent position and do not like to move. On forcible movement, they have stiff gait and wobble, hence this is called as stiff lamb disease.

Respiratory form where the muscles of respiration like diaphragm and intercoastal muscles are affected. The animal may show symptoms of respiratory distress.

The cardiac form: In this type, animals show considerable weakness, inability to stand, rapid pulse and low blood pressure. Since the heart is affected and weakened, exertion brings on repertory distress and even death. In animals with cardiac involvement alone, sudden death occurs without any other symptoms.

Grossly those muscles which are continuously active namely diaphragm and intercoastal muscles show the changes. The muscles are bilaterally affected and are pale like fish flesh. The whole muscle bundles may be affected but only a part of it will show the change. The muscles become hard and wooden. The paleness is due to loss of myoglobin which is excreted in the urine. The change in colour is also due to change in optical characteristic of the muscle protein when it becomes coagulated. Pneumonia, oedema, hydrothorax, chronic venous congestion of liver and hydropericardium are found. Heart shows yellowish or grey streaks or patches the ventricle is more often affected.

Histologically the muscle fibers are swollen with loss of striations and with wide spread hyaline degeneration (Zenker's degeneration). These progresses to coagulative necrosis, fibers are fragmented and may completely disappear. Marked sarcolemmal proliferation is present. Calcification also is seen. In the same way lesions are also found in the cardiac muscle.

Azoturia

(Equine myoglobinuria, Monday-morning sickness, parlayatic haemoglobinuria)

This is seen in horses which are in well nourished condition. This is seen in animals suddenly and in horses going to work after complete rest for a few days but maintained on full work-rations. This happens usually on Mondays where the horse is being rested on Sunday. The animals suddenly stop, sweat, shiver and show great suffering from pain and in the lumbar region. The affected muscles are swollen. The involved muscles are gluteal, lumbar andfemoral muscles. These become hot, hard and board like. Soon the animal passes coffee coloured dark brown coloured or black urine since it contains large quantities of myoglobin. Animals lie d down and soon die. Those that survive are weak and it takes on time for them to recuperate and for the atrophic muscles regain their normal state.

Pathogenesis:

In normal msucle contraction, muscle glycogen is converted to pyruvic acid. Due to inadequate oxygen only $1/5^{th}$ of this is oxidized to CO_2 and H_2O to liberate energy. The rest is converted into lactic acid which is converted into glycogen in the liver and used again.

Because muscle fatigue can be caused by glycogen depletion under anaerobic or partly anaerobic conditions, fatigued muscle often contain large quantities of lactic acid. Lactic acid produced during muscle contraction generally passé into the blood stream and is transported to the liver, because the muscle cells contain only small amounts of the enzymes to convert lactic acid to glucose. Consequently during contraction or activity, muscles cells use glucose from the blood stream and break down the glycogen to glucose they contain to form lactic acid for energy for contraction. The liver removes the lactic acid from the blood stream, converts it back to glucose using energy in its process, and then passes the glucose back into the blood stream for use by the muscle cells. During rest, the muscle cell removes glucose from the blood stream and uses it to rebuild the glycogen stores.

When the animal is at rest but wellfed, the muscles are well stored with glycogen. When it is peat to work suddenly much of the glycogen is converted to lactic acid in them as said above, large amounts of this stimulate extreme contractions of the muscles which become hard. In the contracted state the muscles blood circulation is further reduced. Under this hypoxic conditions more of lactic acid is from pyruvic acid which still further contracts themselves and so greater curtailment of blood flow occurs leading to still greater reduction of oxygen supply.

Thus a vicious cycle is established, the net result being that the muscles do not get sufficient amount of oxygen and nutrition and some necrosis results. Necrosed muscle liberates myoglobin which is excreted in the urine. Large masses of myoglobin in the urine appear to produce renal blockage, renal ischemia and lower nephron nephrosis, wherein the epithelium of the distal convolute tubules as well as the Henle's loops are degenerated, some of which become necrosed and desquamated. Renal vasoconstrictions that may be caused by these factors

responsible for the haemoglobinuria produce renal ischemia. This condition causes degenerative changes in the tubules and so anuria and fatal uremia results.

Grossly the affected muscles are swollen, pale and have increased amount of interstitial fluid. The affected kidneys are swollen and on section the cortex is brownish and the medulla has reddish streaks. Urine show granular reddish casts and a few hyaline casts.

Histologically the changes in the muscles are those of Zenker's degeneration in which the muscle becomes a homogenous hyaline mass without striations. The fibers are fragmented. All the constituents' muscle fiber may vanish except the sarcolemma and fibrous stroma. In animals that survive regeneration may occur.

In **kidneys** the lesions are found mostly in the distal tubules. Similar changes are seen in the epithelium of Henle's loop. The lumen of the tubules may contain, besides the desquamated cells, masses of myoglobin. These form granular pigmented casts. Death is due to renal insufficiency leading to uremia.

Myasthenia

Two clearly defined types of myasthenia gravis occur in animals, a congenital disease in which acetyl choline end plate receptors are few in number, and the acquired disease in which a normal number of end plate receptors are blocked by circulating anticholinesterase receptor antibodies. In the congenital group, which accounts for 10% of cases in dogs, the puppies show clinical signs early in postnatal life. It leads to a failure of formation of acetyl choline receptors and development of shallow secondary clefts in the end plate.

Among the cases of acquired myasthenia are disproportionate number of dogs and cats with thymoma, and this is also seen in human beings. The thymus normally contains cells with internal muscle components, and they apparently present the muscle antigen when the immune system become aberrant or when thymoma develops. Animals become very weak and may develop a voice change. The disease is fatal.

Metabolic myopathy: Muscular dystrophy characterized by glycogen storage occurs as part of systemic glygenosis in cattle and dogs. Histologically increased levels of glycogen can be demonstrated in muscle, but the changes in the muscles do not reflect the greatly reduced exercise tolerance, tremors and inco-ordination. These may be due to deficient lysosomal glycosidase activity.

Discoid degeneration: This develops when hypoxia plays a major part in the production of muscle lesions. The muscle striations, but not their entire fine feature are preserved and the fiber beings to separate the Z bands. The z bands of several adjacent sarcomeres may break, but more often 3-10 sarcomeres remain intact before the next break occurs, perhaps on the opposite side of the fiber. This makes the muscle fiber brittle.

Downer syndrome

This is a muscle ischemic syndrome. This is due to application of external pressure by variety of objects on muscles of the parts of the body. In humans it is due to prolonged anesthesia, muscle, joint or bone damage causing prostration, or metabolic or neurolgic disease causing paresis. Cows are most frequently affected as downer animals, partly because of their weight and their muscle bulk and partly because they are subject to diseases in which paresis is common. Horses usually suffer from this type of muscle ischemia as a result of having been anesthetized for several hours while lying on a hard surface.

The pathogenesis of the downer syndrome depends on the fact that pressure within muscles caused by the weight of the body on them may rise to levels considerably higher than both venous and arterial pressure. Muscles of limbs in a flexed or tuck position are particularly susceptible. Some regions of muscle which are in closest contact with the floor or with bones may be pressure balanced, but the intramuscular pressure created within skin and facial sheaths of the limbs soon serves to collapse veins causing congestion, and then collapses arteries. This blood exclusive ischemia creates changes in tissues, which soon resemble the changes described for the compartment syndrome, and leads to further oedema and more intramuscular pressure. Other nerve damage leading to peroneal nerve paralysis and flexed rear fetlock or a dropped shoulder leads to Downer cow syndrome in cattle. As time passes and as the pressure is removed, the affected limb continues to swell as oedema fluid increases under returned arterial flow. The limb usually extends involuntarily perhaps because the flexor muscles are rendered uncontractile by ischemic anaesthesia. Swelling is reduced slowly and may be accompanied by fixation of skin to the underlying necrotic muscle. The formation of venous or arterial thrombus may slow or obstruct return. The formation of heaemorrhages and haematomas as arterial blood pressure return to damaged vessels may further slow effective revascularization.

On postmortem muscles are dark and often hameorrhagic. The boundaries of necrotic muscles show competent regenerative repair.

Physical injuries of muscle: Traumatic injuries of muscles are common and may be the result of external trauma. Or they may due to rupture of muscle or tear of the fascia as occurs occasionally in violent contractions, rarely in over extension. The histology appearnace of traumatic injury includes sarcolemmal rupture with adjacent intact fibers showing hyaline and granular degeneration.

Tumors of muscle tissue

Myomas : It is a benign tumor composed of muscle tissue. Rhabdomyoma is a tumor of striated muscle tissue and leiomyoma of smooth or nonstriated muscle.

Summary

Diseases of skeletal system

Bone: bone development-Osteoblasts-functions-Embryology of bone—Development in cartilage—Osteodystrophic diseases— Relationship to calcium and phosphorus haemostasis and vitamin D—Bone effects—Poultry—Reaction of bone to injury—osteitis, periosteitis. Osteomyelitis. Fractures—Healing of fracture—- Factors responsible for healing of fractures-Non-alignment of the two ends of bones— Tumors of Cartilage and Bone—Osteoma — Giant cell tumors (Osteoclastomas)—. Diseases of joints—(synathroses (diarthroidal joints)—Arthritis—Acute arthritis—causes—Non-infectious arthritis: Immunological mediated— Hygromas of carpal joint -capped elbow

Diseases of skeletal system

Bone: Bone develops from haemopoieitc system, as well from fibroblastic system. Osteoclasts are derived from haemopoieitc system and osteoblasts, osteocytes, chondroblasts and chondro cytes from stromal fibroblastic system. The stem cells from stromal fibroblast system are called Osteoprogenitor cells. They are responsible for creating haematopoietic microenvironment chacteristics of bone. Mesenchymal cells in other tissues are called inducible osteogenic precursor cells in recognition of their osteogenic ability when an appropriate inducer is present. Osteoprogenitor cells are the source of chondrobalsts, osteoblasts and fibroblasts of bone. Either a physical factor or genetic factor may operate in differentiation. Ischemia and hypoxia favors cartilage formation, whereas development of bone is stimulated by a good blood supply and high oxygen tension. Developmental of fibroblasts from Osteoprogenitor cells is stimulated by tension and prolonged hyperparathyroidism. Some of the growth factors are involved in differentiation of mesenchyma cells whether it should become a fibroblast, chondroblasts or osteoblasts. These growth factors are derived from bone marrow cells and are either monoines or of lymphokines. The monokines are interleukin-1 and tumor necrosis factor. Interleukin-1 stimulates bone resorption.

The collagenous matrix is known as osteoid. It is produced by the principal cell type of bone the osteoblasts, a cell that lines bone forming surfaces. These cells later become entrapped within the matrix and are termed osteocytes. Osteoblasts contain alkaline phosphatase and have receptors for parathyroid hormone. Osteoclasts which are multinucleated cells are concerned with the bone resorption, and are found along bone surface osteoclasts which are multinucleated cells are concerted with bone resorption and are found along bone surfaces; osteoclasts are associated with small resorption cavities, termed How ship lacunae. These cells are rich in id phosphates and lack receptors for parathyroid hormone. The non collagenous proteins produced by osteoblasts include phospho proteins, osteonectin, osteofontin, osteocalcin, bone protelglycan, bone morphogenicity as

protein, bone sialoprotein and bone protein lipid. The collagen fibers of bone are arranged in an orderly parallel fashion. This is termed as lamellar bone. In Th foetus the collagen fibers are deposited in an irregular fashion termed woven bone.

Bones formed under two different situations; one is intramemrbranous bone formation in which fibroblast appearing cells of the periosteum gradually diffenrtiate into osteoblasts or bone forming cells and osteocytes. This occurs with flat bones of head and pelvis and along the periosteum surface shafts (diaphysis). Next one is formation by endochondral ossification where cartilaginous material is involved information of bone. Development and growth of long bone involve both endochondral and intramemrbranous ossification. Endochondrial ossification entails the proliferation, maturation, hypertrophy and modeling of cartilage. The physis is the principal seat of endochondrial ossification. It is often called the growth plate or epiphyseal plate. The terminal part of bone separates the physis from the epiphysis. So long as the bone is growing it must maintain its basic shape. The integration of continuous endochondral ossification with maintenance of shape involves a process of remodeling which depends on resorption and formation of mineralized bone and cartilage. Most of the bone formed during the growth period by the periosteum of farm animals and large dogs is laminar bone.

The classical structure of the diaphysis is osteons or Haversian system. This is long, about 100 to 500îm in diameter with a vascular canal (Haversian canal) in the center. {Primary osteons are formed in the preexisting spaces between other bony structures. Formation of secondary osteons is preceded by creation of resorption spaces. Whereas primary osteons often irregular spaces, secondary osteons tend to be ellipsoidal circular in cross sections.

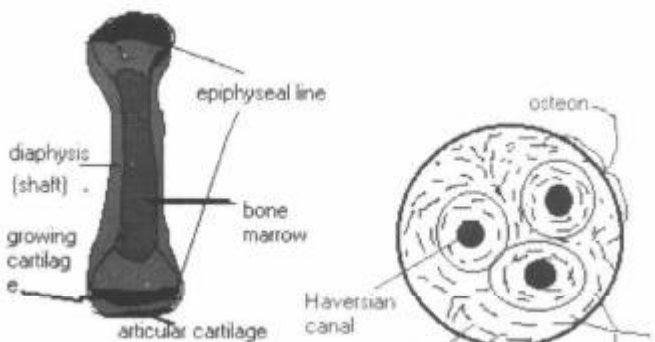
Osteoblasts: Osteoblasts produce and mineralize matrix called osteoid. In sections they are separated by narrow matrix free clefts. Their nuclei are located at the end of a cell. 10% of osteoblasts are enclosed in matrix and become osteocytes and others probably die. The productive life of lamellar osteoblasts in human is around 3 months. Effect of parathormone on osteoblasts is to reduce collagen synthesis. Osteoblasts have receptors to calcitrol. Osteoblasts are important in calcium haemostasis and allow transfer of calcium without phosphate in blood. The bone lining cells, under the control of parathyroid hormone, regulate the exchange of extracellular fluid by increasing the potential difference between bone fluid and extracellular fluid.

Osteocytes: Osteocytes are formed from osteoblasts; a few develop by metaplasia from fibrocytes. Osteocytes of mature lamellar bone are flat or plump oval cells with many branching processes, which fill the canaliculi and anastomose with those of other osteocytes. Osteocytes line in cavities called lacunae. Osteocytes survive more than 35 years. Calcitonin stimulates osteocytes to deposit mineral

in perilacunar bone. Pituitary growth hormone, thryoxine, oestrogens and various growth factors also stimulates osteocytes.

Osteoclasts: Osteoclasts are related to monocytes and macrophage but differs in that osteoblasts contain tartarate resistant isozymes. Typical osteoclasts are a large cell with acidophilic cytoplasm and contain nuclei from 2 to 100. Osteoclasts are active for about a month. The empty space where osteoclasts seen are termed as How ship's lacunae. They have acidophilic cytoplasm and have branching processes. Carbonic anhydrase isozymes II is present in the osteoclastic cytosol. Osteoclasts do not have parathyroid hormone receptors, but how they act in resorbing calcium is not known. Osteoclasts do possess receptors for calcitonin. Calcitonin also cause decrease in the number of nuclei per osteoclasts.

Bone matrix: It consists of organic matrix without calcium. Bone matrix consists of collagenous and non-collagenous proteins which are mainly glycoproteins and proteoglycans. Lamellar osteoblasts contains 90% type I collagen chemically differs from that of skin and tendon. Woven bone is first formed and later followed by lamellar bone. Osteoblasts synthesize vitamin K dependent protein and are called osteonectin. Serum proteins constitute upto 1/3 of the organix matrix of bone. Vitamin C is necessary for the supply of 4-hydroxy proline which stabilizes collagen molecule. When it is deficient collagen is either not produced or is produced in defective form. Copper deficiency and aminonitriles intake results in defective collagen synthesis and lead to skeletal deformities. Corticosteroids administration depresses osteoblasts.



STRUCTURE OF LONG BONE

The organic matrix of bone is 90 to 95% collagen fibers, and the remainder is a homogenous medium called ground substance. The collagen fibers extend primarily along the lines of tensional force. These fibers give bone its powerful tensile strength. The ground substance is composed of extracellular fluid plus

proteolglycans, especially chondroitin sulfate and hyaluronic acid. The crystalline salts deposited in the organic matrix of bone are composed of principally calcium and phosphate and the formula for the major crystalline salts, known as hydroxy apatites. Ca^{++} 10 -x(H20')2x ? $(P0_4)_6/(OH)_2$

Each crystal is about 400 A long, 10 to 30 A thick, and 100 A wide and is shaped like a long, flat plate. The relative ratio of calcium to phosphorous can vary markedly under different nutritional conditions. The calcium and phosphorus ratio on weight basing varying between 1.3 and 2.0

Magnesium, sodium, potassium and carbonate ions are also present among the bone salts.

Each collagen fiber of compact bone is composed of repeating periodic segments every 640 A along its length; hydroxyapatite crystals lie adjacent to each segment of the fiber, bound tightly to it. This intimate bonding prevents shear in the bone; that is, it prevents the crystals and collagen fibers from slipping out of place, which is essential in providing strength to the bone. In addition, the segments of adjacent collagen fibers overlap each other, also causing hydroxyapatite crystals, to be overlapped like bricks keyed to each other in a brick wall.

The collagen fibers of bone, like those of tendons, have great tensile strength while the calcium salts which are similar in physical properties to marble, have great compression strength. These combine properties plus the degree of bondage between the collagen fibers and the crystals, provide a bony structure that has both extreme tensile and compressonal strength. Thus, bones are constructed in exactly the same way that reinforced concrete is constructed. The steel of reinforced concrete provides the tensile strength, while the cement, sand and rock provide the compressional strength. Indeed, the compressional strength of bone is greater than that of even the best reinforced concrete, and the tensile strength approaches that of reinforced concrete.

Embryology of bone

Development in membrane the earliest indications the formation of a condensed mesenchymal membranous sheet composed of spindle shaped cells arranged in parallel rows. Subsequently by the secretion of these cells collagen fibers are deposited in between the cells which become arranged in single layers with increased cytoplasm along isolated groups of these fibers. These mesenchyme cells become modified in their character and are called osteoblasts which help in the deposition of calcium salts in the intercellular substance carried by the blood stream and aided by vitamins, especially vitamin d. with; the calcification, bony spicules are deposited in the primitive mesenchymal membranous sheet except on it superficial surface where the undifferentiated mesenchyma sheet becomes condensed to form the periosteum. A development process, the bony spicules increased in size and number and invade at the neighbouring membrane. The

mesenchymal cell soon the deeper aspect of the periosteum become modified to form osteoblasts which further help in the deposition of successive layers of sub-periosteum new bone. As a result some of the osteoblasts become engulfed between the layers of new bone, forming bone cells, which occupy Interstial space called lacunae.

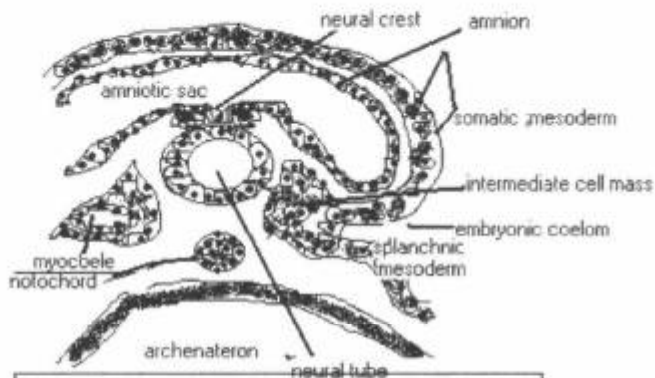
Development in cartilage: In early embryonic life, the bones to develop in cartilage are represented by cartilaginous bars which become transformed into bones by the process of ossification which begins at about the 8th week of foetal life by the appearance of a primary centre of ossification near the middle of a bone. By the process of ossification the cartilaginous element undergoes destructive and degenerative changes. With the appearance of the centre of ossification, the cartilage cells in the centre of a bone enlarge and calcium salts carried by the blood stream become deposited in the intercellular ground substance. This is followed by the degeneration of the cartilage cells and the space left by degenerated cells are called primary areolae. Subsequent to the degeneration of the cartilage cells and calcification of the matrix, the condense mesenchyme on the surface of the bone forms the periosteum. The deeper layers of the mesenchyma cells of the periosteum become ossified to form the osteoblasts which help in the deposition layer of subperiosteal compact; bone and thereby increasing the girth of the bone.

Near the centre of ossification a vascularised tuft form the deeper layer of the periosteum penetrates the calcified cartilaginous matrix carrying groups of mesenchyma cells from the periosteum. Some of these mesenchymal cells become modified into osteoclasts and chondroblasts which help in the absorption and removal of the cartilaginous matrix whereas others are modified into osteoblasts which arrange themselves along the persistent cartilaginous strand and help to deposit successive layers of cancellous bones with spaces in between them known as secondary areolae.

In the case of long bones, on either side of the primary ossifies centre, the cartilage cells enlarge and become arranged in parallel rows. Subsequent to calcification of the cartilaginous matrix these enlarged cartilage cells are absorbed and removed and the process of ossification extends from the primary centre with the development of new capillaries and osteoblasts. The cartilage cells at the extremities of long bones proliferate rapidly and become closely packed with very little matrix in between the proliferated cells. As the process of ossification extends towards the ends from the primary ossify centres, these proliferated cartilage cells in close proximity to the site of ossification become enlarged and arranged in rows. With the calcification of the matrix, these cells degenerate and are absorbed before the spread of ossification with the advent of fresh capillaries and osteoblasts in the usual manner. The process of ossification by the primary centre is completed at birth except its two extremities which remain cartilaginous and are further ossified from secondary centres of ossification. The cartilage cells at the extremities proliferate in two directions, namely longer columns proliferate

towards the diaphysis increasing its length and the shorter columns towards the secondary one epiphyseal centre increasing its size.

As the subperiosteal new bone formation take place from the deeper layers of the periosteum absorption of the cancellous bone takes place in the interior forming the medullary cavities of the long bones. Later on the cartilage cells at the junction of diaphysis and epiphysis become compressed and thinned out forming a plate of cartilage called the epiphyseal cartilage, where active bone growth take place and with the completion of the ossification it disappears and union takes place between the epiphysis and diaphysis.



a transverse section of embryo showing the neural tube, notochord and the parts of secondary mesoderm

In mammals the notochord almost entirely disappears, they remains forming the pulpy substance (nucleus pulpous) of the intervertebral fibro cartilage. The vertebral column is developed from the paraxial mesoderm which primarily lies as a longitudinal column on either side of the notochord and the neural tube. This paraxial mesoderm in the region of the hind brain and the trunk undergoes segmentation. These segments are called the primitive segments or somite and as many as 38 of them have been recognized from the cranial to the caudal end. In the region of the hind brain 3 or 4 such segments appear and the rest in the trunk region. Each of these primitive segments is prismatic on transverse section. In the centre of each segment develops a cavity develops called the myocoele of the somite, which enlarges and splits the segment into an apical and a basal portion. The basal or the dorsilateral portion of each somite becomes detached from the apical portion which remains as a plate with an incurved ventral dorsal end. This is called the muscle plate or myotomme from which the skeltal muscles of the body are developed. In the apical or ventro medial portion of each primitive segment called the scelrotome, the cell rapidly proliferate and surround the notochord and the nerualtube from either side, and will develop into the axial skeleton. Each segmental scelrotome differentiates into a cranial half with loose

mesodermal cells and a caudal half in which the fusiform angular mesodermal cells are more condensed. The caudal half of each scelrotome fuses with the cranial half of the succeeding one forming a mesodermal oar blastema vertebra. The proliferation of the caudal half the scelrotome which surrounds the notochord forms the mesodermal basis of the body of a vertebra and its dorsal out growth one on each side which surrounds and enclosed the neural tube will formed the mesodermal rudiment of the arch of the corresponding vertebra.

Disorders of skeletal system

Amelia-complete absence of four limbs

Brachia absence of anterior limbs

Apodia- absence of posterior limbs

Promelia- peripheral part of skeletal limbs is absent

Phocomelia- Absence of bones of the upper arm and fore arm, thigh and lower legs with the bones of distal part of the extremities are present.

Micromelia- Denotes the various the limbs of skeleton are present but abnormally small.

Peodactyly denotes the absence of some of the toes or parts of toes

Adtyly signifies absence of all toes on a limb

Brnachydactylly- abnormal shortness of toes

Syndactyly- Fusion of the bones hand or foot or faulty separation of the rudiments of digits in the foetal hand or foot.

True dwarfism (nosomia) - False dwarfism-in osteogenesis imperfecta and also in Myxoedema, this is seen.

Overgrowth- Normal gigantism; this is due to abnormal persistence and activity of epiphyseal cartilage. Tissue to pituitary affection called Acromegaly gigantism or disease of gonads (eunchooidism)

Polymelia-duplication of limbs, proximal to the basopodium

Polydactyl: Multiplication of the terminal part of the limb-distal to the basopodium

Lordosis: Curvature with convexity directed ventrally. This is common in domestic animals because of the horizontal l position of the body. The lordosis generally involves the terminal part of the thoracic and lumbar spine. The spinous processes maybe so approximated that they rub against one another.

Kyphosis: Curvature with convexity directed dorsally. Rare in animals common in man. The curvature is generally in the lumbar and caudal regions of the thoracic region. The pulling of heavy loads is generally regarded as responsible for carp back in horses.

Scoliosis, lateral curvature is generally seen in an association with Kyphosis or lordosis inset cases as a congenital and very frequently inherited malformation.

Osteodystrophic diseases

These following osteodystrophic diseases in animals and as well humans have been reported. To know fully about the osteodystrophic diseases first brief physiological response of the hormones to govern the calcium and phosphorus metabolism as well relative factors also have been discussed including bone formation in subsequent paragraphs.

Relationship to calcium and phosphorus haemostasis and vitamin D

The general function of vitamin D is to elevate plasma calcium and phosphorus to a level that will support normal mineralization of bone as well as other body functions. Evidence also suggests a regulatory role of vitamin D in immune cell function.

The two hormones, thyrocalcitonin and parathormone function in a delicate relationship with 1, 25-(OH) 2, D3 to control blood calcium and phosphorus levels. Production rate of 1, 25 (OH) 2, D3 is under physiological control as well as dietary control. Calcitonin, contrary to other two, regulates high serum calcium levels by depressing gut absorption and halting bone demineralization and reabsorption in the kidney. Vitamin D brings about an elevation of plasma calcium and phosphorus by stimulating specific pump mechanisms in the intestine, bone, and kidney. These three source of calcium and phosphorous thus provide reservoirs that enable vitamin D to elevate calcium and phosphorous level in blood to level that are necessary for normal bone mineralization and for other functions ascribed to calcium.

Intestinal effects: It is well known that vitamin D stimulates active transport of calcium and phosphorus across intestinal epithelium. Parathyroid hormone indirectly stimulates intestinal calcium absorption by stimulating production of 1, 25-(OH) 2 D3 under conditions of hypocalcaemia. The vitamin D3 is transferred to the nucleus of the intestinal cell, where it interacts with the chromatin material. In response to the 1, 25-(OH) 2-D3 specific RNAs are elaborated by the nucleus and when these are translated into specific proteins by ribosome, the events leading to enhancement of calcium and phosphorous absorption occur. In the intestine 1, 25-(OH) 2, D3 promotes synthesis of calcium binding protein and other proteins and stimulates calcium and phosphorus absorption. Phosphate is also transported against electrochemical potential gradient involving sodium response to 1, 25-(OH) 2, D3.

Bone effects: During a vitamin D deficiency, organic matrix of bone fails to mineralize, causing rickets in the young and oteomalacia in adults. Vitamin D plays another role in bone that is mobilization of calcium from bone to the extra cellular fluid compartment. It is an active process requiring energy, and presumably

it transports calcium and phosphorous across the bone membrane by acting on osteocytes and osteoclasts.

Kidney effects: There is evidence that vitamin D functions in the distal renal tubules to improve calcium reabsorption. It is known that 99% of filtered load of calcium is reabsorbed in the absence of vitamin D and parathyroid hormone. This 1% is under the control of 1, 25 (OH) 2, D3 in improving renal absorption of calcium. With intact parathyroid and without vitamin D, renal tubular resorption of inorganic phosphate decreases, thereby increasing phosphate clearance and resulting in hypophophetemia, although the parathyroid maintain a normal plasma calcium levels. With adequate vitamin D greater reabsorption of phosphorus by the renal tubule occurs. Without intact parathyroid vitamin D actually increased renal loss of phosphorous.

Consequent to the deficiency of vitamin D there is failure of calcium salt deposition in the cartilage matrix. These following changes are also seen. Failure of cartilage cells to mature, leading to their accumulation rather than destruction; compression of the proliferating cartilage cells; elongation, swelling and degeneration of proliferative cartilage; abnormal pattern of invasion of cartilage by capillaries.

Rickets- in young animals; Osteomalacia- in adult animals; Osteoporosis in adult and aged animals; Osteodystrophia fibrosa (von Reklinghausen's disease) consequent to the deficiency of calcium due to metabolic disturbances and as well nephritic conditions (rubber jaw syndrome in dogs) as well excess intake of phosphorus in animals like Bran disease (Miller's disease) have also been discussed.

Calcium and phosphorus deficiency in young ones leads to rickets and in adult's osteomalacia. In young ones deficiency results in inhibition of growth, a loss of weight and reduced appetite, before characteristic signs in the bone system become apparent. There is decreased mineralization of bones, resulting in lameness and fractures.

During periods of inadequate intake, withdrawal of mineral does not take place equally from different parts of skeleton. The spongy bone, ribs, vertebrae and sternum, which are the lowest in ash are the first to be affected, together with the cancellous ends of the longs bones. The compact shaft of long bones, such as humerus, femur and tibia and of small bones of extremities is the last reserves to be used. In severe and prolonged failure of adequate nutrition, the tension of the muscles pulls the weakened bones out of shape.

The skeletal changes in different species are weak bones, causing curving and bending of bones, enlarged hock and knee joints, tendency to drag hind legs, and beaded ribs and deformed thorax. Onward signs of rickets include the following skeletal changes, varying somewhat with the species depending on anatomy and severity. Weak bones cause curving and bending of knees (bowed legs), enlarged hock and knee joints, tendency to drag hind legs; beaded ribs (rachitic rosary),

with swelling of costo-chondral joints, beaded ribs and deformed thorax with bent sternum (crooked sternum). Although there appears to be difference between species in the susceptibility of different bones to such degenerative changes, differences that probably, reflect bodily conformation. Spongy part of individual bones, and bones relatively rich in such tissue, are first and worst affected. The vertebrae and the bones of the head suffer the greatest degree of resorption. Next come the scapula, sternum and ribs. The most resistant bones are metatarsal and shafts of long bones.

Reduced intake of or feed efficiency will reduce weight gain or production of milk and eggs. Fertility is likely to be reduced in females, animal may appear listless and may have dull, dry hair cots, and pica; depraved appetite may eventually occur.

Poultry: Death occurs in phosphorus deficiency cases. A less severe deficiency causes rickets and growth failure. Clinical signs include cessation of egg production, reduced feed consumption and efficiency, reduced eggshell quality, decreased breaking strength, egg specific gravity, shell thickness and shell weight. Inferior egg quality, blood spots, yolk mottling, decreased egg size and weight; impaired reproduction (reduced hatchability, dead weak or deformed offspring), decreased mating activity, delayed sexual maturity. Skeletal abnormalities include bone resorption, cage fatigue, osteoporosis, rickets, oteomalacia, soft beak, osteodystrophia fibrosa, paralysis, muscular stiffness, lameness, beaded ribs, enlarged and painful joints, weak bones, easily broken or bent bones, misshapen bones, arching of back and muscular rigidity, stiffness, shaft of bone bent outwards (bowed legness).

The causes are deficiency of calcium in the diet, improper of calcium and phosphorous, failure of absorption of calcium, formation of insoluble complexes where calcium oxalates and phytates present in some green leaves and grains respectively may form insoluble compounds in monogastric animals and are lost in the faeces. Excess of oxalic acid in leaves and excess of lactic, tartaric and malic acids in silage bind calcium in large quantities. Similarly acid break down products of proteins bind calcium if food is too rich in protein. In too coarse food greater amounts of hipppuric acid is formed from cellulose. Too rich or poor fat reduces the utilization of calcium. Reduced body movements also are contributory causes.

When compounds like sulfur as coccidiostats they are combine with calcium to form insoluble compounds which are sot in the faeces.

Steatorrhea, where in excess fats in feed prevents utilization of calcium forming calcium soaps which lost into faeces. This is common in humans with enteritis infections. Since Vitamin D absorption is also there with calcium, vitamin D deficiency also sets in. Renal disease where in nephritis, phosphates are not excreted as it should and so accumulated in the blood and body. The excess phosphate ones are excreted through the intestinal tract, where they combine

with calcium to form insoluble compounds which are lost in the faeces. Increase requirements in growing animals.

Osteoporosis: In this disorder there is a reduction in the bony matrix. The matrix what is present is fully mineralized and the bones become porous and brittle, as in this condition destructive processes exceed the production in the remodeling of bone. Biochemical plasma calcium and phosphorus level are normal.

The causes are senility where is decreased osteoblastic activity or decreased oestrogens are seen. Especially in females this is common after menopause where circulating oestrogen levels are reduced. Lack of proteins or losses are seen in renal disorders; decreased production as in liver disease or defective absorption as seen in intestinal disorders. Proteins are essential for the formation of osteoid without which bone cannot be formed. Deficiency of vitamin A; deficiency vitamin C; local pressure on bone may cause atrophy as in seen in tumors and with cysts like Coenuris cerebralis and hydatid cysts that are present in the bone marrow and pulsating aneurysm within the vertebrae. Osteoporosis occurs also in disuse where in lack of exercise to bone as in seen in immobility where activity of osteoclasts and osteoblasts are there.

Loss of nerve supply to the part results in paralysis and so the part cannot be moved and osteoporosis results. Deficiency of trace elements like copper deficiency in dogs, manganese deficiency in pigs and zinc delinquency in fowls. In hyperthyroidism osteoclastic activity is increased and in hyperparathyroidism there is increased resorption of bone.

In Cushing's syndrome there are excessive gluco-corticocids probably suppresses the osteoblastic activity, wherein body of vertebrae are affected.

Lead poisoning in sheep and goats cause osteoporosis.

Grossly the bone appears lighter and thinner and atrophied. The cortex is thinner but the marrow cavity is wider. Bones become brittle and so are prone to fracture.

Histologically the bony trabaculae are thinner and decreased number of osteoblasts is seen. Osteoclastic activity and numbers are normal.

Reaction of bone to injury

As a result of insult the endochondral ossification is impaired in growing bone. Weight bearing effect is the bone. Insult of this results in disruption of mechanical forces with heaemorrhages. Sequence of bone formation is interfered and widespread production of new bone by injured or stimulated periosteum.

Inflammation of the bone is called osteitis, and that of periosteum is periosteitis. Inflammation of bone marrow is known as osteomyelitis. Inflammation of vertebrae is spondylitis.

Osteitis and osteomyelitis may be acute or chronic. Acute purulent osteomyelitis

is always caused by bacteria which gain entry into the bone in the following ways, either by direct extension through compound fractures, through gun shot and other wounds. By lymph vessels in draining neighbouring purulent areas such as purulent arthritis, purulent periosteitis and purulent osteitis media. Infection also spreads through the blood stream from suppurating lesion else where and in pyemia.

The causative organisms for osteomyelitis are *Staphylococci, Streptococci, Spherophorus necrophorus, Erysipelothrix rhusiopathiae, salmonella and Cryptococcus neoformans.*

Acute periosteitis may be non-suppurative usually caused by trauma and is seen in horses as sore shins due to working on hard roads. Grossly in periosteitis the usually inflammatory reaction is seen in the periosteum, hyperemia with purulent exudates accumulating between the cortex and periosteum. The exudates may separate periosteum from the bone and necrosis of the cortex results. Periosteum may be ruptured, liberating the pus into the nearby tissue. Since periosteum is in continuity with the endosteum and medulla, pus may pass on to these structures. In such an event, necrosis of the bone occurs due to separation of both periosteum and endosteum on which the nutrition of the bone depends.

In suppurative osteomyelitis pus is found in the medullary cavity and it may burst through the cortex. But more often such a drainage is difficult and the condition in progresses to a chronic stage. In the young growing animals abscesses are found at the costo chondral joints and in the epiphysis plates.

The necrosed bone is separated from the healthy bone by the action of osteoclasts and a sequestrum is formed. Osteoblasts nearby are active and produce new bone which forms a case, as it were around sequestrum and this is known as involucrum. Pus is discharged to the outside from the sequestrum through small openings in the involucrum called cloacae. The Sequleae are fractures occur due to extensive destruction of the bone, or it may result in chronic osteomyelitis. I suppurative osteomyelitis is extensive and present for a long time, Amyloidosis of different organs are observed. Resolution and healing with timely treatment occurs. In acute suppurative arthritis due to extension of infection to the neighbouring joint resulting in metastatic abscesses and filly death may also supervenes due to pyaemia and septicemia.

Chronic osteomyelitis results with persisting osteomyelitis cases or with traumatic injury or concussion or bacteria of low virulence that penetrates the bone marrow through the wounds like Actinomyces, brucella, mycobacterium and salmonella lesions and with fungi like coccidioides mycosis. In the case of chronic trauma and concussion exosteosis reulsts.This is formation of granulation tissue of bone. Just as fibrosis occurs in chronic inflammation of soft tissue chronic inflammation results in formation of new bone. Esentially this results in chronic ossifying periosteitis.

In the horse special names are given to exostoses occurring in certain location like ring bone: If the exostoses is found on the 1st or 2nd phalanx. This is painful condition causing lameness.

Splint: Exostoses at tendon of metacarpal o rmetatarsal bone, not usually painful and so no lameness is seen.

Spavin: Exostoses on the media portion of the distal tarsal bones cause lameness as the bony growth punches the cuneal tendon, which passes over it. The exostoses or osteophytes have the structure of a compact bone, but do not have Haversian system.

The lesions produced by bacteria in chronic osteomyelitis are granulomas. Histologically in chronic osteomyelitis, centres of pus are surrounded by granulation tissue and inflammatory cells, consisting of mostly of mononuclear and a few giant cells. Due to activity of the osteogenic layer of the periosteum new bone is formed and so the shaft is thickened and marrow narrowed-osteosclerosis. In actinomycosis and tuberculosis is there in rarefaction of bone-rarefying osteitis. In T.B there is extensive destruction of bone with the formation of caseous material but new boner is not formed.

Fractures

A fracture is a break in the continuity of bone.

Varieties of fractures; simple fracture: Fracture of bone without an opening over the overlying skin.

Compound fracture: Fracture with an opening on overlying skin.

Comminuted fracture: Fracture where the bone has been broken into number of pieces.

Impacted fracture: When one fragment of fractured bone is firmly driven into the other.

Greenstick fracture: Here one side of the bone is broken while the other is intact as occurs when a green stick is bent.

Pathological fracture: The fracture is not due to trauma only but due to some existing bone diseases like osteosarcomas and developing tumors of bone marrow.

Articular fracture: When joint surfaces of bone are involved.

Depressed fracture: In the skull where the involved bone is depressed below the surfaces.

Linear fracture: Here the bone is split length wise.

Transverse fracture: Fracture at right angles to the axis of the bone.

Multiple fractures: Here two or more lines of fracture of the same bone but not

communicating with each other.

Oblique fracture: The fracture break extends in an oblique direction.

Condylar fracture: Affects the distal ends of humerus of femur or proximal tibia. Condylar fracture as medial or lateral.

Articular fracture: Articular fracture indicates subchondral bone.

Avulsion of fracture generally caused by muscular contractions.

Fractures are classified anatomically as to location in the bone, epiphysis, metaphysical and Diaphyseal.

Fractures are also classified according to the plane of fractured surface.

Spiral fracture is the one which is the fractured surface is spiral and is produced by torsional stress which fractures the bone along the line of maximum sheer.

Oblique fracture: The fracture surface form an angle with the axis of shaft.

Comminution indicated more than two fragments or potential fragments are present.

A closed fracture is one in which the fracture surface does not communicate with the skin or mucoummebrnaes.

An open or compound fracture is a discontinuity occurring in the bone which communicates between the fractures surface and the skin or mucous membrane.

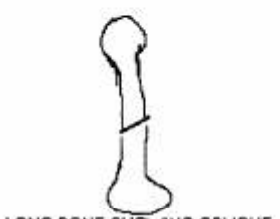
A pathological fracture is a discontinuity occurring in the bone at an area of weakness covered by pathologic process in including a tumor, infection or metabolic diseases.

A stress or fatigue fracture is the response of bone to repeated stresses, none of which by itself is sufficient to cause fracture. In soldiers forced to walk 2nd and 3rd metatarsal bone is fracture.

A compressed fracture results when a compression force causes compaction of bone traculae resulting in decreased lengthy or width of a partition of a bone.

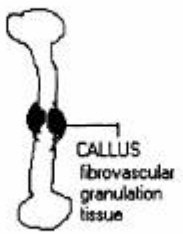
Greenstick fracture is an incomplete fracture with the opposite cortex intact.

A torso fracture is arising in which one cortex is intact with buckling or compacting of the opposite cortex. Diaphyseal fracture- Midshaft fracture- fracture of metaphysic -epiphyseal fracture.



LONG BONE SHOWING OBLIQUE FRACTURE

COMMINUTED FRACTURE



HEALING OF FRACTURE

Healing of fracture

Along with fractured bone, there is hemorrhage as the blood vessels nearby are torn and ruptured. Moreover the capillaries of the Haversian canals also contribute to the hemorrhage. Because of ischemia due to cessation of local circulation, bone cells die and these incite an inflammatory reaction. The accumulated blood clots and in twenty four hours this clot is invaded by fibroblasts and capillaries from the periosteum and is organized. This fibrovascular tissue is strong enough to keep the two broken ends together and is known as soft tissue callus. Callus is Latin for a hard substance. Thus callus is fibrous vascular granulation tissue developed to heal the fractures bone.

Osteoblasts derived mostly from the deeper layer of the periosteum invade the blood clot along with the capillaries and within 4 or 5 days trabecular or formed around central spaced which become Haversian canals. This is the osteoid laid down by the osteoblasts. This osteoid is well formed the end of 2nd week. Osteoblasts are also formed metaplasia of the fibrous tissue. Later calcium salts are deposited on the osteoid to form bone. The newly formed bony tissue unites the two ends of the fracture bone and is known as provisional callus.

The callus is formed by the periosteum and located sub-periosteally is called external callus. That is present in the medullary regions and is called internal callus and that between the end of the shaft of the intermediate callus or in line callus.

The callus formed is larger than the outlines of the bone and so bulges on the periosteum side. In the beginning there is no orderly arrangement of the trabaculae and Haversian systems. Later the provisional callus is removed by osteoclasts and remodeled by osteoblasts into regular bone. This is called definitive callus. It may take several months for this definite or hard callus to form. Finally during the remodeling processes, excesses of callus are removed.

If the gap between the two ends of a broken bone is too wide, the fibro blasts of provisional callus may become cartilage cells by metaplasia and this later converted into bone endochondral ossification.

Factors that interfere with healing:

1. **Non-alignment of the two ends of bones:** Due to this deformity excessive callus formation and displacement occur.
2. **Infection:** This is common in compound fractures, leading to necrosis and osteomyelitis which retard the process of healing.
3. **Deficiency of calcium, phosphorous, vitamin D and proteins:** These may occur in dietary deficiency, starvation, metabolic or infectious diseases.
4. Presence of foreign bodies hinders normal and rapid healing. These extraneous objects like bullets, muscle, fat or clothing.
5. **Fragments of necrotic bone:** This is more common in comminuted fractures, where necrotic bone acts as a foreign body, producing inflammation and preventing healing.
6. **Inadequate immobilization:** A false joint or pseudoarthrosis may occur if the fractured ends are not firmly immobilized. This provisional callus is not sufficiently mineralized and so permits bending at the fractured area.
7. **Senility:** In older animals, healing is a slow due to decreased vascualrity and retarded metabolic processes.
8. **Pathological:** Presence of osteodystrophy or neoplasms prevents healing of fractures.

Pulmonary osteoarthropathy (Marie's disease)

This occurs frequently in humans and dogs. The lesions are found in the lungs and bones are also affected. Bones are affected and formation of new bone under the periosteum that is periosteal hyperosteoses. As the osteophytes formation is not even, the bony surface is rough. Osteophytes increase resulting in bony excrescences. In the lung foci of new bone formation is seen.

The causes are due to lack of oxygen to bone cells. In brief the pathology laid in this way. When heart and lungs are involved in chronic diseases, there is interference in vascular supply of extremities and there is development of passive congestion in these areas. This type of lesions is also seen in neoplastic diseases, Spirocerca lupi infection in dogs and with Dirofilaria infections. Anoxia probably

with some obscure toxins is responsible for this. It is also; though those skeletal changes are the result of reflex vasomotor disturbances in limbs, secondary to circulatory disturbances.

Tumors of Cartilage and Bone

Chondromas and Chondrosarcoma

These tumors consist of primarily of neoplastic cartilage cells. They occur in places where cartilage is normally present i.e., at the epiphysis of long bones of the extremities, the costo-chondral and chondro-sternal junctions, and in the cartilage of the nasal passages, larynx, trachea and bronchi. Tumors that develop on the surface of the cartilage and project under the periosteum of the bone are known as Chondromas, while those that remain the interior or substance of a cartilage or bone are known as enchondromas.

Incidence: Chondromas are one of rare tumors of animals. Dogs are the most commonly affected among animals and in these mammary gland is the most common site. In the mammary gland, the myoepithelial cells which are toti-potential cells are responsible for the metaplastic change and development of Chondromas. The epiphysis of long bones, the chondro-coastal and chondro-sternal articulations as well as the bronchi, trachea and larynx are the places mostly affected.

Grossly Chondromas are large in size and may be multi-nodular. Majority is encapsulated and may have rounded contour. They are bluish white and on section are of translucent appearance. Some may show cysts due to degeneration. Foci of calcification may be present.

Histologically, Chondromas may show very cellular appearance, consisting of round or ovoid cells set in a bluish matrix. The cells are arranged singly but not in groups of four or eight as in the normal cartilage. Strands of fibrous tissue separate the tumor into lobules.

Chondrosarcoma are more cellular and the cells often show pleomorphism. At the periphery may be seen the immature spindle shaped cells while the centre may be found fully differentiated cartilage cells. Mitosisis frequent. Hyperpalstic nuclei contain many nucleoli. Blood supply is found in the connective tissue only but none in the cartilage. So large areas of tumor may be necrosed and calcified. Metastases are commonly seen in the lungs.

Osteoma and Osteosarcomas

Osteoma is hard tumors composed of bone. They are frequently found on the head. They are usually nodular and encapsulated. Depending on the hardness, Osteoma is divided into two varities as Osteoma eburneum or compact Osteoma or Osteoma spongiosum or spongy Osteoma.

Compact Osteoma is commonly found more often in the skull, scapulae and pelvic bones. Spongy Osteoma is found near the ends of long bones like humerus and femur etc.

Grossly Osteoma is small, hard, slow-growing, sharply defined and encapsulated. They are round or elliptical in shape. The bone in the vicinity of an osteo-sarcoma usually shows extensive destruction. This is because the bone has a tendency to undergo demineralization, whenever active growth is present.

Histologically the structure of the bone with lamellar arrangement is noticed. Sometimes Haversian canals may also be seen. In some cases it is difficult to differentiate Osteoma from ex-ostoses, which arises from the periosteum of bones due to inflammation and degeneration. Sometimes bone may be formed in muscles, heart, and lungs by metaplasia of fibrous tissue in these places and this must be differentiated from osteomas.

Osteosarcomas are also being called as osteogenic sarcomas. This is a highly developed malignant tumor and arises wherever bony origin is there. Dogs are probably the animals most commonly affected. Large breeds of dog are more affected. Osteosarcomas in the dog may be either skeletal or extra skeletal. They must be differentiated from inflammatory formation of bone i.e., exostoses.

The limbs are the sites of predilection.

Grossly, the tumors are round or ovoid in shape and may replace much of the normal bone. The marrow cavity may be invaded and occupied. The tumors may be hard or soft, containing spicules of bone and cartilage. They may be white, yellow or pink in colour.

Histologically, the tumor is very cellular. The neopalstic cells are pleomorphic being round, spindle and polyhedral. The cells are arranged in compact masses. Tumor giant cells are present. The tumor cells possess hyperchromatic nuclei each with a single nucleolus. Numerous mitotic figures are present. Spicules of new borne may be encountered. Numerous thin walled blood vessels are present. Metastases are found in the lungs mostly, and other tissues are not affected much. Spread is common by blood stream.

Giant cell tumors (Osteoclastomas)

These are believed to be arising from the osteoclasts. These tumors are not common among animals. As the tumor grows by expansion, absorption of the bone takes place leaving a thin cortex. When such bone is broken, gives an egg shell crackling sensation. This is also called as egg shell crackling tumor. Giant cell tumors are slow growing and do not metastasize.

Histologically numerous giant cells similar to osteoclasts are found amidst a ground substance containing oval spindle cells. Arrangement of the nuclei in the giant cell is at the centre and not at the periphery as seen with foreign body giant cells

of the inflammation.

Diseases of joints

Joints or articulations are structures in which two or more bone or cartilages are united. Depending on the tissue which unites them, they maybe classified as fibrous, cartilaginous or synovial joints.

Fibrous joints (synathroses) comprise sutures, syndesmoses and gomphoses. Sutures occur in the skull, are formed by fibrous tissue, and permit continued growth of the bones they unite by virtue of osteogenic cells at their borders. Syndesmoses unite skeletal structures by fibrous, elastic or fibroblastic tissue. When the original tissue becomes ossified with age a synostosis is formed. Such unions occur between the shafts of the tibia-fibula, and of the radius-ulna in some species. Gomphoses are really not joints, since the term refers to the fibrous unions of teeth, which are not skeletal structures, to alveolar bone, by the periodontal ligament.

Cartilaginous joints (amphiarthroses) are united by hyaline or fibro-cartilage or a combination of two. There are two types. A synchondrosis is a temporary joint in which hyaline cartilage is replaced by bone at maturity. The epiphyseal cartilage which unite two centres of ossification occurs in the basocranium, The second type of cartilaginous joints is the symphysis, where the uniting tissue is fibro cartilage, at least during some stage of the joint's existence. Examples are the pelvic symphysis and the joints between vertebral bodies.

Synovial joints (diarthroidal joints) are characterized by a joint cavity, a synovial membrane lining a fibrous capsule, and mobility, which is facilitated by Articular plates on the ends of bones forming the joint. Simple synovial joints unite two articular surfaces; composite joints unite more than two. Some synovial joints also have ligaments, while others contain cartilaginous discs or marginal cartilage encircling the rim (acetabulum with femoral joint).

The basic components of synovial joints are capsules and ligaments, synovial memebranes, synovial fluid, and articular cartilage with special structures, including fat pads, synovial fossa and cartilaginous discs in some joints.

Articular capsule and ligaments are composed of fibrous tissue, interlaced collagen, and reticular fibers with cant elastic and ground substance and a few fat cells, histiocytes, and leukocytes. The tissue is poorly supplied with blood vessels, which, together with its unyielding density, limits its expression of inflammatory phenomena and its capacity for repair. Repair may eventually may be complete. Both ligaments and capsules are well provided with proprioceptive and pain end organs, the latter accounting for some of the pain of arthritic diseases.

Fibrous capsules vary in their thickness and strength depending on the demands placed on them. Fibrous capsules form sleeves around the joints, enclosing the

articular structures. Their inelastic quality aids the proper location bone ends and helps to restrict movement, especially near the extremes off or the range of movement of joint. In this the ligament as it, their shape and position being in accord with the functions of the joint. The limited elasticity of capsules and ligaments, although necessary for restriction of joint movement, means that excessive or prolonged tension may stretch the structures irreversibly.

Fibrous capsules and ligaments are attached to bone either directly or indirectly but attachment to each other or to other internal and peri-articular structures. Some of the fibers are attached to periosteum and others become incorporated in bone. Whereas excessive tension on ligaments may rupture them, avulsion fracture or detachment of ligaments is more likely, especially in osteodystrophy. Much of the restrictive to motion in stiff joints, including those of arthrogryposis rises in the fibrous capsules rather than in synovial or articular structures. Abnormalities mobility of joints may be prominent in osteogenesis imperfecta of claves and lambs. Laxity of capsules and ligaments occur sin a number of metabolic diseases, especially the osteodystrophy associated with calcium and phosphorous deficiencies, and that provide degenerative changes are into advanced, tone is rapidly restored to these structures with correction the deficiency.

The specialized lining synovial cells have a variable appearance and arrangement by both light and electron microscopy. Where the synovial membrane is subjected to pressure from adjoining structures, the subintimal layers is fibrous, and the lining cells generally resemble the underlying fibroblasts. The synovial cells overlying adipose and areola tissue are similar to each other and may form one to 3 layers. Two main cell type war disintinguished by light and electormicroscopy. TyepA cells are more numerous and tend to be located onto the surface of the synovial membrane. They have irregular cytoplasmic and nuclear outlines, long cytoplasmic processes, and contain extensiveGolgi apparatus, granules and micro pinocytotitic vesicles. TypeA cells are phagoyctic and akin to macrophages. Type B cells tend to be located deeper in the synovial membrane and have smoother cytoplasmic and nuclear outlines. Their cytoplasm contains large amount of endoplasmic reticulum and a relatively extensive Golgi apparatus. Many of them contain granules and vesicles similar to those in type A cells. Type B cells produce hyaluronic acid. Other cells are intermediate between the A and B type. In proliferative stage type A cells are less and intermediate cells are more. There is no basement membrane to synovial and there are not tight junction or desmosomes between the synovial cells. Instead they are arranged in granular inter-cellular matrix which contains fine fibrils, which are similar to fibrils in the cytoplasm of type A or B and some collagen fibers. The discontinuous lining may be part of the reason that particulate matter and bacteria can rapidly gain access to the subsynoival tissues and joint cavity. The abundance of capillaries and lymphatics probably so facilitate this movement.

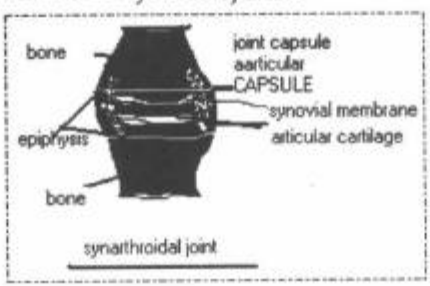
The synovial membrane is freely permeable in either direction to molecules of small dimension, which may be removed by the capillaries and lymphatics. Particulate material is also readily removed by phagocytes. Hyperemia of exercise and inflammation hastens the exchange. The removal of articulate material form the joint and it deposition in the subintimal layer is a continuous process of removal of debris. When the volume of debris is large in diseased joints, it presence which contributes to the swelling and fixation diseased joints. Synovial membranes have a great regenerative ability, following biopsy, great proliferative ability in certain disease states.

There is a gradual transition from the synovial membrane to the periosteum and cartilage margin and the intima is well periosteum and cartilage margin and in this well vascularised where it extends on to the cartilage surface. Its marked proliferative ability probably is correlated with its vascualrity, and it is in this area that tension, or altering slipping and osteophytes formation occurs in arthritis and arthropathy. Hyperplasia and development of new villi occur with age and size and give the synovial membrane a velvety appearance. Cartilaginous metaplasia occurs in the stroma of the synovial membrane.

In chronic synovitis, lymphocytes which may be arranged in follicles or as diffuse infiltrations and plasma cell accumulate in hypertrophic synovial villi. In septic arthritis local antibodies may be secreted into the synovial fluid. Transfer of serum antibodies to synovial fluid is probably in significant in normal joints.

Synovial fluid is generally regarded as a protein free dialyste of plasma to which hyaluronate, glycoprotein, immunoglobulins, lysosomal enzymes, and other unidentified macromolecules are added by synovial cells. There is a blood-synovial barrier exists whose function depends on the presence of fenestrations in the synovial capillary and probably on at the intimal cells and the hyaluronate in their supporting stroma, which act as a filter of various molecules.

The volume, composition, and viscosity of synovial fluid vary markedly from joint to joint and between the same joints in different animals. Exercise and inactivity increase and decrease the amount of fluid the volume of synovial fluid in joint. Increased amounts of fluid and changes in its physical properties from a clear viscous material to a cloudy or water substance are consistent with inflammation or degeneration of synovial joints.



Arthritis

Inflammation of joints is called arthritis. Inflammation of hip joint is called coxitis while that of stifle joint is gonitis. Arthritis may be acute or chronic.

Acute arthritis

Causes:

1. Contusion or strain in which there is stretching of the joint capsule.
2. Bacteria enter either through the blood stream or by extension from neighbouring tissue and or through punctured wounds. In calves , *Streptococcus, Escherichia coli, Actinomyces pyogens, salmonella species, Mycoplasma bovis* and *Corynebacterium pyogenes*, in foals *Shigella equirulis* and *streptococci, Klebsiella species and salmonella species* in sheep *staphylococci* and *corynebacterium* and in pig's *streptococci , Erysipelothrix rhusiopathiae,Streptococcus, Haemophilus spp, Mycoplasma species and Brucella abortus* infections, in dogs *Staphylococcus species, Streptococcus species, and Escherichia coli.*
3. Trauma usually produces a serous type of inflammation in which there is increased production of synovial, distending the joint capsule.
4. Bacterial arthritis could be called as non-suppurative or suppurative.
5. In non-suppurative arthritis there are acute serous or serofibrinous exudates and the causes are Erysipelothrix rhusiopathiae in sheep and pig and Haemophilus influenza Suis in pigs.
6. Grossly exudates contain yellowish flakes, which are often compressed into flat structures which float in the joint fluid. The synovial membrane is thickened and studded with heaemorrhages.
7. Histologially hyperemia and neutrophilic infiltration are common. Articular cartilages are eroded.

Grossly all the symptoms of an acute inflammation are seen notably swelling of the joint. White, yellow or green pus may be present in the joint depending on infecting organisms. Mycoplasma infections produce thin and colorless exudates in joints.

In suppurative arthritis the articular cartilages are destroyed. This condition is usually associated with navel ill. The bacteria localise in the joints because of the rich blood supply there and also probably to the weak defenses in that region. Suppurative osteomyelitis, necrosis and caries of bone results. Particles of disintegrated bone are found in the pus, like grains of sand. Sometimes, the pus may be discharged through a break in the skin resulting in an open joint. The articular cartilages maybe inflammed and eroded. Synovial fluid which is increased is purulent. There may be inflammation of peri articular tissue.

Histologically infiltrations of neutrophils are observed. In young animals this is unfavorable as pain is excruciating, fibrosis and ankylosis of the joint will result.

Chronic serous arthritis: Due to destruction of the articular cartilage, there may be fibrous adhesion between the two articular surfaces. Subsequently the two bones may fuse together producing ankylosis of the joint.

Tuberculous arthritis is characterized by granulomatous inflammation and is manifested in three forms. These are miliary form, where miliary nodules are found in the synovial membrane. The neighbouring tubercles may coalesce and project into the joint cavity as pearls.

Infiltrating tuberculosis is seen in cattle, c characterized by diffuse tuberculosis granulation tissue containing epitheloid cells and giant cells.

Caseating tuberculosis synovitis with caseation but without specific grnaulation stage.

In Mycoplasmal arthritis of swine grossly, there is increased serosanguinous synovial fluid in the femero-tibial, coxo-femoral, cubitalor scapula-humeral joints. The synovial membranes are swollen, hyperemic and discolored but the joint capsule and articular surfaces appear normal. Histologically hyperplasia of synovial swelling cells, villous hypertrophy and extensive mononuclear infiltration are noticed.

Chlamydial poly arthritis in calves is severe; both naturally and experimentally showed high mortality. Affected calves are weak at birth, suggesting intrauterine infections. In these animals there is fever, anorexia, reluctance to stand or movie and welling of joints develop in 2 to 3 days and death occurs 2 days to 2 weeks after onset of signs. All or many joints are affected and those of limbs most severely. The subcutaneous and adjacent peri-articular tissues are oedematous with clear fluid, and this extends also around tendon sheaths. Surrounding muscle is hyperemic and oedematous with turbid yellow grey fluid and strands of fibrin and adheres to the synovial. Other organs show changes of septicemia.

Mycoplasma mycoides sub species mycoides which causes contagious bovine pleuro pneumonia in adult cattle and buffaloes also cause polyarthritis and endocarditis in calves.

Non-infectious arthritis: Immunological mediated; immunologically mediated noninfectious arthritis is a form of inflammatory joint disease in which the stimulus for inflammation is either local and persistent immunological disturbances centered in the synovial of the affected joint or joints or an immune mediated disease centered elsewhere in the body. The synovial involvement in majority of cases is secondary and the products of immune response are transported through the blood to the joints where they become lodges in the walls also the synovial capillaries initiate a local inflammatory response. The presence of neutrophils is into characteristic feature in the joint capsule in this type of inflammation. This may cause erosive or non-erosive arthritis. The erosive pattern includes rheumatoid like arthritis of dogs, polyarthritis of greyhounds and feline chronic

progressive polyarthritis. The nonerosive patterns includes polyarthritis of dogs and cats with systemic lupus erythematous; idiopathic polyarthritis which is identical to systemic lupus erythematous except for an absence of serological abnormalities found in that disease.

Ring bone- This is a condition of degenerative atrophy affecting the inter-phalangeal articulation of horses, resulting in ankylosis and lameness. Articular ring bone is a condition wherein articular cartilages may be destroyed resulting in ankylosis due to union of the articular ends of the bones by grnaulation tissue which become ossified. More often there is chronic inflammation of the periosteum and the ligamentum apparatus due to repeated concussion and these results in peri articular ring bone, in which the exostoses occur as a ring round about the ends of bones. Some times these peri-articular exostoses may fuse bridging the joint and fixing it.

Spavin: This is arthropathy of the tarsal joint affecting its distal and medial parts. Ankylosis may results. The condition starts with degeneration of the cartilages of the 2nd and 3rd tarsal bones. Subsequently other tarsal and metatarsal bones are involved.

The normal white or bluish cartilage undergoes degeneration, becoming opaque and fibrous. It breaks down and ulcerates. Granulation tissue from the exposed bone grows and fuses with that growing from the opposite end. When this becomes ossified, the joint becomes ankylosed. No peri articular changes may be noticed. So such a condition is known as occult spavin.

Ankylosing spondylosis: In this condition, the small vertebral articulation becomes Ankylosed. Affected bulls show posterior weakness and ataxia, or paralysis after dismounting from service. The onset of signs is associated with fracture of vertebral bodies and of the Ankylosing bone. The line of fracture tends to follow a large penetrating vessel to the intervertebral disc, which is frequently separated, and the to diverge across the dorsal corner of one or other vertebra. Ankylosing spondylosis: In is common in adult sows. The ankylosis may be confined to the ventral aspect of vertebral bodies. Any factor which permits abnormal mobility of intervertebral articulations has the potential to stimulate osteophytes formation and spondylosis: In cats with vitamin A deficiency vertebral ankylosis has also been reported.

Protrusion of inter-vertebral discs:

Embryology of vertebrae formation: Vertebrae are in fact each is formed by contribution from two somites of each side. Blocks into which paradoxical mesoderm is segregated to each side of neural tube and notochord. Together with ribs and sternum, they are produced from the medial positions of somites known as sclerotomes. Muscles of vertebral column are derived from lateral portions of somites, the myotomes. Each myotomes attracts a single nerve that

grows from the adjacent neural tube. It was formerly believed that the connective tissue component of skin- the dermis is derived exclusively from 3rd portions of somites, the dermatomes.

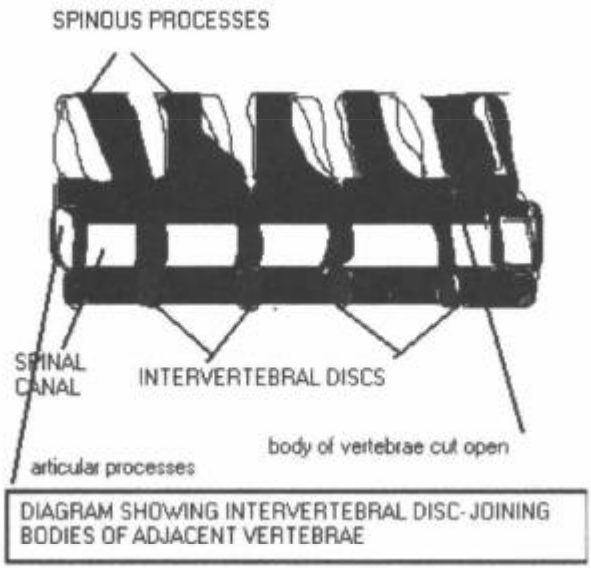


DIAGRAM SHOWING INTERVERTEBRAL DISC- JOINING BODIES OF ADJACENT VERTEBRAE

Protrusion of intervertebral disc condition is met within man and dogs.

The vertebral bodies, with the exceptions of the first two cervical, are united by intervertebral discs. The discs in association with the articular facets permit some movement between the vertebrae, and the central portions, which are hydrophilic and normally turgid, are useful shock absorbers. A cross section of normal disc reveals that its centre is composed tough jelly like mass, tenacious pulposus, which are remnants of primitive notochord. Normally the intervertebral disc consists of a central nucleus pulposus which is semisolid mucoid connective tissue. This is enclosed in thick fibrous covering the annulus fibrosus.

The discs are attached to the ends of vertebrae in the same manner as articular cartilages are attached to the epiphyses. The ventral longitudinal ligaments fuse with the annulus fibrosus of each disc as it passes. The dorsal spinal ligament lying in the vertebral canal fuses with the dorsal part of the annulus fibrosus, except in the thoracic region between the 2nd and 10th ribs; in this region the conjugal ligaments, which connect the heads of correspond ribs, cross the floor of the canal between the annulus fibrosus and the dorsal longitudinal ligament. The conjugal ligaments fuse with and reinforce the dorsal partition of the annulus fibrosus. These anatomic relations have a considerable bearing on the consequences of degenerations of the discs. Due to violent trauma and degenerative changes in senility, there may be a rupture in the annulus, from which the nucleus pulposus

escapes and becomes displaced. Usually two forms of displacement occur namely dorso-lateral prolapse of the nucleus pulposus into the spinal canal and ventral prolapse beneath the spinal ligaments. In this variety due to formation of osteophytes ankylosing spondylosis: In results.

In the dogs, those having long vertebral column and humans who are tall and frequently travel will get this condition. In females, the relaxin hormone liberated during pregnancy makes the ligaments loose as well disc protrusion is common in with repeated pregnancies. This is not common with animals.

In the chondrodystrophic breeds namely *Dachshunds, Pekingese and French Bull dogs* at a very early stage, the nucleus pulposus become cartilaginous, which later becomes denigrated and calcified. So the nucleus pulposus, which is normally a gel and so able to withstand shocks and transmits pressures firmly to the annulus fibrosus, becomes transformed into a cheesy mass which crumbles easily. This material transmits pressure to localised points of the annulus, which also undergoes degeneration. Its lamellae become hyalinised and later split. In other breeds the above changes occur in id or late life.

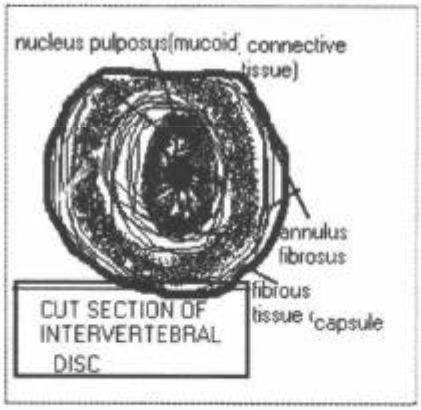
In non-chondrodystrophic breeds, the initial degenerative changes occur later in life and consist of fissures in the annulus fibrosus, which stimulates vascularisation. At this stage, the nucleus pulposus is normal. Degenerative changes in the annulus progress from within outward, independent of the nucleus, and the annulus is converted into foci to a structureless, granular mass with unmasked lamellae, which are thick and prominent and progressively frayed and disrupted. After middle age, the nucleus is gradually toughened by a concentric deposition of collagen fibers. This fibrous transformation is regarded as a maturation changes on which degeneration may be superimposed. The degeneration takes the form of necrosis in which dystrophic mineralisation seldom occurs. Prolapse associated with this form of degeneration are associated with partial rupture of the annulus and bulging of the dorsal surface of the disk.

The displaced nucleus pulposus presses uppon there spinal cord producing nervous lesions. The protrusion of the disc may occur at any level, but occurs more frequently in the lumbar region or in the posterior thoracic region. Complete paralysis of the posterior region may be noticed. Pressure on the spinal cord may produce heaemorrhages and necrosis in the involved areas. Wallerian degeneration of the nerves may be noticed in the spinal nerves arising from the affected region as well as demyelination of nerve tracts.

Since the dorsal part of the annulus is thinner than the ventral, the great majority of displacement occurs dorsally toward or into the spinal canal. Most disc prolapses either in thoracic-lumbar or in the cervical regions.

Symptoms are excruciating pain with exaggerated reflex; movements of hind legs which may be intermittent or occur over long periods. Partial paralysis of the

limbs. And violent reaction to stimuli which is of spastic type. Rapid progressive paralysis and early death due to respiratory failure occurs in animals and man in severe conditions.



In dogs prolapsed discs are the most common cause of spinal pain, paresis and paraplegia in dogs. Affected animals are usually males aged 3-6 years. However, other syndromes do occur, including ventral herniation,embolism of disc material to the spinal cord, disc explosions associated with trauma.

Bursitis

Inflammation of the bursa over the joints is bursitis. This is of frequent occurrence in animals. Hygromas of carpal joint in cows and capped elbow or hock joints of horses. The causes are trauma especially if repeated, infection like brucella infections as seen with hygromas and fistulous withers in horses.

Grossly the inflammation may be serous, serofibrinous or purulent. Trauma produces serous type and one example is the serous bursitis of hock joint in horses. This is called bog spavin.

Poll evil is the inflammation of the bursa between ligamentum nucahe and atlas and axis.

Fistulous withers are the affection of bursa between the ligamentum nucahe and the thoracic spines. The inflammation is suppurative granulomatous one in which fistulae open on the surface of the skin. Causes are trauma, parasites like *Onchoerca cervicalis or Brucella abortus and Actinomyces bovis*. The suppurative granulomatous reaction is attributed to the two organisms, infection occurring haematogenously.

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Chapter 11

Diseases of Integument, Skin, Ear, Hoof, Nail and Horn

Diseases of Skin

Histological structure of skin-Epidermis-stratum Ultrastructuraly stratum granulosum stratum cornuem. Keratinocyte- Merkel cells- Melanocytes-Langerhans cells Other peculiarities of skin-The dermis Hair follicles anagen hair follicle- Sweat glands First type of sweat glands-Parakeratosis -Dyskeratosis-Hypoplasia Atrophy-Acantholysis-Hyperplasia-Dyskeratosis-folliculitisis Mycotic diseases of skin-Cutaneous mycoses

Diseases of Skin

Skin or integument is the single largest organ of the body. The word integument is of Latin origin, and means covering. Representing the physical barrier between the environment and the organism, the skin performs many important functions. The skin prevents fluid loss, and keeps opportunistic organism from invading the more vulnerable underlying soft tissues. Its functions in temperature regulation through neurlogic communications between hypothalamus and cutaneous vasculature. Skin reflects a wide variety of systemic disorders, most notably certain metabolic, viral, inflammatory and endocrine diseases.

Keratocytes in addition to the building blocks of theepidermis, conduct important paracrine communication function through the secretin of important cytokines. Thus skin serves important functions in the over all immune surveillance system of the body.

Histological structure of skin

Epidermis is the most superficial layer of skin and is composed of stratified squamous epithelium, composed primarily of keratinocyte with smaller number of scattered dendritic, Langerhans cells, melanocytes, Merkel cells and migrating lymphocytes.

The stratum basal is the deepened and germinative layer of the epidermis. It consists of single layer of cells, which are usually more cuboidal basal cells are mitotically active. The mitoses usually occur in some animals during sleeping periods. Basal cells express a specific set of keratin filaments K_5 and K_1. They are

express surface receptors belonging to the integrin and cadherin families. These molecules mediate cell to cell and cell to substrate adherence and have profound influence on keratinocyte growth and differentiation. This contain row of distinctive cuboidal cells with hyerchromatic nuclei just on the epidermal side of the basement membrane.

Above stratum basale lie the stratum spinosum. It is composed of polyhedral cells and these cells assume a more flattened morphology. Numerous inter cellular junctions between keratinocyte are called as desmosomes. The stratum spinosum is usually between 2 and 5 cells thick in hairy skin, thinner in dogs and cats than in cattle, horses and pigs but usually 29 cell layers thick in foot pad areas of canine or feline. Ultrastructuraly the cytoplasm of the stratum spinosum cells are filled with keratin filaments, anchored to the cytoplasmic membrane at the desmosomal junction. These intermediate filaments are approximately 8 nm in diameter and comprise acidic and basic subunits, which assemble in pairs. The precursor protein for the cornified envelope is also produced with stratum spinous but is inactive.

The stratum spinosum and stratum basale together are simultaneously referred to as the Malphigian layer.

The *stratum granulosum* is often discontinuous and only one cell thick in the haired skin upto 8 cell thick in foot pads. It is composed of nucleated flattened keratinocyte which are distinguished by the blue black granules of keratohyaline. These contain profilaggrin, the precursor of matrix protein which eventually glues together the keratin filaments.

The *stratum cornuem* is composed of many layers of flattened terminally differentiated dead cells. The cell thickness in animals may be around 50 cell layers. In the stratum cornuem profilaggrin forms flaggrin, and heavily cross links microfilaments of keratin. The cornified cells are bound together by an insoluble lipid rich extracellular matrix as bricks are bound by mortar. Transglutaminase enzymes are critical to the cross linking of the cornified envelope precursor proteins such as involucrin, keratolinin and loricrin. These form along with the intercellular lipids the critical permeability barrier.

Keratinocyte make up 85% of the epidermis; the remaining cells resident in the epidermis are melanocyte (5-8%), Langerhans cells (5%), Merkel cells and indeterminate dendritic cells. The epidermis is the most superficial layer of the skin and is composed of stratified squamous epithelium composed of primarily of keratinocyte with smaller number of scattered dendritic Langerhans cells, melanocytes and Merkel cells and migrating lymphocytes. The keratinocyte differentiate as they progress from the deeper portion of the epidermis to the surface, where they die leaving their cytoplasmic keratin protein as the cornfield layer. In hairless region in some domestic animals, the next layer to stratum cornuem is the stratum lucidum. It is composed of flattened anuclear keratinocyte

and as it name implies, has a somewhat translucent appearance compared to the most superficial keratin.

Melanocytes are dendritic cells within the epidermis that make melanin, the pigment of the skin. Melanocytes are numeorus in the hair follicles, except in white animals. Melanocytes have processes. The melanocytes extend their dendritic processes around adjacent keratinocyte, forming an epidermal-melanin unit. Melanin is transferred to the keratinocyte, and the pigmentmigrates to the surface with the differentiating cells. These cells are formed embryo logically from the neural crest and migrate to the epidermis during foetal development. There they tend to populate the basilar regions of the epidermis, but their dendrites extend for significant distance between keratinocyte throughout the stratum basale and spongiosum. Melanin is produced by a tyrosine dependent pathway, thus melanocytes synthesis tyrosinase and packed melanin in specialized cytoplasmic organelles called melanosomes. Skin colour is impaired by the transfer of these melanosomes from melanocytes to keratinocyte. Thus it is these pigments containing keratinocyte that absorb and disperse damaging energy form ultraviolet light.

Merkel cells are found sporadically throughout the epidermis. Merkel cells are found in the epidermis. In humans they are more abundant in areas typically involved with sensory perception such as the face or hands. Clusters and solitary Merkel cells are frequently in intimate association with myelinated nerve fibers. The presence of neuropeptides such as vasoactive intestinal polypeptide and metenkephalin like protein, has been localised to these granules, which along with their close association with nerve terminals, has prompted investigators to propose that either have a role in signal transduction for mechanoreceptors, sub serve a neuromodulator function by influencing action potential threshold of adjacent sensory nerve terminal or perhaps provide trophic navigational signals to developing neuronal axons. These Merkel cells contain typical dense core neurosecretory cytoplasmic granules and function as mechanoreceptors.

Langerhans cells are suprabasilar bone marrow derived dendritic cells found in all squamous epithelia, including the follicular epithelium of skin. They constitute 2 to 8% of epidermal cells and share number of properties of mononuclear phagoyctic system. Langerhans cells represent a group of bone marrow derived immune cells with potent antigen processing cells. Langerhans cells are the members of monocyte-macrophage system and are the major antigen presenting cells of epidermis. They reside not only in the epidermis but also migrate after antigenic stimulation to the local lymph nodes. They are important cells in contact sensitization. These could be demonstrable gold chloride preparations. They are positive to ATPase and alkaline phophatase stains. Langerhans cells typically express class II; major histocompatability complex and Cluster differentiation molecules.

Intraepidermal lymphocytes: These form as members of the skin immune system. 2 % of T-cells are present in the skin. These bear CD8 positive markers and function as suppressor or cytotoxic cells.

Immunoglobulin super family: In the immunoglobulin super family are two endothelial adhesion proteins. These are, intercellular adhesion molecule -1(ICAM-1), vascular cell adhesion molecule (VCAM-1). Intercellular adhesion molecule contributes to the endothelial adhesion of most leukocytes cell types, including neutrophils, monocytes and lymphocytes. They appear later than E. selectin, and persist for longer period. The temporal expression of these four endothelium adhesion proteins in response to cytokine stimulation provides a mechanism for the first cell that is neturophil to arrive at the site of tissue damage.

Integrin family: Complement components and TNF-α induce a family of cell surface glyco-proteins on leukocytes designated as β_1 integrins. These are the lymphocyte function related antigen-1 (LFA, CD *11\CD 18).* LFA-$_1$ served as the leukocyte receptor for the endothelial, ICAM-$_1$ proteins. Beta-$_1$ integrins are compounds of group of six adhesion proteins; called very late antigen proteins (VLA) induced by lymphocytes on primary antigenic stimulation. VLA-$_4$ (very late antigen-4) is expressed on resting lymphocytes and monocytes and these are act as ligands for VCAM-$_1$ (Vascular cell adhesion molecule).

Other peculiarities of skin

When injured or appropriately stimulated, the epidermis can produce pro-inflammatory molecules which have profound effects on the underlying dermal vasculature. Variety of chemicals and ultraviolet rays can induce keratinocyte to secrete cytokines tumor necrosis factor- α, IL-8, and IL-1 in vitro. In addition these agents are able to induce keratinocyte expression of E-selectin, the ligands for which is leukocyte function associated molecules. These keratinocyte derived cytokines and ICAM-1 then begin to start the inflammatory response. First keratinocyte derived cytokines (IL-1) and TNF- alfa can induce the nearby dermal vasculature to express the adhesion molecules, E-selectin. VCAM and ICAM-1 and these endothelial adhesion molecules interact with their respective leukocyte receptor, thereby causing leukocyte margination and subsequent migration from the vasculature. Second once brought to the site these extravasated leukocytes may do one of the two things either they can remain in the dermis, where they can amplify stimulatory signals to the epidermis or alternatively they can migrate along IL-8 directed chemotactic gradients to the epidermis, where LFA-1 expressing leukocytes will adhere to ICAM-1 expressing keratinocyte. There they can either provide growth or stimulatory signals to keratinocyte or damage them by cell type specific cytotoxic mechanisms. Thus it is clear thatcells residing in the epidermis and dermis interact in concert with one another to maintain or manifest pathologic changes in the skin. Thus many more agents or environmental stimuli which have the capacity to induce keratinocyte elaboration or expression of

inflammatory cytokines or important adhesion molecules.

Dermis: This is divided into superficial and deep layers. The dermis is composed of collagen and elastin fibers embedded in glycosamino-glycans rich ground substance. Collagen, elastin and most of the glycosamino-glycans are produced predominantly by the dermal fibroblasts.

Dermal collagen fibers are predominantly of type I and III collagen. Collagen types IV and VII are constituents of basement membrane zone, the latter comprising the anchoring fibrils. Collagens types IV and V are also present around blood vessels and hair follicles. Type V has been described forming network around fiber bundles of type I and III collagen. Type VI is distributed throughout the dermis. Elastic fibers compose less than 1% of dry weight of skin.

The fine collagen bundles in the **superficial dermis** tend to be parallel to their surface. In the deep dermis, the collagen bundles are approximately three times thicker than those of the superficial dermis and form a closely packed and interwoven layer.

The principal glycoamino-glycans of skin are hyaluronic acid and dermatan-suflate, with contribution from chondroitin-4 and chondroitin-6 sulfate and heparin which is released from mast cells. Most of these are associated with proteins and hence called as proteolglycans. These large proteoglycans are interspersed with within the firbous matrix and fill the interstitial space. The proteoglycans are important in maintining the normal hydration of skin. Hygroscopic properties of hyaluronic acid molecules are responsible for this.

The dermis contains cellular elements like mast cells in addition to fibroblasts. Mast cells reside around blood vessels and are extremely variable in number. Cat skin contains around 20 mast cells per high power filed. Normal dogs these are around 4-12 cells. The granules derma mast cells stain metachormaticaly with toludine blue that is blue to pink appearance. Dermal mast cells are thought to play an important role in the initiation of inflammatory and immune responses in the skin, because they secrete, on appropriate simulation, tumor necrosis factor - α. This induces the adhesion molecule of ELAM-1 on vascular endothelial cells promoting adhesion of immune cells to dermal vessels. T-lymphocytes, dermal dendritic cells and marophages are present around post capillary venules.

Cutaneous vasculature is dividing into intercommunicating superficial, middle and deep plexuses. The deep plexues occur at the subcutaneous dermal junction, the middle plexus lies at the level of the sebaceous glands. The superficial plexus sends capillary loops to the dermo-epidermal junctions. Lymphatics are present into the superficial dermis and around adnexa. Nerve fibers in general follow blood vessels.

Hair follicles occur in triads. There are two types of follicle simple and compound. The first refers to a single primary follicle. Compound follicles comprise a grouping

of primary follicles surrounded by smaller secondary follcels. Simple hair follicles occur in cattle and horse, while sheep and goats, dogs and cats have compound hair follicles. In sheep compound follicles comprise large central primary hair with two or more lateral primaries each surrounded their secondary hairs.

Hair follicles undergo cyclic growth divided into three phases namely anagen actively growing, catagen, transitional, and telogen resting. The base of the anagen follicle rests at the junction of the dermis and subcutis. The telogen follicles are found closer to the epidermis than the anagen follicle bases in all species.

Catagen the intermediate involution phase is relatively rapid so that few hairs in this stage are seen in the normal skin that is less than 7%. The basement membrane zone of the degenerating follicle becomes folded and wrinkled to form the thick hyaline membrane known as glassy membrane. Eventually the dermal papillae move up to the hair germ.

Telogen or resting hairs are attached to the hair germ by the club, which holds the hair in place until it is dislodged by the next generation hair. The dermal papilla remains a small ball of dermal mesenchyme beneath the inconspicuous hair germ. These germ cells have been considered to represent the resting progenitor cells population for the next cycle of hair growth.

The anagen hair follicle comprises the dermal papilla, the hair matrix within the hair bulb, the hair shaft and the inner and outer root sheaths. The hair matrix surrounds the inductive dermal papilla with its primitive mesenchymal cells. In pigmented hairs, large number of melanocytes lies between their matrix cells. The hair matrix produces both the hair and the internal root sheath. The internal root sheath which comprises three layers namely, a cuticle, Huxley's and Henle's layer. This hardens first so as to form a rigid tube of internal root sheath protein, which protects the zone of keratinisation in the newly forming hair shaft. Huxley's layer contains large brightly eosinophilic granules known as tirchohyalin. These granules contain a high concentration of arginine, precursors of citruline which is probably involved in cross linking of the keratin of internal root sheath. The hair shaft has in addition to the outer cuticle a cortex and medulla. The cortex consists of fully keratinized spined shaped cell oriented parallel to the hair shaft. Hair keratin is hard α- keratin. It is composed of 7.5 nm diameter filamentous proteins rich in cysteine and tyrosine. The filaments are embedded in globular matrix proteins. The external root sheath is continuous with the axe of the hair bulb, which is continuous with the hair matrix. The basement membrane zone of the external root sheath is thin in anagen hairs. It is invested by a sheath of dense fibrous connective tissue.

The skin is an integral part of the organism. Many diseases of the skin are the direct result of metabolic or nutritional disturbances or of functional or anatomic diseases of internal organs, particularly of the gastrointestinal tract, the liver, pancreas, the endocrine glands and the nervous system. On the other hand certain

inflammatory processes of the skin due to infection to chemical irritation may give rise to hepatic, digestive and other visceral disturbances and dermatoses and internal disorders may occasionally constitute concomitant expression of some underlying systemic diseases.

The sebaceous glands are halocline glands which develop as part of the hair follicular complex. Each primasry hair has its own sebaceous gland, which usually comprises 2-3 simple alveoli opening via squamous epithelium lined ducts into the upper part of the hair follicles. The secondary hair follicle usually shares sebaceous glands. Free sebaceous glands may occur on skin such as the lip and anus. Large sebaceous glands occur where the density of hair follicles are less. Other functions attributed to sebum include inhibition of surface microbial growth, prevention of microbial invasion, and protection against high temperatures by promoting light reflection from glossy coat and protection against surface desiccation. Sebum may be produced form sebaceous gland just like hair from hair follicles.

Sweat glands: There are two types of sweat glands. These are coiled tubular glands. First type of sweat glands goes with hairs. These are found in all hair skinned areas. These are associated with primary hair follicles. These are apical glands because part other secretions come from lining epithelial cells of alveoli. Sweat production involves cell death (holocrine secretion), vesicle exocytosis, active ion and water transport.

Second type of sweat glands are seen where hairs are not there. These are found on the foot pads and hoof of animals. Specialized nasolabial glands occur in the dermis of the ruminant muzzle. The mucous secretion are elaborated from these glands.

Arrector pili muscles are smooth muscles which insert on bulge in the external root sheath of the hair follicles. They are largest in the areas where the hair are often erect, such as along the dorsum in cats and dogs. The muscle fibers are often vacuolated in older animals.

Dermatitis manifests all the hall marks of inflammation. In this there is vascular dilatation, oedema and leukocyte infiltration. How the skin responds to injury depends upon where the inciting agent or injury occurs, the type and nature of the insult, and the duration, location to specific skin structures, and severity of the inciting agent.

Parakeratosis is a type of hyperkeratosis and is characterized by proliferative stratum cornuem containing pyknotic nuclei of keratinocyte. It is incomplete carnification at the level of stratum cornuem.

Hyperkeratosis is an increased thickens of the stratum cornuem.

This may be orthokeratosis (anuler) or parakeratosis (nucleated).

Hyperkeratosis occurs in ectoparasitism, zinc responsive dermatoses, vitamin-a responsive dermatoses, thallium toxicity, and dermatophytosis. Diffuse orthokeratosis is seen in endocrinopathy, nutritional deficiencies, secondary seborrhea and developmental abnormalitieslike icthyosis, hyotrichosis and colour mutant alopecia.

Hypokeratosis is a decreased thickness of the stratum cornuem.

Dyskeratosis is premature and faulty keratinisation of individual cells Dyskeratosis cells are characterized by eosinophilic swollen cytoplasm and condensed dark stained nuclei.

Hypergranulosis and hypogranulosisindicate an increased or decreased thickness of stratum granulosum.

Hyperplasia is an increased thickness of non cornified epidermis due to an increased number of epidermal cells.

Acanthosis: Presence of thickened epidermis is defined as acanthosis. This is common in inflammatory diseases of skin. Here the proliferative rate of keratinocyte is increased. Increased production of keratinocyte with decreased desquamation from the surface ultimately leads to hyperkeratosis. Increased thickness of stratum spinosum. Rete ridge formation wherein epidermis appears to project downward into the underlying dermis. This is commonly seen in chronic inflammatory diseases of skin.

Hypoplasia is decreased thickness of the noncornified epidermis due to a decreased number of cells.

Atrophy is decreased thickness of noncornified epidermis due to a decreased size of cells.

Spongiosis of the epidermis is characterized by a widening of intercellular spaces with increased intercellular bridges giving the involved epidermis a spongy appearance. Severe intercellular oedema leads to rupture of intercellular bridges and formation of spongiotic vesicles within the epidermis.

Intracellular oedema or hydropic degeneration of the epidermis is characterized by increased size, cytoplasmic pallor and displacement of nucleus to the periphery. Severe intracellular oedema may result in reticular degeneration and intra-epidermal vesicles.

Acantholysis is loss of cohesions between epidermal cells resulting in intraepidermal clefts, vesicles and bullae. The process may also involve the outer root sheath of hair follicles. Acanthoysis may be caused by severe Spongiosis, hydropic degeneration, proteolytic enzymes release due to neutrophilic or eosinophilic infiltration, in neopalstic transformation of squamous cells and in actinic keratosis.

Vesicles also known as blisters or bullae are fluid filled cavities. Vesicles are generally 5mm in diameter or smaller, whereas bullae are greater than 5 mm in diameter and develop in any layer of the epidermis or beneath the epidermis. Vesicles may form from Acantholysis, epidermal or dermal oedema, degeneration of basal cells, or other processes such as frictional trauma or burns, which cause q alack of cohesions between the epidermal cells or between the epidermis and dermis. The location of vesicles or bullae is suggestive of certain diseases. Most of the viral infections like foot and mouth disease in cattle and pigs, vesicular diseases of swine.

Pustules or microabscesses present in Intraepidermal and sub epidermal areas and are filled with inflammatory cells.

Hyperpigementation of skin which is focal or diffuse and confined to the stratum basale or present throughout all epidermal layers. It is common condition in chronic inflammatory conditions as well due to hormonal dermatoses and in melanomas of skin.

Hypo pigmentation occurs in leukoderma, vitiligo, toxic effects of certain chemicals on melanocytes like mnobenzzyl ether of dihydroquinone present in rubbers and plastic, inflammatory disorders, hormonal disorders, hydropic degeneration of dermatoses.

Pigmentary incontinence is loss of melanin pigment from the basal layer due to the damage to the cells of basal layer, and the accumulation of pigment in macrophages in the upper dermis. This is a non specific lesion associated with inflammation. However it is also seen in diseases which specifically damage the basal layer, such as lupus erythematous. The term leukotrichia means decreased pigmentation of hair and leukodrma a decreased pigmentation skin.

Hyperplasia: It is an increase in the number of cells in the epidermis. The most important hyperplasia is that of stratum spinosum, called acanthosis. Hyperplasia is a common response to a variety of chronic stimuli, and occurs in various types.

Psoriasiform hyperplasia: In this epidermal projections extend downward into the dermis to inter-digitate dermal papillae.

Papillated epidermal hyperplasia wherein downward growth of the epidermis and finger like projections are increased.

Pseudo-carcinomatous hyperplasia is seen in squamous cell carcinoma, such as increased mitotic figures and keratin pearls, but without invasion through the basement membrane. Also there is differentiation of the epidermal cells. This is seen in skin damaged by chronic radiation due to repeated stimulation or by chronic ulcers.

Dyskeratosis is the term used to describe the morphological features of premature or abnormal keratinisation in the viable layers of the epidermis that is the stratum

spinosum. Dyskeratosis keratinocyte have brightly eosinophilic cytoplasm containing keratin filaments and a pyknotic nucleus. Dyskeratosis occur in squamous cell carcinomas.

Fibroplasia is the formation of fibrous tissue in increased amounts in dermis.

Desmoplasia is the fibrous tissue reaction seen in neoplasms. Sclerosis or scar is the end part of fibrosis.

A hamartoma is a tumor like malformation composed of an abnormal mixture of tissue elements or an abnormal proportion of single elements.

Folliculitis is the inflammation of hair follicles. Nevus literally means spot or birth mark. It usually refers to pigments moles. A nevus is a circumscribed stable malformation of skin.

Furunculosis (penetrating or perforating Folliculitis): It signifies hair follicular rupture.

Follicular inflammation *is caused by* bacteria, parasites, demodectitic, stephanofilariasis spp, atopy in canines, food allergy, seborrhea dermatitis, and widespread inflammation is called panniculitis. It is due to extension of dermal inflammatory processes.

Psoriasis form Exfoliative dermatoses: A rare idiopathic Exfoliative dermatitis resembling large plaque Para psoriasis seenin dogs and cats. Large erythematous, scaly, irregular plaques are found in a more or less symmetric distribution over the trunk and proximal limbs. Superficial dermatitis associated with epidermal hyperplasia, multifocal hyerperkeratosis and lymphocytic infiltration. Scaling, alopecia crusting are seen on ventrum, perineum, face and pinnae. Pruritis is absent. There is superficial Perivascualr dermatitis is seen.

Pemphigus: Pemphigus refers to a group of autoimmune skin diseases characterized clinically by pustules, vesicles, bullae, erosions and ulcers, histologically by loss of adhesion between cells (Acantholysis) and immunologically by the development of auto antibodies directed against surface antigens of keratinocyte of various stratified squamous epithelia including skin, muco cutaneous junctions or mucosa, oesophagus and vagina. The antigen against which antibodies are directed are integral membrane glycoproteins and vary depending on the form of Pemphigus. This is characterized by deposition of immunoglobulin with or without complement on the surface of keratinocytes.

Mycotic diseases of skin

The fungus that affects skin and produce inflammmation. Fungal diseases are divided into the cutaneous mycoses, the subcutaneous or intermediate mycoses and the deep or systemic mycoses. The cutaneous mycoses wherein the nonviable keratinized tissues are involved. The intermediate mycoses are caused by a wide

range of saprophytic fungi, which induce disease only when introduced into subcutaneous tissues by penetrating cutaneous wounds. In the deep or systemic mycoses cutaneous lesions characterized by nodules, ulcers, fistulas and abscesses are seen. Histologically granulomatous or pyogranulomatous dermatitis and panniculitis occur. Systemic mycoses include opportunities infection of imunosuppressed hosts by organisms such as Cryptococcus, Blastomycosis, Coccidioidomycosis and histoplasmosis. Severity of mycotic disease is the outcome of the host fungus interplay. Less virulent organisms may cause disease only in weakened hosts. Candida cause severe disease in imunosuppressed hosts.

Cutaneous mycoses

Candidiasis is an opportunistic infection. Dermatophytosis results from superficial infection of the keratinised layers of the skin and its appendages:

Trichophyton equinum in equines, *Trichophyton mentagrophytes and Trichophyton verrucosum in bovines, Microsporon canis, Microsporon gypsum and Trichophyton mentagrophytes* causes the skin infections.

Diseases of integuments - Limbs

Lameness

Basic concept of bovine lameness

Cows and buffaloes do not change the pattern of locomotion to any great extent on any particular surface unless they have some pain or discomfort. Such abnormalities of walking may also have adverse consequences for muscles or bones or may increase the likelihood of injury. An animal may give up its social position and reduce the number of times it walks to obtain resources. In extreme circumstances, a cow may reduce its consumption of food and water to avoid painful experience during walking. Lameness has multifactorial etiology.

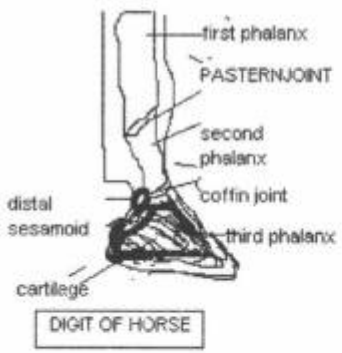
Lameness after infertility and mastitis, the biggest cause of economic loss to the dairy farmers. Digital lameness is related to parturition or may not be related to parturition. Acute laminitis occurs during preparturient period or immediately up to one month after parturition.

One to three months after parturition is may be either due to chronic laminitis or due to solar ulcerations or due to white line disease.

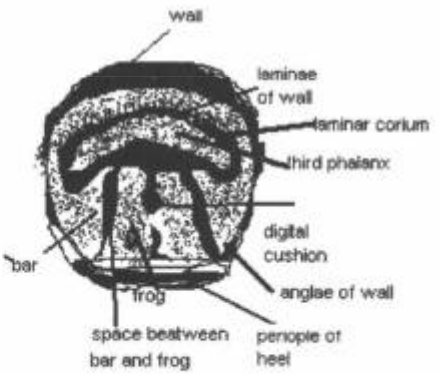
Laminitis also occurs due to certain causes unrelated to parturition such as hoof erosions, punctured sole and hoof wall damage.

Digital lameness is also related to age. Thus lameness can be seen in young calves, older cows and at any age. In young calves it maybe due to horn affections such as acute laminitis, in older cows it is due to chronic laminitis that sets in due to hoof erosions, white line disease, hoof deformities and solar ulceration or may be due to interdigital hyperplasia of keratin.

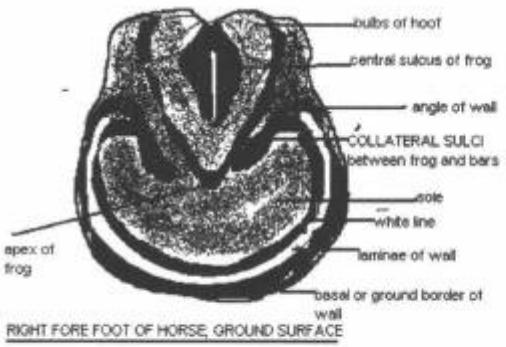
Trauma to sole, sand cracks to hoofs or to hoof wall tissue may occur at any age of the animal. Lame cows have been shown to be more susceptible to other diseases such as mastitis. A painful lameness causes reduction in appetite. The cows produce less milk and lose weight. Using up fat and muscles it will be Thinned down.



DIGIT OF HORSE

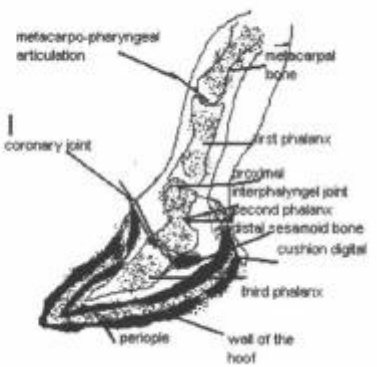


CROSS SECTION OF FOOT OF HORSE CUT PARALLEL WITH CORONARY BORDER



RIGHT FORE FOOT OF HORSE, GROUND SURFACE

SAGITAL SECTION OF DIGITAL PART OF FORELIMB OF OX



In horse: The hoof is the horny covering of the distal end of the digit. It is convenient to divide for description into three parts, termed the wall, sole and frog.

The wall is defined as the part of the hoof which is visible when the foot is placed on the ground. It covers the front and sides of the foot, and is reflected posteriorly at an acute angle to form the bars. The latter appear on the ground surface of the hoof as convergent ridges, which subside in front and are fused with sole; they

are united with each other by the frog. The wall also is divided as anterior part as toe, medial and lateral parts as quarters and angles as heels. It presents two surfaces and two borders. The external surface is convex from side to side and slopes obliquely from edge to edge. In front the angle of inclination on the ground plane is about 50° for the fore limb, 55°for the hind limb; on the sides the angle gradually increases and is about 100° at the heels. The curvature of the wall is wider on the lateral than on the medial side and the slope of the medial quarter is steeper than that of the lateral ones. The surface is smooth and crossed by more or less distinct ridges which are parallel with coronary border and indicates variation in the activity of the growth of hoof. It is also marked by fine parallel striae, which extend from border to border in an almost rectilinear manner and indicates the direction of the horn tube.

The internal surface is concave from side to side and bears about 600 thin primary laminae, which extend from the coronary groove to the basal border of the wall. Each bears a hundred or more secondary laminae on its surfaces, so that the arrangement is pinnate on cross section. The lamina ear continued on the inner surface of the bars, a and dovetail with corresponding laminae of the corium. The proximal coronary border is thin. Its outer aspect is covered by a layer of soft, light colored horn known as at the periople; this appears as a ring like prominence above and gradually fades out below; at the angle it forms a wide cap or bulb and blends centrally with the frog. The inner aspect of the border is excavated to form the coronary groove, which contains the thick coronary corium. The groove narrows on the ides, and merges at the angles with the periople groove. It is perforated by innumerable small, funnel like openings which are occupied by the papillae of the coronary corium in the natural state. Above the thin border of the wall proper there is a mall periople groove which contains the corium of the periople. At the heel the groove widens and merges with the coronary groove. The basal or ground border of the unshod hoof comes in contact with the ground, in thickens is greatest in front and decreases considerably from before backward on the sides, but there is a slight increase at the angles. At its inner face is united with the periphery of the sole by horn of lighter color and softer texture, which appears on the ground surface of the hoof as the so called white line.

The sole constitutes the greater part of the ground surface of the hoof. It is some what crescent in out line and presents two surfaces and two borders. The internal surface is convex and slopes with a varying degree of obliquely downward to the convex border. It presents numerous small funnel like openings which contain the papillae of the sole corium in the natural state. The external or ground surface is the converse of the preceding. It is normally arched and more strongly in the hind than in the fore foot; in heavy draft horses the sole is commonly less curved than in the lighter breeds and may even be flat. The surface is usually rough. The

convex border is joined to the wall by relatively sot horn that is white line on the ground surface of the hoof. The concave border has the form of deep angle which is occupied by the bars and the apex of the frog. The parts of the sole between the wall and bars are termed its angles.

The frog is a wedge shaped mass which occupies the angle bounded by the bars and sole, and extends considerably below these on the ground surface of the foot. It is having four surfaces, a base and an apex. At internal surface bears a central ridge, frog stay which is high posteriorly and subsides abruptly in front. On either side there is a deep depression which is bounded outwardly by the rounded ridged foramen by the junction of the frog with the bars and sole. The external or ground surface presents a central sulcus. The base is depressed central and prominent at the sides, where it unites with the angle of the wall; the junction here is covered by the expanded periople and constitutes the bulb of the hoof.

The hoof is composed of epithelial cells which are more or less completely keratinized except in its deepest part, the stratum germinativum; here the cells have not undergone cornification and by their proliferation maintain the growth of the hoof. The cells are in part arranged to form horn tubes which are unite by intertubular epithelium and enclose medullary cells and air spaces. The external layers comprised the periople and the strum tectorium. The periople is composed of soft, no pigmented tubular horn and become white when the hoof is soaked in water. It is continuous with the epidermis of the skin above, and extends downwards a variable distance. Usually it forms a distinct band somewhat less than an inch wide, except at the heels, where it much wider and caps the angle of inflection of the wall forming the so called bulb of the heel. The stratum tectorium is a thin layer of horny scales which gives the outer surface of the wall below the periople its smooth, glossy appearance. The middle layer forms the bulk of the wall, and is the densest part of the hoof. Its horn tubes run in a parallel direction from the coronary border to the basal border. In dark hoofs it is pigmented except in its deep part. The laminar layer is internal; it consists of horny laminae and is non pigmented. The primary laminae are narrow and thin at their origin at the lower margin of the coronary groove, but become wider and thicker distally. At the junction of the wall and sole they are united by interlaminar horn to form the white zone or line. Only the central part of the laminae becomes fully keratinized. They are composed of no tubular horn in the normal state. The sole consist of tubular and intertubular born. The tubes run parallel with those of the wall land very much in size. The frog is composed of relatively soft horn, which is much more elastic than that of the wall or sole and is not fully keratinized. The horn tubes in it are slightly flexuous. The hoof is nonvascular and receives it nutrition from the corium. It is also destitute of nerves.

In Ox: The hoof are four in number on each limb, cover the ends of the digits. Those of the chief digits confirm in general way to the shape of the third phalanges, and each may be regarded as having three surfaces. The abaxial surface is convex from side to side and is marked by ridges parallel with the coronary border. Its anterior part is concave from edge to edge, and the angle which it forms with the ground is about 30°. The interdigital surface is concave and grooved; it touches the opposite claw only at its ends. The basal or ground surface consists of two parts, namely a slightly concave sole, which is pointed in front and widens behind, and a prominent bulb of soft thin horn, which is continuous above with the skin. The hoof may be regarded as consisting of three parts, periople, wall and sole. The periople surrounds the coronary border in the form of a flat band, which is about half an inch wide, except at the heels, where it widens to cover the entire surface. The wall forms most of the abaxial part of the hoof and is reflected in front upon the interdigital surface. It thins out toward the bulb or heel, which appears, as stated above, to consist of the thin expansion of the periople. The sole occupies the angle of inflection of the wall; it is continuous without demarcation with the periople of the bulb. The periople corium bears relatively on papillae. The coronary corium is much less developed than in the horse and its papillae are short. The laminae are much narrower and are more numerous than in the horse; secondary laminae are not present. The corium of the sole is not marked off behind form that of the periople; it pail ear every small close together. The corium of the bulbs is separated from the flexor tendon by mass elastic fatty tissue which is analogous with the digital cushion of the horse. The papillae here are long and often compound. The accessory digits bear short conical horn capsule which resembles in general way those of chief digits, and have similar corium which covers one or two nodular vestigial phalanges. From these a fibrous and descend obliquely on the volar aspect of each chief digit and is attaché below to the distal phalanx and sesamoid bones. Sending fibers to the elastic pad of the hell.

Lameness due to joint affections: Infectious arthritis, luxation and subluxation of patella leads to lameness in cattle. Stifle joint – upward fixation of patella. The limb is intermittently locked in extension by the middle patellar ligament acting in concert with the medial patellar ligament, thus causing patella to become fixed over the medial femoral tracheal ridge.

Partial separation of synarthroidal joint surface is termed subluxation. Complete separation is called luxation. These conditions are associated with parturition or soon after dystocia. Sacroiliac luxation and subluxation also occurs. Clinical signs include mild ataxia and weakness in hind quarters or severe posterior paresis and recumbency as shown in luxation.

Coxofemoral luxation is common in dairy cattle and usually traumatic in origin. A cow after dystocia develops bilateral obturator paralysis; goes down with both

hind legs abducted, and either immediately or as a result of struggling to stand results in a unilateral Coxofemoral luxation. Bilateral cases are rare.

The common direction of abnormal movement of the femoral head is dorsal and cranial, the head lying along the lateral aspect of ileal shaft. The animal is usually unable to bear the weight on the leg, which is rotated so that both stifle and digits are directed outwards.

Wounds: Common sites of wounds results in the lameness are the lower limb, from the carpus and hock distally. Degloving injuries, a large flap of skin is pulled back away from the underlying tissue is responsible for lameness in all animals. Severe haematomas on leg are also responsible for lameness in animals.

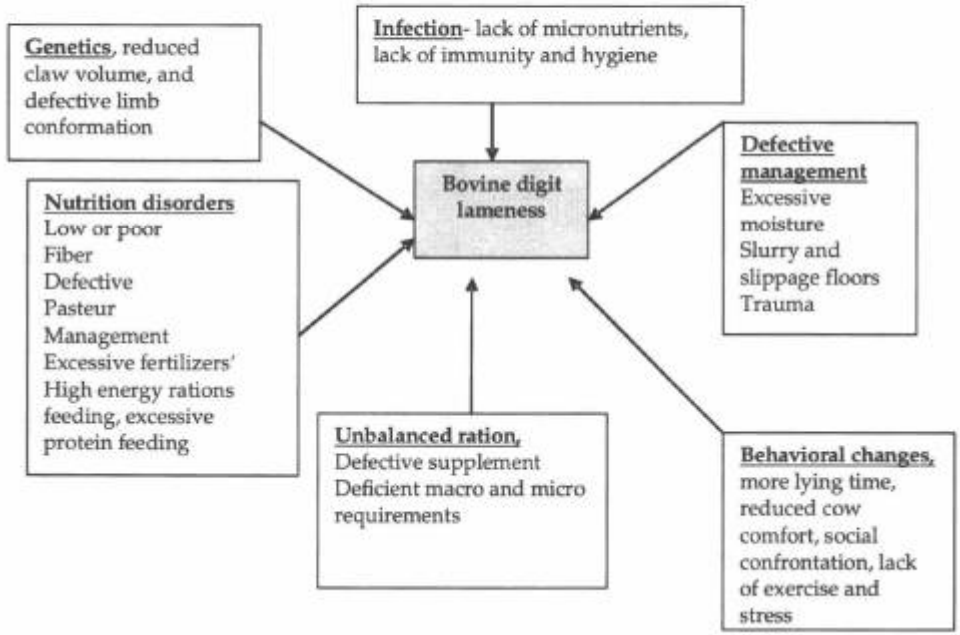
Haematomas: Severe blunt trauma can result in vascular damage leading to the formation of large subcutaneous or intramuscular haematomas. Injury to the claw capsule results due to trauma. This results in severe lameness. Injuries involving the coronary band are more serious. The hoof wall that grows down after the injury may be abnormal but may be quite functional.

Other factors that contribute to bovine lameness:

1. Abductor group muscles are involved in downer cow syndrome.
2. There is gastroenemius rupture and the hock is flexed.
3. Fracture of radius and ulna, articular deformity of radio-carpal and tibio tarsal joints.
4. Fractures of proximal and middle phalanx
5. Septic arthritis of fetlock
6. Humoral fractures and tibial fractures
7. Laminitis in cattle is also due to lactic acidosis, due to liberation of high levels of histamine. The histamine coming from disturbances in gastrointestinal tract or uterus.
8. Amount of fiber in the rumen
9. When protein content of fed is more than 30%. The excess protein may be converted to amino acids and ammonia. Alternatively protein may be degraded to toxic entities or may cause some allergic reaction.
10. Breed susceptibility: Friesian cattle are more susceptible to laminitis.
11. Exercise: Lack of exercise lack of movement also is conducive to lameness due to pooling of blood in the claws. Factors that interfere with exercise also cause lameness.
12. When compensatory drop in acid digestible fibers.
13. Mechanical factors: External trauma or abnormal claw or limb configuration. Mechanical forces applied to the sole of the claw result from a permutation of claw size and shape, body weight, conformation of limbs, claw hardness

and the quality of the surface over which the animal walks.

14. Deficient keratinisation: Zinc, copper, and methionine are essential for keratinisation. Therefore deficiency of minerals affect the quality of hoof produced.
15. Changes in the lamellar region, changes in the sole due to hemorrhages in the horn, double sole, ulcers in the sole and toe, white line separation and whole deformity of claw. Deformities of claws occur in chronic laminitis. A chronic laminitis claw is characteristically deformed and is referred to as slipper foot. Multiple changes occur as alternate grooves and bridges vie the claw q wash board appearance. The hoof broadens and flattens. The horn wall, normally parallel to the dorsal surface of the distal phalanx, gradually changes its direction of growth to curve away, producing a concave dorsal wall as said earlier. The corium becomes wedge shaped on section. The distal phalanx sinks away from the horn capsule in a distal direction. In chronic laminitis successive episodes of laminitis may prevent the restitution of the wall structure because this would require enough time for the whole length of the wall to go out. The lamellae widen in chornic laminitis, claws as a result of hyperplasia eventually producing a widened and vulnerable white line.
16. Chronic displacement of the distal phalanx induces an increase of pressure in the corium. This pressure is constant, and mild enough to cause sclerosis of the wall of blood vessels rather than tissue necrosis. Mantles are formed around nerve bundles. Thrombi may occlude blood vessels; young animals may recover more readily from a laminitis incident, possibly because these individuals are still able to develop collateral circulation to take over the function of damaged vessels. Nevertheless, each time an animal suffers an episode of laminitis, more scar tissue is formed and the animal is able to recover from the next insult.
17. A diffuse proliferation of scar tissue in the corium is a consistent accompanying future in chronic laminitis. Grossly one may observe that the adipose tissue cushions in the heels are replaced by thick connective tissue layers. These reduce the elasticity and movement capacity of the weight bearing corium.
18. Yet another sequel of the chronic compression and sclerosis of the corium under the distal phalanx in these chronically laminitis claws are that this layer becomes obviously thinner than normal. The cushioning function is reduced, and the compression is transmitted to the sole and heel horn to produce two further morphological features. The sole becomes convex and bulges so called dropped sole. A typical deep oblique furrow forms in the sole heel junction, passing roughly along the border line. Bulb is drawn downwards. Heel gets softer.



Lameness in horses

These additional factors are also bringing about lameness in horses.

1. Thrombosis of the posterior aorta or iliac.
2. Intermittent lameness disappears with rest.
3. Shivering and involuntary movements of limbs and tail.
4. Stringhalt- involuntary flexing of the hock of one or both hind limbs during progression.
5. Curb- is an inflammation and thickening of plantar ligament. This produces an enlargement of posterior surface of the limb.
6. Capped hock; for a swelling that occurs on the tuber calcis. The tissues affected are skin and subcutaneous tissue.
7. **Bog spavin:** Chronic distension of joint capsule of the tibial articulation as result of chronic synovitis.
8. Bone spavin or chronic deformans of tarsal bones.
9. **Rupture of perioneum tertius:** This tendon unites the stifle and hock joint. This is due to overextension of hock joint.
10. Fracture or defect of fibula.
11. Lateral luxation of patella to upward areas.
12. Seroma is characterized by the presence thin fluid that is tinged with blood

so that it is reddish brown in color.

13. Fracture through epiphyseal cartilage
14. Growths on stifle joint
15. Femoral paralysis affecting quadriceps femoris muscle
16. Spastic paresis of hind limb
17. Dislocation Coxofemoral articulation
18. Coxitis that is inflammation Coxofemoral articulation.
19. Trochontric bursa is affected.
20. Epiphyseal separation of head of femur especially in young horses.
21. Hoof affections like interdigital necorbacillosis involvement
22. Interdigital skin hyperplasia
23. Interdigital dermatitis
24. Verrucose dermatitis
25. Digital dermatitis
26. Pododermatitis- solar ulcerations
27. Punctured sole
28. White line separation
29. Heel erosions
30. Transverse sand cracks
31. Fracture of distal phalanx

Diseases of horns

Horns: Horns enclose the horn processes of the frontal bones. They vary greatly in size, form and curvature. The root or base of the horn has a thin edge which is continuous with the ordinary epidermis. It is covered by a thin layer of soft horn similar to the periople of the hoof of the horse. Near the root of the horn it is encircled by variable rings. Towards the apex the thickness of horn increases till it becomes practically a solid mass. The horn consists of mainly of tubules which are very close together, except at the rings, where there is more intertubular horn. The corium of the horn is united to the horn process by periosteum which is and bears long, slender papillae; in the body of the horn it becomes thin and the papillae are smaller, but increases in size apically. Rudimentary papillated laminae also occur.

Diseases of ear

Tympanic membrane: Auditory ossicle: Cochlea:- organ of Corti -Mechanism of hearing:. Development organ of hearing: Development of external ear: Development of the middle ear (tympanic cavity), the pharynges-tympanic tube (auditory tube) and the tympanic antrum: Development of the internal ear or the

labyrinth: the internal ear -Otitis externa: auricular haematomas -Otitis media:

Diseases of ear

Hearing like many somatic senses, is a mechanoreceptive sense, for the ear responds to mechanical vibration of sound waves in the air. Ear receives sound waves, discriminate their frequencies and finally transmits auditory information into the central nervous system. Diseases of hearing covers under three headings namely defects of hearing, otitis media and otitis externa.

The ear is made up of three division, the external ear, consisting of the pinnae or auricle and the external acoustic meatus; the middle ear, consisting of the tympanic cavity, with its contents, and the Eustachian tube, with its diverticulum, the guttural pouch and the internal ear or labyrinth, consisting of an acoustic part, the cochlea and a nonacosutic part, the vestibular organ. The cochlear supplied by the cochlea branch of the acoustic nerves contains the receptors for the sense of hearing. The essential function of the external ear is to receive sound waves of the middle ear, to modify them and to facilitate other passage to the perilymph of the internal ear and thus to the sound receptors in the cochlea.

Auricle or pinnae: The function of this structure is to collect sound waves, which are then transmitted to the tympanic membrane by way of the external acousticmeatus. The mobility of auricle enhances it value as a collector of sound waves by enabling it to be turned in the direction of the sound.

Tympanic membrane: Completely separating the external acoustic meatus from tympanic cavity, or cavity of the middle ear, is a thin septum known as tympanic membrane. It is composed of three layers, the external layer is continuous with the skin lining the external acoustic meatus; the middle layer is composed of radially and circularly arranged connective tissue fibers; the internal layer is continuous with the mucous membrane of the tympanic cavity. Attached to their internal surface of the membrane is the manubrium or handle of the malleus, the first of the auditory vesicles. Vibrations of the tympanic membrane are in this way transmitted to the chain of bones and to the perilymph. An important feature of the tympanic membrane is that it is periodic, that it has no inherent period of vibration and therefore can transmit any frequency without modifying it.

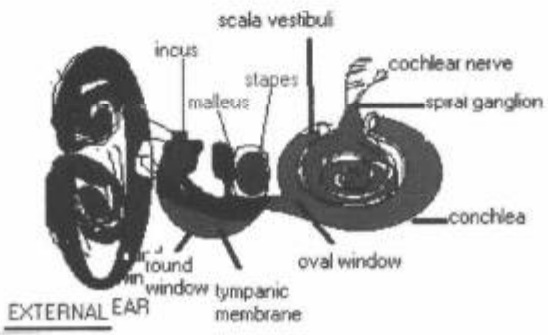
Auditory ossicle: These are three small bones, the malleus, incus and stapes, found in the tympanic cavity. They comprise a chain extending from the tympanic membrane to the fenestrae ovalis. Through them the vibrations of the tympanic membrane are transmitted to the perilymph of the labryinth.The malleus, the first bone in the chain is, as noted above, attached to the tympanic membrane by means of the manubrium. The head of malleus articulates with the head of the incus. Several ligaments held to hold the malleus in place. The incus presents a head, which articulates with the head of the malleus and two processes. A ligament attaches the shorter process to the wall of the tympanic cavity. The long processes

articulate with the head or the stapes. The foot plate of steppes is inserted into the oval window. The whole margin it is attached by a membrane. In transmitting the vibrations of the tympanic membrane to the perilymph, the auditory ossicle acts as a bent lever. Since the manubrium of the malleus is longer than the long processes of the incus, it is evident that the vibrations of the tympanic membrane are transmitted to the perilymph with increased force but with decreased amplitude.

Eustachian tube and guttural pouch: Connecting the tympanic cavity with the pharynx is the Eustachian tube, hose presence ensures that the air pressure in the tympanic cavity shall be the same as that on the outside the body. Ordinarily closed, at in man, the pharyngeal aperture of the tube is opened during swallowing. Therefore should an inequality of atmospheric pressure on the two sides of tympanic membrane result, it can quickly be corrected by deglutition. The function of guttural pouch present in it in enquires signifies the movement of air into handout of the pouch during respirations.

Hearing: when a body surrounded by air is thrown into vibrations, adjacent air molecules are made to vibrate, or move to and fro, thus producing alternating phases of compression and refraction. Then the air adjacent outward from the vibrating body, in three dimensions, in the form of a wave. The spread of wound waves in air varies somewhat depending on the temperature the average at ordinary temperatures being about 1100 feet per second. Physically sounds differ as to frequency, intensity, and wave form. Frequency refers to the number of vibrations per second and is perceived as pitch. The intensity of a sound wave depends on both the frequency and multitude of the vibration. Intensity determines the loudness of the ousnd. Wave form refers the presence or absence of overtones, which determines subjectively the quality, or timbre of a sound.

Cochlea: the acoustic labyrinth or cochlea contains the receptor for the sense of hearing. it consist essential of a spiral bony tube wound several times around a bony supporting pillar and a much smaller tube, known as



the tympanic membmae, the ossicualr system of the middle ear, the inner and external ear.

Cochlear duct, contained within the bony tube. The cochlea is a system of coiled tubes, with three different tubes coiled side by side, the scala vestibule, the scala media and the scala tympani. The scala vestibule and scala media are separated from each other by Reissner's membrane is also called as the vestibular membrane and the scala Tympanitis and scala media are separated from each other by the basilar membrane. On the surface of the basilar membranes lies a structure, the organ of Corti, which contains a series of mechanically sensitive cells, the hair cells. These are the receptive end organs that generate nerve impulses in response to sound vibrations. It is found the organ of Corti with it sensory hair cells and the termination of the cochlear nerve. The cells of origin of the cochlear nerve fibers are bipolar nerve cell stituated in the spiral ganglion. The spiral ganglion is located in the modiolus. The peripheral branches of these nerve cell end in relation to the hair cells of the organ of Corti. The central branches end in the ventral and dorsal cochlear nuclei of the pons.

The cochlear duct, somewhat triangular in cross section, begins in the vestibule and extends the length of the bony canal, to whose walls its base and apex are attached. Forming one side of the cochlear duct and separating its cavity from that of the scala vestibule is the delicate vestibular membrane. Forming the other die of the duct and separating its cavity from that of scala tympani is the much firmer basal membrna situated on the inner side of the basilar membrane and running its entire length is highly specialized, the organ of Corti. The basilar membrane is composed of large number of fibers whose length increases and shoe tension apparently decreases from the base to the apex of cochlea. The membrane is believed to be the structure that receives the sound waves in the perilymph and thus cause s stimulation of the hair cells and their associated nerve endings in the organ of Corti.

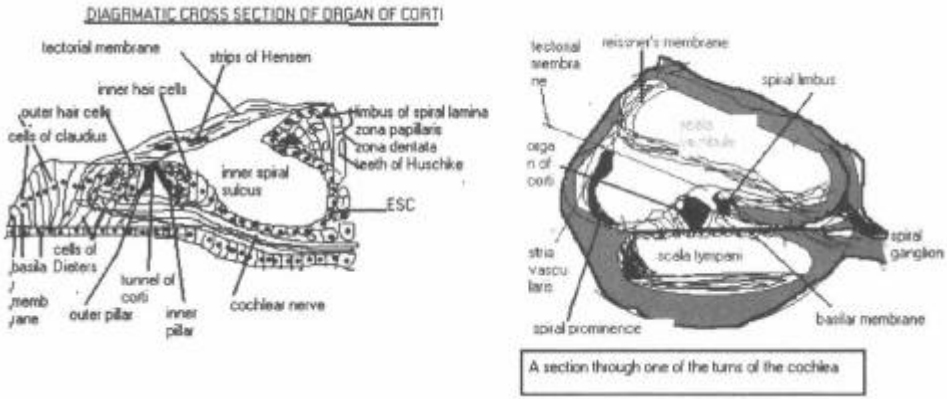
The cochlear duct, filled with endolymph communicates with the saccular through the canalis reunions. The scala vestibule and the scala tympani filled with perilymph, communicate with each other at the apex of the cochlea, the helicotrema. At the base of the cochlea bathe scal vestibule communicates with the vestibule. The scala tympani end at fenestrae rotunda, which is closed by membranes, the secondary tympanic membrane. By it elasticity this membrane compensates for pressure changes in the perilymph as a result of the impact delivered to the latter by the stapes at the fenestrae ovalis. This however may; not represent its sole function.

Organ of Corti: This is very complex sensory epithelial structure, extending from the beginning to the end of the cochlear duct, rests upon the basilar membrane. It is composed of supporting cells of several kinds, sensory epithelial cells known as the auditory hair cells, the tectorial membranes, and the fibers of the cochlear nerve. The hair cells are the structures by which sound wave area converted into nerve impulses. The free ends of these cells posses stiff cilia, while the basal cell ends are related to the terminal fibrils of the cochlear nerve. It is estimated that

there are more than 20,000 hair cells in the organ of Corti and about as many fibers in the cochlear nerve. The cilia of hair cells project, near its free margin, into the tectorial membrane, a gelatinous pad covering the outer surface of the organ of Corti. At its other margin this membrane is attached to the wall of the cochlea at the spiral lamina.

Mechanism of hearing: Sound waves entering the external acoustic meatus throw the tympanic membrane in vibration. The waves so generated are transmitted mechanically across the tympanic cavity by action of the auditory ossicle. The movements of the foot plate of the stapes set up waves in the perilymph of the labyrinth, which cause the basilar membrane, less likely, the tectorial membrane-to vibrate. These fine movements cause change of pressure on the cilia of the hair cells, probably by bending them; and nerve impulses are set up in the nerve terminations at the bases of the cells. Nerve impulses thus aroused are transmitted to the central nervous system. Some of the impulse stimulates auditory reflex centers in the brain stem another reach the auditory area in the cerebral cortex.

The cochlea show potential changes, known as the micro phonic effect, which may concerned in stimulating the nerve terminations. The potential changes result from pressure variations caused by the sound waves and are probably piezoelectric effects. They should not be confused with the spike potentials shown by the nerve fibers.



A section through one of the turns of the cochlea

Development organ of hearing: The organ of hearing consists of a conducting apparatus formed by the external and middle ears and a receiving apparatus called the internal ear.

Development of external ear: The external ear consists of the external auditory meatus and the auricular or the pinnae. The dorsal end of the first branchial cleft becomes funnel shaped and from it the whole of the external auditory meatus is developed. From the medial end of this a solid ectodermal cord grows inwards about the 2nd and 3rd months and abuts against the lateral part of the floor of the

tubotympanic process. By the break-in down of central cells of this cord, about 7th month, the meatus is deepened and the same ectodermal cells at the medial end of the meatus form the outer lining of the tympanic membrne. The meatus which lies between the first and second arches are supplied by the nerves of both these arches namely the mandiubular and the facial nerves. The auricular branch of the vagus is possibly a vestigial remnant of the lower animals. The auricular or pinnae is formed by the fusion of certain tubercles and fold developed around the dorsal part of the first branchial cleft about the 6th week of embryonic life. Thus along the caudal edge of the 1st branchial arch 3 tubercles are developed numbered from the ventral to the dorsal side as 1, 2 and 3. Along the cranial edge of the second branchial arch 3 other tubercles are developed numbered from the ventral to the dorsal sides as 4, 5 and 6. These latter are bounded behind a curved fold of the integument called the auricular fold. From the enlargement and fusion of the 2nd and 3rd tubercles and their fusion with auricular fold behind, helix is developed. The antihelixes is formed by the enlargment and fused of the 4th and 5th tubercles. The 6th tubercle develops into the antitragus. The lobule is probably developed from an extension of antitrageal elevation. The auricular tubercles may not fuse completely, resulting in the presence of fistulae between them. The posterior-superior pointed angle of the auricular of the lower animals is represented as a tubercle on the infield posterior margin of human ears called Darwin's tubercle. Muscles of the external ear are derived from the plasma sheet and hence are innervated by the nerve of the sheet which is the facial nerve.

Development of the middle ear (tympanic cavity), the pharynges-tympanic tube (auditory tube) and the tympanic antrum: the auditory tube and the tympanic cavity are developed from the 1st and 2nd pharyngeal pouched which altogether form areas called the tubo-tympanic recess at the end of the 2nd month of foetal life between the 1st and 3rd arches, the 2nd arch being pushed to the lateral wall of the proceses. The floor of this recess is formed by the 1st and 2nd branchial arches and the 3rd branchial arch forms its posterior boundary. The medial or pharyngeal end this recess becomes narrowed to for the auditory tube (pharyngo-tympanic) tube and the lateral or distal end is dilated to form the tympanic cavity. The tympanic is formed by the floor of the tubo-tympanic recess lying lateral to the dilatation which forms the tympanic cavity. It is limited internally by the endoderm of the tubotympanic recess and its external lining of ectoderm is derived from the ectodermal outgrowth of the 1st cleft from which at the medial part of the external auditory meatus is developed. The fibrous layer of the tympanic membrane is derived from the intervening mesoderm. The membrane being contributed by the 1st and 2nd arches is supplied by the vessels and nerves of those arches. The malleus and iscus are developed from the dorsal end of the mandiubular (Meckel's) cartilage and the muscle of the malleus-the tensor tympani is developed from the mesoderm of the first arch which accounts for its nerve supply by the mandiubular division of the 5th nerve which is the nerve of the first arch, which accounts for its nerve supply by the mandibular division of the 5th nerve which is

the nerve of the 1st arch. The stapes is developed from the dorsal end of the 2nd branchial arch or the hyoid arch and the muscle of the stapes, the stampedes, is developed from the mesoderm of the 2nd arch which explains its nerve supply by the 7th nerve which is the nerve of the 2nd arch. These three ossicle of the ear develop in the mesoderm of the roof other tympanic cavity but they are subsequently invaginated into the cavity pushing the endoderm lining in front of them and being invested by. The tympanic antrum develops as a backward extension of the tympanic cavity, during the 6th and 7th month of foetal life. The portion the tympanic cavity above the level of the tympanic membrane, containing the head of the malleus is called attic or epitympanic recess. The mastoid air cells are developed as evagination of the lining membrane of the antrum at birth.

Development of the internal ear or the labyrinth: The internal ear consists of an osseous or bony covering enclosing the membranous labyrinth. The epithelial lining of the membranous labyrinth is developed from the surface ectoderm. Soon after the formation of the lens vesicle a depression occurs in the surface ectoderm opposite the middle of the hind brain called the auditory pit (otic pit), in a line with the dorsal end of the first branchial cleft. The ectoderm forming the floor of this pit become thickened and the margins of the pit coalesce converting it into cyst called the otic vesicle or oocysts resembling the lens vesicle. Part of the lining epithelium of the otocyst becomes differentiated into ciliated sensory epithelium. Detached cells of the neural crest forming the ganglia of the clear and vestibular division of the 8th nerve become closely applied to wall of the otocyst. One of the processes of these nerve cell become connected with the air cell of the sensory epithelium of the otocyst and the other processes collectively forming the vestibular and cochlear nerves will end in the hind brain. This cyst which sill develop into the membranous labyrinth become detached from the surface ectoderm and become embedded in the sub adjacent mesoderm which later transforms into cartilaginous otic capsules which develops into the bony labyrinth. At first it has a circular shape soon it becomes oval, containing fluid called endolymph. Otoliths are formed within it later. From the middle of the dorsal surface an elongated hollow protrusion occurs which forms subsequently the ductus endolympaticus and the blind end of it's dilates to form the saccus endolympaticus

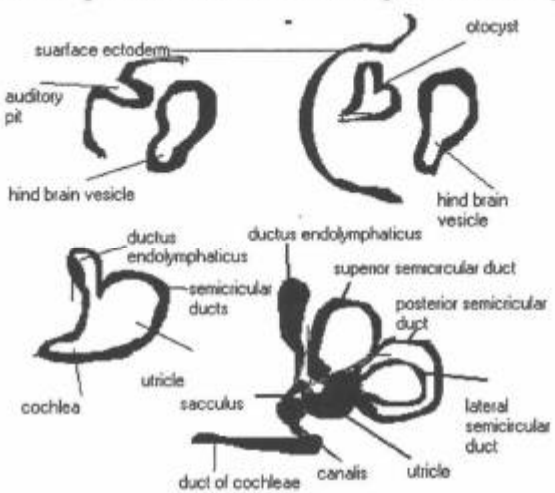
Differentiation of ductus cochlerias: At about the 5th week, the ventral part of the otocyst is prolonged for wards as a hollow diverticulum which is the rudiment of the ductus cochlerias. It is at first straight but as it elongates it become coiled on itself like the shell of a snail for nearly two turns and three quarters. The organ of Corti which sets up auditory impulses are developed within it as a modification of the ecodermal lining forming the hair cells or the sensory cell around which the cochlear nerve fibers commence.

Development of semicircular ducts: From the dorsal portion of the otocyst three discs like hollow protrusions occur on 3 planes. The walls of the central parts of these protrusions become apposed and degenerate whereas their peripheral parts

remain patent communicating with each other and with the cavity of the central part of the otocyst. The superior semicircular duct is the first to form and then the posterior and lastly the lateral duct. The 3 ducts open into the otocyst by 5 openings as the is a common opening for the medial end of the superior and the upper end of the posterior semicircular duct. One of the ends of each duct becomes ampullated.

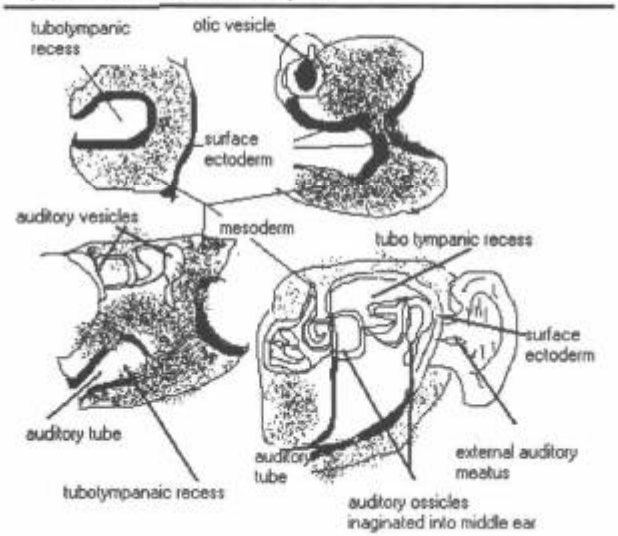
After the differentiation of the ductus cochlerias and the semicircular ducts from the ventral and dorsal parts of Th otocyst the remaining intermediate part of the otocyst undergoes a subdivision into two intercommunicating smaller sacs. This subdivision by a constriction which gradually deepens so that the smaller bag called the saccule lays ventrally and is demarcated from the larger bag called the utricle which lies dorsally. The constriction as it deepens extends into the proximal part of the ductus endolympaticus so that the two bags into long communicated directly but by a Y-shaped tube. The vestibular end of the ductus cochlerias which now communicates with the saccule is also constricted to form the canalis reuniensn. The semicircular ducts now open into the dorsal segment of the vestibule that is the utricle. The epithelial cells in connection with the termination of the vestibular nerve become modified into sensory organs as in the aristae ampullaris of the semicircular ducts, in the maculae of the utricle and the saccule. The utricle saccule and the semicircular ducts are the vestibular of balancing part of the labyrinth giving information regarding the position and movement of the body.

Development of bony labyrinth: The layer of mesoderm which lies in immediate apposition with the membranous labyrinth is transformed into its fibrous wall. This remaining mesodermal investment of the membranous labyrinth is tranformed into a cartilaginous capsule in the 2nd month by the inducing periphery of the



THE DEVELOPMENT OF INTERNAL EAR

the development of middle ear, external audiatory meatus, the tympanic membrane and the auditory tube



otocyst. But the layer of cartilaginous lying in contact with the fibrous wall of the membranous labyrinth reverts to a precartilagenous state in which reticulum of a protoplasmic processes develops. This constitutes the perilaymaptic space containing perilymph. The surrounding cartilaginous capsule is then ossified to form the bony labyrinth.

Otitis externa: Auricular haematomas occurs as a consequence of trauma usually forms excessive head shaking by dogs with otitis externa. Dogs and pigs with pendulous ears are affected much. Haematomas usually develop on the concave side of the pinnae and are initially fluctuant but become firm as the haematomas organizes. As it is converted to granulation tissue by fibroblastic and capillary growths, the lesion becomes hard. Subsequent fibroblastic contraction may result in disfigurement of pinna.

Alopecia of pinnae is also common dogs and cats. The precise cause is not known.

Otitis externa is common in dogs, cats and goats. In cats and goats ear mite infestation causes this. In dogs complicated etiology is involved. Trauma and bacterial infections is responsible for this. The ear mite involved in dog is otodectes cyanotis. Psorotes cuniculi is the ear mite of rabbits.

Middle ear infections: Otitis media: It is the inflammation of tympanic cavity within temporal bone. The bacteria enter through the Eustachian tube or through the perforation of tympanum.

Otitis interna is due to result of infection spreading from middle ear.

Otitis media: It is the inflammation of the tympanic cavity within the temporal bone. The cause is always bacterial. The organisms reach the poorly drained cavity via the Eustachian tube or following perforation of the tympanum. The clinical signs are head a tilt, circling and ataxia suggesting involvement of internal ear.

The lining epithelium of tympanic cavity shows hyperemia, oedema and ulceration. Neutrophils exuding from the reactive vessels under the epithelium enter the tympanic cavity joining the initially serous or serofibrinous exudates to make to progressively more purulent. Exudates may temporarily drain into the pharynx via the Eustachian tube which is soon sealed by inflammatory swelling of its epithelium. Severe cases lysis of tympanum or rarely the one on the ventral floor of the tympanic bullae. Chronic inflammations are characterized by inspissations of exudates, lysis of the ossicle and occasionally the tympanum and spared to inner ear and brain stem.

Deafness: Conductive deafness is due to interference with the conduction of sound to the sensory end organ of Corti. Sensorineural deafness results from maldevelopment or degeneration of the sensory organ, eight nerve, or auditory path ways within the brain. Any lesions that interferes with vibration of the tympanic or ossicle interferes with the vibration of tympanum or ossicle causes vibration of the oval windows interferes with the establishment of fluid waves within the endolymph. Nerve deafness usually involves the organ of Corti. Hereditary deafness is recorded in several breeds of animals. The carnivore ear is completely developed at birth and continues to mature for 2 to 4 weeks.

Senile deafness: Many animals become hard of hearing as they reach old age. This phenomenon called presbyacusis is more frequently observed in old dogs. In humans the loss of hearing is progressive from about 40th year of life and particularly affects hearing of high tones. This age related degeneration of epithelial tissues within the cochlea and of the spiral ganglion, a process that may be accelerated by excessive noise, arteriosclerosis, and nutritional factors. The essential lesions are atrophy of all epithelial structures within the cochlear duct and the associated auditory nerves as well as neuronal atrophy within the spiral ganglion. Stria vascularis atrophy or atrophy of the basal membrane supporting the organ of Corti is also responsible in producing deafness in animals.

Acoustics and chemical ototoxicity: Noise either a sudden loud noise or as moderate but prolonged environment background, causes degeneration of the sensory hair cell necrosis and even outright disruption of the organ of Corti or Reissner's membrane by mechanical trauma, mediated via fluid waves within the endolymph that must be the otic equivalent of tidal waves.

The ototoxic chemicals are aminoglycosides antibiotics like gentamycin, streptomycin, kanamycin, neomycin; Overdosing with decreased renal function markedly increases the risk of toxic injury to the nerve. Cats are particularly susceptible and vestibular toxicity like defective posture, balance and gait precedes

hearing loss.

Diuretics like furosemide, bumetanide and ethacrynic acid are chemically related and all are ototoxic to dogs and cats.

Acetyl salicylic acid (aspirin) and its derivatives are ototoxic for humans and several laboratory animals.

The antibacterial anthelminatic agent, hygraomycin-B causes permanent deafness in dogs. The antiseptic combination of chlorhexidine and cetrimide is toxic both vestibular and cochlear cells in dogs.

Vestibular dysfunction: Vestibular function is characterized by head tilt and falling towards the affected side, ataxia without weakness, and nystagmus. The lesion may be in brain or in the vestibular apparatus or both. Animals with vestibular dysfunction caused by brain lesions as in listeriosis or canine distemper usually show other signs of neurological dysfunction. Since vestibular signs are more readily detected than is partial hearing loss, mild lesions of the inner ear are more frequently associated with vestibular abnormalities than with hearing deficients.

Neoplasms

Neoplasms of ceruminous glands are seen in dogs and cats. Adenomas are smooth, nodular or pedunculated. Histologically adenomas are well differentiated tubular and cystic growths. The epithelial cells are cuboidal and eosinophilic. Cartilaginous tumors of ears are also common in dogs.

Squamous cell carcinoma of the pinnae in dogs and certain times canine histiocytoma are present on to the skin of dogs and cats.

DISEASES OF EYE

Refractive power of the crystalline lens - Embryology: Development of eye:Development of lens- Development of the vitreous body, hyaloids membrane and zonules ciliary- Development of sclera and corena, choroid ciliary body iris and aqueous chamber- Retina- The lens- Congenital diseases of eye; Defective organogenesis; Diseases of cornea; Corneal wounds: Anterior synchia; Posterior synchia Diseases of lens; cataract,. Cortical cataracts, Nuclear cataracts-. Disorders of lens -Aphakia- Microphakia- Iridocyclitis: Inflammation of iris and ciliary apparatus Anterior uveitis: posterior uveitis; Chorioretinitis Endopthalmitis Diseases of retina: Retinal separation. Diseases of Eyelids; Infectious keratoconjunctivitis; Eye tumors; Ocular Squamous cell carcinoma in cattle

DISEASES OF EYE

The eye ball is situated within the bony cavity, known as orbit. The front portion is protected by the eyelids within orbit are surrounded by muscles and a thick padding of retrobulbar fat.

The bony orbital rim is complete in some species. It is incomplete in other. The term closed orbit is used when the bony orbital rim surrounding the eye ball is complete. Closed orbit is seen in man, horse, cattle and camel. An open orbit is an orbit with the bony rim incomplete so that part of it is made up a fibrous ligament. Open orbit is seen in cat, elephant, pig, dog and birds.

The anterior segment of eye is the portion of eye consisting of eye lids, conjucntiva, cornea, iris, and pupil and the anterior capsule of lens.

Eyelids: The front portion of eye ball is protected by eyelids. The border of eyelids contains eye lashes. The third eyelid is a piece of elastic cartilaginous structure situated at the inner canthus of eye.

Conjunctiva: It has two parts that is palepebral conjunctiva lining the inner surface of the eyelid and bulbar conjunctiva attached to the eye ball. The epithelial lining of conjunctiva is continuous with the epithelial lining of conjunctiva.

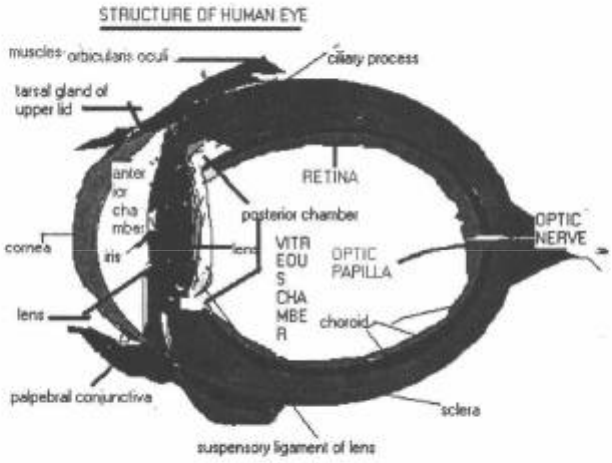
Lacrimal gland: It secretes tears. It lies in a depression beneath the supraorbital process. It opens into the conjunctival fornix by means of small openings. The tears lubricate the epitheialial surface of the cornea. The excess tears is drained through the two puncta lacrimalis situated at the inner canthus of the eye into the lacrimal sac and form the lacrimal sac to the nasal cavity through lacrimal duct. The conjunctiva epithelium is continuous with the epithelium of larcimal canal and epithelium lining the cornea.

Harderian gland: The harderian gland resembles lacrimal gland, situated on the inner surface of the third eye close to the anterior border.

Tarsal glands: Modified sebaceous gland situated within the tarsal plate. Ducts of these glands open along the free border of the eyelid.

Lens system of the eye: The eye is optically equivalent to the usual photographic camera, for it has a lens system, a variable aperture system (the pupil) and a retina corresponds to the film. The lens system of the eye is composed of the interface between air and the anterior surface of the cornea. The interface between the posterior surface of the cornea and the aqueous humor, the interface between the aqueous humor and the anterior surface of the lens and the interface between the posterior surface of the lens and the vitreous humor. The refractive index of air is 1.0 and the cornea is 1.38, the aqueous humor is 1.33, the lens is1.40 and the vitreous humor is 1.34.

In the reduced eye a single lens is considered to exist with its central pint 17 mm in front of the retina and to have a total refractive power of approximately 59 diopters when the lens is accommodated for distant vision. The anterior surface of the cornea provides about 48 diopters of the eye's total dioptic strength for three reasons. The refractive index of the cornea is a markedly different from that of air, the surface of the cornea is farther away from the retina than are the



surfaces of the eye lens and the curvature of the cornea is reasonably great. The posterior surface of the cornea is concave and actually acts as a concave lens, but, because the difference in refractive index of the cornea and the aqueous humor is slight, this posterior surface of the cornea has a refractive power of only about-4 diopters, which is neutralizes only a small part of the refractive power of the other refractive surfaces the eye.

The total refractive power of the crystalline lens of the eye when it is surrounds by fluid on each side is only 15 diopters of the total refractive power of the eye's lens system. If this lens were removed form the eye and then surrounded by air, its refractive power would be about 150 diopters. Thus it can be seen than the lens inside the eye is not nearly as powerful as it would be outside the eye. The reason for this is that the fluids surrounding the lens have refractive indices not greatly different from the refractive index of the lens itself, the smallness of the hindrances greatly decreasing the mount of light refraction at the lens interfaces.

In exactly the some manner that a glass lens can focus an image on a sheet of paper, the lens system of the eye can also focus an image on the retina. The image is inverted and reversed with respect to the object. However the mind perceives the objects in the upright position despite the upside down orientation the retina because the brain is trained to consider inverted image as the normal. The refractive power of the crystalline lens in them can be voluntarily increased from 15 diopters to approximately 29 diopters in young children. This is the total accommodation of 14 diopters. That is moderately convex lens is changed to very convex lens.

Normally lens is composed of a strong elastic capsule filled with viscous, proteinaceous but transparent fibers. When the lens is in a relaxed state, with no tension on its capsule, it assumes a spherical shape, owing entirely to the elasticity

the lens capsule. Approximated around 70 ligaments attach radially around the lens, pulling the lens edges towards the edge of the choroid. These ligaments are constantly tensed by the elastic pull of their attachment to the choroid, and the tension on the ligaments causes the lens to remain relatively flat under normal resting conditions of the eye. At the insertion of the ligaments in the choroid is the ciliary muscle, which has two sets for smooth muscle fibers, the meridian fibers and the circular fibers. The meridian fibers and extend from the corneo-slceral junction to the insertions for the ligaments to the choroid approximately 2 to 3 mm behind the corneoscleral junction. When these muscle fibers contact the insertion of the ligaments is pulled forward, thereby releasing a certain amount of tension on the crystalline lens. The circular fibers are arranged circularly all the way around the eye so that when they contract a sphincter like actin occurs, decreasing the diameter of the circle ligament attachments and allowing the ligaments to pull less on the lens capsule. Thus contraction of both sets of smooth muscle fibers in the ciliary muscle relaxes the ligaments to the lens capsule, and the lens assumes a more spherical shape, like that of a balloon, because of elasticity of its capsule. When the ciliary muscle is completely relaxed, the dioptic strength of the lens is as weak as it can become. On the other hand when ciliary muscle contracts as strongly as possible, the dioptic strength of the lens becomes maximal.

The circular muscle is controlled mainly by the parasympathetic nervous system but also to a slight extent by the sympathetic system. As a person grows older inhuman beings, the lens lose its elastic nature and becomes a relatively sold mass, probably because of progressive denaturation of the lens proteins. Therefore, the ability of the lens to assume a spherical shape; progressively decreases, and the power of accommodation decreases from approximately 14 diopters shortly after birth to approximately 2 diopters at the age of 45 to 50. Thereafter the lens may be considered to be almost totally nonaccomodating, a condition known as presbyopia.

Once a person has reached the state of presbyopia, each eye remains focused permanently at an almost constant distance; this distance depends on the physical characteristics of each individual's eyes. Obviously, the eyes can no longer accommodate for both near and far vision. Therefore, to see clearly both in the distance and nearby, an older person must wear bifocal glasses with the upper segment normally focused for far seeing and the lower segment focused for near seeing.

Embryology: Development of eye

Development of retina and optic nerves: Even before the closure of the fore-brain vesicle two lateral hollow diverticula project from the alar lamina at the junction of the telencephalon with the diencephalon towards the sides of the head. These are called the optic vesicles and the hollow stalks by which they communicate with forebrain vesicle are called the optic stalks. The opening of

communication with fore brain vesicle subsequently closes by the end of 5th week and the original site of the optic evagination is marked by the optic recess in the floor of the 3rd ventricle. The blind ends soon enlarge to form the optic bulbs. The distal wall of each optic bulb becomes invaginated by the developing lens and the bulb assumes the shape of a cup called the optic cup, the distal and proximal walls of which remain in an apposition, with a potential space between them which is the remains of the cavity of optic vesicle. The invagination extends also along the ventral aspect of the cup into the distal part of the optic stalk giving rise to a groove or cleft in that situation called the choroidal fissure. Into the fissure at about 5th week, mesoderm enters the in which the central artery of the retina and the hyaloid artery are developed. During 8th week, the margins of the choroidal fissure close. But sometimes it persists and is then associated with a deficiency of the choroid and iris at the situation giving rise to a gap called congenital coloboma of the choroid and the iris.

With the closure of choroid fissure the optic cup becomes complete and from it the retina is developed. The outer convex layer of the cup forms the outermost pigmented layer of the retina, as the cells in the mantle layer develop pigment granules and are arranged in single layer. From the inner invaginated layer of the cup kept its peripheral part the remaining layers of the retina is developed. Thus the rods and cones are arranged close to the pigment cells in the outer layer of the cup, and the ganglion cells are arranged against the marginal zone of the inner layer of the cup, and between these the other cells often inner nuclear layer are developed. The fovea centralis, though apparent in the 3rd month of foetal life, is not well differentiated till the 3rd month after birth. The condition called the detachment of the retina causing blindness is the detachment of the outer pigment layer from the inner layer containing rods and cones which fall inwards with the nervous layer, with the accumulation of fluid in the primate cavity of the optic vesicle. From the spongioblasts the supporting cell is developed. The axis cylinder processes the ganglionic layer pass through the marginal zone of the inner layer of the cup and leave the cup as optic nerve fibers through the optic stalk. The optic stalk lined by a single layer of columnar cells, become solid by the orifice trait of its cells and by the invasion of the optic nerve fibers. The two optic stalks converge and partial decussation of the fibers takes place forming optic chiasma. From the chiasma the optic tracts develop and diverge to establish connections with the mid brain and the diencephalon.

The peripheral part of the optic cup remains thin, the outer layer being represented by the single layer of pigmented cells and the inner layer also by a single layer of columnar cells. This thin peripheral part of the retina consisting of two layers of cells only is continued up to the margin of the pupil. Thief portion of it opposite the ciliary body is called the pars ciliary reitna, while the portion lining the back part of the iris is called pars iridica retina. Limiting membrane is devoted on both the surfaces of the retina.

Development of lens: The lens is ectodermal in origin. About the 5th week of embryonic life, the surface ectoderm overlying the optic vesicle thickens as a circular patch which becomes depressed centrally. The margins of the depressed thick ectoderm fuse, forming a closed ectodermic sac called lens vesicle. The vesicle becomes detached from the surface ectoderm and sinks into the adjacent mesoderm. It enters the optic cup and lies at first in apposition with the inner invaginated layer of the cup. The optic cup said to have an inducing organizing property to influence and control the development and the invagination of the lens. As the lens recedes from the inner layer of the cup, the interval between it and the cup is occupied by the tissue which develops into vitreous body. The cells forming the posterior wall of the lens vesicle become elongated transversely and lose their nuclei forming the lens fibers. The cells of the anterior wall of the lens vesicle remain small and retain their nuclei forming the epithelial lining of the anterior surface of the lens. Owning to elongation of the cells of the posterior wall, the cavity of the vesicle becomes obliterated. The superficial lenticular cells will form a cuticular membrane called the capsule of the lens.

The lens carries with it a covering of mesoderm which is at first very vascular. The portion of it covering the posterior surface of the lens is supplied by the terminal l part of the hyaloids artery and the part in front of it is supplied by ciliary vessels from the front part of the choroid. This vascular mesodermal covering is called the capsule vesiculosus lentis. With the atrophy of the vessels coming form the choroid, and of the hyaloids artery, at the 6th month. This vascular capsule of the lens atrophies by the 7th month foetal life. Sometimes however the part anterior to the lens persists after birth as the papillary membrane.

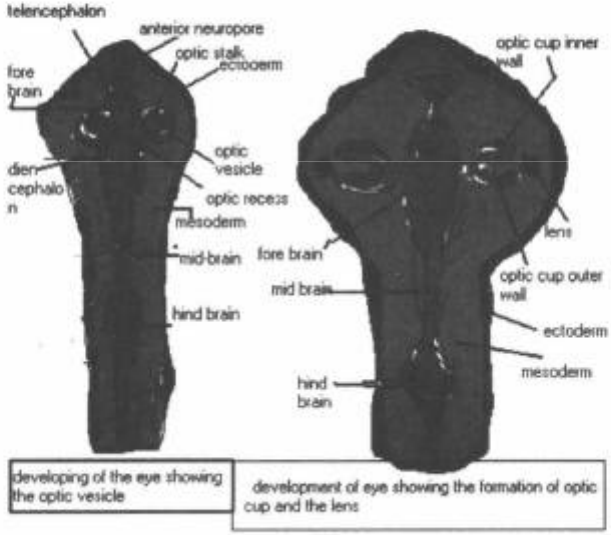
Development of the vitreous body, hyaloids membrane and zonules ciliary: As the lens recedes from the inner layer of the optic cup the gap between it and the lens becomes filled up by network of protoplasmic processes derived partly from the marginal zone of the optic cup antiparty from the posterior layer of the lens vesicle and both of these elements are ectodermal origin. With its is mixed up some amount of mesodermal tissue carried into the interior of the cup through the chorial fissure as well as round the equator of the lens. All this contributes that formation of the vitreous body, which is thus partly ectodermal den partly mesodermal in origin. Some embryologist believe that the vitreous body is entirely ectodermal in original having no mesodermal contirbution. The peripheral layer of the vitreous body become condense to form the hyaloids membrane. Futher condensate of the is peripheral layer opposite the ciliary body forms the zonules cilairis. Originally the hyaloids artery passé through the vitreous body to the posterior surface of the lens to supplies casual capsule. But the artery atrophies during the 6th month the track of the artery, however, still persisting as the hyaloids canal. The persistent remnant of the hyaloids artery may interfere with the vision.

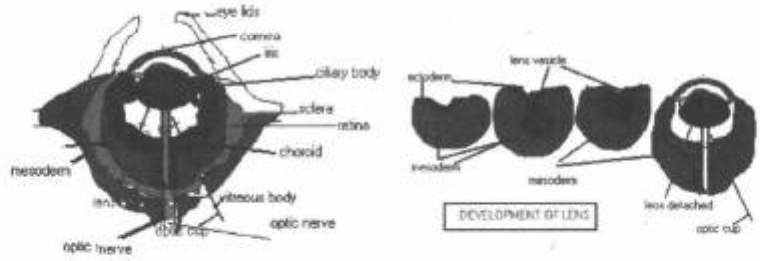
Development of sclera and corena, choroid ciliary body iris and aqueous chamber: The mesoderm around the optic cup and the lens becomes condense to form the fibrous and the vascular tunics of the eye balls. Between the 2nd and 3rd month of fetal life, the condensed mesoderm will form the sclera and the choroid, the anterior part of the choroid being modified to form the ciliary body and the ciliary processes. About the 4th month of foetal life the ciliary processes develop as 60 or 70 folds or plications of the Pars ciliaris retinae invaded by the mesoderm of the choroid. In the mesoderm which intervenes between the lens and the surface ectoderm, a cleft appears which forms the aqueous chamber. The condensed mesoderm in front of the cleft forms the transparent cornea and is continuous behind with the sclera which forms the posterior part of the fibrous tunic. The zonules of Zinn and the suspensory ligament of the lens are developed from radial fibrils stretching between the ciliary body and the lens with its capsule. About the 4th month, the iris is developed as a forward growth of the anterior margin of the optic cup thereby subdividing the aqueous chamber into anterior and a posterior chamber, the latter being between the iris and the lens. The stroma of the iris is contributed by the mesoderm which is continuous with the choroid.The iris is continuous behind with the anterior part of the vascular tunic namely the ciliary body and the choroid. The aqueous humour is formed at the 6th month of foetal life by a secretion of the retinal epithelium covering the cilairy proceses, the ciliary muscle composed of circular and radial fibers is also developed in this mesoderm. The cells of the vascular tunic pigmnted, the dilator and sphincter muscles of the pupil are however ectodermal in or inbeing developed from the pigment layer of the pars iridica retinae or the thin al portion of the optic cup. The facis bulb oar the fascialsheath of the eye ball is developed from the mesoderm surrounding the eye ball and is separated forth sclera by a tentialo lymph space. The metalliclustre called the tapetumlucidum found in atheiterori of the ox eye is due to the presence of layer of the fibers developed on thee retinal surface of the choroid. It is absent in the human eye.

Development of eyelids and the conjunctiva: During the 7th week of embryonic if, the eyelids develop as two cutaneous folds, upper and lower with a core of mesoderm within which form the tarsal plates. These folds approach each other and fuse by their free margins at the 3rd month. They remain fused till the end of the 6th month. At the 7th month the fused margins again separate forming the free eyelids. The inner surfaces are lined by ectoderm which forms the palepebral conjunctiva and is reflected over the front of the cornea to form the bulbar conjunctiva; the line of reflection forms the conjunctival fornix. The eye lashes develop from the margins of folds, before their separation and the sebaceous and Meibomian glands develops as ectodermal outgrowths from the hair follicles. The sweat glands form as downgroths from surface ectoderm. The muscles of eyelids are developed from the 2nd or the hyoid arch at the end of the 2nd month and hence supplied by the facial nerve. The levator palepebral superiorisa muscle

of the upper eyelid supplied by the occulo motor nerve is a detached portion of the superior rectus muscle of the eye ball.

Development of the larcimal apparatus: The larcimal glands develop as solid buds or out growths from the epithelial cells of the conjunctiva from the lateral part of the superior conjunctival fornix during 9th week of foetal life. These buds branch and become canalized forming the alveoli and ducts of the larcimal gland. The nasolacrimal duct begins as a thickening of the ectoderm at junction the lateral nasal and maxillary processes. This thickening forms a solid cellular cord which sinks beneath the surface ectoderm and becomes canalized, the lower part of which it opens into the olfactory fossa. The upper end of this hollow tube becomes dilated and remains blind forming the larcimal sac. Two lateral diverticula take place from the lacrimal sac which opens at the margins of the eyelids near the medial ends. These are the upper and lower larcimal ducts or canliculi and their opening at the margins of the eyelids form the punctate lacrimalia.





The cornea: The cornea of domestic animals is a horizontal eclipse varying from 0.6 to 2.0 mm in thickness among the various species. In general the larger and older the animal, the thicker the cornea. It appears as a structural and physiological modification of sclera and when chronically injured my lose the specialized features of cornea and resemble limbic sclera. Embryologically the epithelium is derived from surface ectoderm, and the stroma is from neural crest mesenchyme in contrast mesenchyme in contrast to the vascular mesenchymal (non-neural) origin for sclera.

Cornea consists of non-keratinized and non-pigmented surface epithelium, avascular, cell poor stroma composed of very thin collagen of type I fibrils arranged in orderly lamellae and a high degree of stromal dehydration maintained primarily by a sodium-potassium dependent adenosine triphosphatase. This dehydration is passively protected by the hydrophobic corneal epithelium and by the lack of stromal vascualrity.

The reaction of cornea to injury is strongly influenced by the anatomic and physiologic relationships of cornea. The acutely injured cornea cannot respond with acute inflammation because it lacks blood vessels. Instead oedema may result from injury to the corneal epithelium or endothelium. With long stand corneal disease, the cornea may undergo metaplasia to resemble limbic sclera and thus acquire the full range of inflammatory responses available to vasuclarised tissue. The corneal irritated epithelium undergoes epidermal metaplasia with the appearance of rete edges, basal pigmentation and surface keratinisation. The stroma acquires capillary network and dermis like irregular fibrous tissue. This results in loss of transparency of cornea.

Corneal injury may result form physical or chemical trauma, microbial agents, increased intra-ocular pressure and rarely from inborn errors of metabolism.

Corneal oedema: This is due to inhibition of lacrimal secretions or failure of electrolyte extrusion by the corneal endothelium. The oedematous cornea is opaque and is thickened, Percolation of stromal fluid into the epithelium results in the intercellular oedema known as bullous keratopathy.

Corneal wounds: These are defects involving epithelium, an epithelium and surface stroma loss, the heal by epithelial sliding and regeneration of these cells. This begins within a few hours and is greatly enhanced by the secretion of fibronectin from adjacent injured epithelium. Healing of shallow, uninfected corneal ulcer is rapid. Deeper defects heal by epithelial proliferation from sides and replication combined with stromal fibrous tissue proliferation. Within a few hours of the insult, neutrophils reach the wound via the tear fill, attracted by protease released by injured epithelium. They migrate into the stroma and control bacterial contamination, degrades damaged collagen, and stimulates fibrous tissue proliferation degraded damaged collagen and stimulated fibrous tissue and vascularisation via production various cytokines. The keratocytes adjacent to the

wound undergo fibrous metaplasia and secrete large amount of sulfated ground substance, particularly chondroitin-sulfate. If the defect is not covering by epithelium results in fibrosis of the cornea.

Corneal pigmentation: Due to chronic initiation and is commonly seen in dogs.

Corneal lipidosis is common in dogs. Diets high in cholesterol produce diffuse corneal stromal lipidosis in rabbits. Corneal inflammation is called keratitis. It is divided into epithelial, stroma and ulcerative keratitis. With severe lesions corneal stromal vascularisation, fibrosis and epithelial metaplasia with pigmentation may occur. Keratitis usually results from physical, chemical or microbial injury to the cornea. Cornea may also affected by extension of disease from elsewhere in the eye or adnexa or conjunctiva. Chronic non-ulcerative proliferative inflammation termed as pannus keratitis.

Proteases and collagenases of microbial, Leukocytic or corneal origin progressively liquefy corneal stroma, a process termed kerato malacia. The neutrophils may encircle the liquefying focus as a thick wall of live and fragmented cells. The resulting lesion is then called a ring abscess. Ulcerative keratitis involves cornea, conjunctiva and uvea. Stromal liquefaction that reaches Descement's membrane results in its forward bulging as a descemetocoele.

Keratoconjunctivitis sicca: Necrosis of corneal epithelium caused by desiccation is called keratoconjunctivitis sicca; acute desiccation keratitis is particularly common in calves moribund as a result of neonatal diarhoea or meningoencephalitis and is seen as bilateral, large, shallow, central corneal ulcers. Desiccation keratitis may follow destruction or denervation of larcimal or accessory lachrymal gland in any species by orbital inflammation, drugs, neoplasia or trauma. Squamous metaplasia with resultant inadequacy of secretion may be seen with chronic deficiency of vitamin A. Transient keratoconjunctivitis sicca may accompany acute herpetic keratoconjunctivitis in cats.

Mycotic keratitis is not a specific disease but is often viewed as such because of its consistently poor response as to therapy and tendency to progress to corneal perforation. The offending fungus is usually a member of normal conjunctival flora and usually of Aspergillus spp.

Infectious bovine kerato-conjunctivitis in western countries is seen with squamous cell carcinoma of eye, Moraxella bovis and Mycoplasmal infections.

Ocular Squamous cell carcinoma in cattle; Squamous cell carcinoma of eye occurs frequently in tropical as well in the Western countries in cattle. In U.S.A. around 0.8 to 1.6% of cattle developed bovine ocular Squamous cell carcinoma (cancer eye). Cattle having the following risk factors namely breed predisposition, genetic predisposition, ultraviolet exposure, and non-pigmented orbital skin, exposure to insects, chemicals and viruses. It is known that the incidence increases with increasing intensity of sunlight, and is related to latitude and the amount of hours

of sunshine. Among the viral agents, infectious bovine rhinotracheitis, bovine herpes virus, bovine Papillomas virus have been incriminated. In India, it is observed that working bullocks suffer more than the cows. It is postulated that probably actinic rays of the sun are of etiological importance since bullocks are worked in the hot sun and probably the lower incidence in cows is that they have not been put to work in the hot sun. The actinic rays do play a part in the genesis of the tumor is supported by the fact that the Hereford breed in which the eye pigment is deficient, eye cancer is more common. The pigment filters the actinic rays of the sun.

Gross findings: Ocular lesions are seen as Precancerous plaques on cornea, sclera located at the lateral limbus. These are whitish in colour and are slightly raised and above the surface and are round in shape. In second stage conjunctiva papillomas extend outward over the epithelial surface and have a wart like appearance, which differentiates them from early plaques. In the third stage, this will turn as carcinoma of the corner or sclera. In the last stages, the invasive carcinoma of cornea and sclera may extend to lids in advanced cases, nictitating membrane is affected.

Squamous cell carcinoma is a highly malignant tumor and metastasis occurs in various organs. The secondary are seen in the regional lymph nodes and eye. Plaques and papillomatosis types of eye cancer may probably removed with satisfactory results since these are supposed to be benign stages. One should be cautious in using animals affected with eye and horn cancer for breeding since a genetic predisposition is suspected.

Retina:

The retina is the light sensitive portion of the eye, containing the cones which are responsible for colour vision, and therods which are mainly responsible for vision in the dark. When the rods and cones are excited signals are transmitted through the successive neurons in the retina itself and finally into the optic nerve fibers and cerebral cortex. The functional components of the retina arranged in layers from the outside to the inside as follows. 1) pigment layers, 2) layers of rods and cones projecting into the pigment, 3) outer lining membrane, 4) outer nuclear layer, 5) outer plexiform layer, 6) inner nuclear layer, 7) inner plexiform layer, 8) ganglionic layer, 9) layer of optic nerve fibers, 10) inner limiting membrane.

After light passes through the lens system of the eye and then through the vitreous humor, it enters the retina from the bottom that is it passes through the ganglion cells, the plexiform layer, the nuclear layer, and the limiting membrane before it finally reaches the layer of rods and cones located all the by or. the opposite side of the retina. This distance is a thickness of several hundred microns; visual activity is obviously decreased by this passage through such nonhomogenous tissue. However in the central region of the retina, the initial layers are pulled aside to prevent this loss.

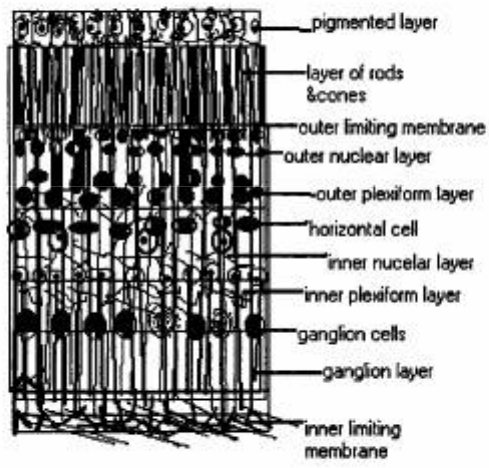
A minute area in the centre of the retina, called the macula and occupying a total area of less than 1 square mm is especially capable of acute and detailed vision. This area is composed entirely of cones, but the cones are very much elongated and have a diameter of only 1.5i in contradistinction to the very large cones located farther peripherally in the retina. The central portion of the macula, only 0.4 mm in diameter is called the fovea; in this region the blood vessels, the ganglion cells, the inner nuclear layer of cells, and the plexiform layers are all displaced tone side rather than resting direction top of the cones. Thus allows light to pass unimpeded to the cones rather than through several layers of retina, which aid immensely in the actual of visual perception by the region of retina.

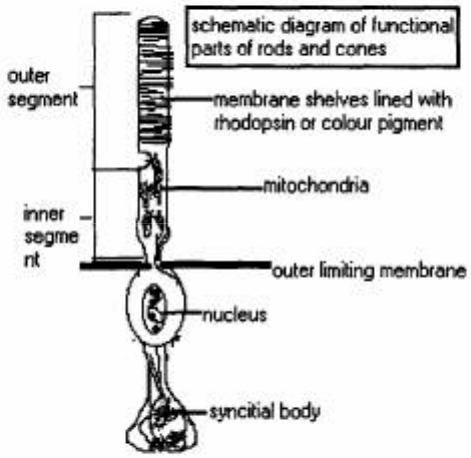
Rods are narrower and longer than cones the photosensitive pigments are incorporated in rods and cones. They are concentrated at each surface of the membrane-both inside and outside surfaces. The four major functions segments of rods are cones are as follows. The outer segment, the inner segment, the nucleus and the synaptic body. In outer segment light sensitive photochemical is found. In case of rods this is rhodopsin and in cones it is one of several photo chemicals almost exactly the same as rhodopsin except for a difference in spectral sensitivity.

The inner segment contains the usual cytoplasm of the cell with the usual cytoplasmic organelles. Particularly important are the mitochondria which provide most of energy for function of photoreceptors.

The synaptic body is the protein of the rod and cone that connects with the subsequent neuronal cells, the horizontal and bipolar cells that represent the next stages in the vision chain.

STRUCTURE OF RETINAL NEURON





Lens:

lens is a flattened sphere of epithelial cells, suspended in the papillary aperture by an equatorial row of suspensory zonules radiating from the basement membrane of the nonpigmented ciliary epithelium in valleys between the ciliary processes and from pars plana. The morphological reaction of lens to injury is very limited due to the simplicity of its structure and physiology and its lack of vascualrity.

The lens is entirely epithelial. Outermost is a thick elastic capsule which is the basement membrane produced by the underlying germinal epithelial clells. The capsule is thickest at the anterior pole and becomes progressively thinner over the posterior half of the lens. The capsules the neonate is thin, but it thickens progressively throughout life.

Below the capsules is a layer of simple cuboidal lens epithelium, which, in all but foetal globes, is found below the capsule of only the anterior half of the lens. The apex of these cells faces inward toward the lens nucleus. At the equator these germinal cells extend into the lens cortex as the nuclear bow, an arc of cells being progressively transformed from cuboidal germinal epithelium to the enlarged spindle shape of the mature lens fibers. The bulk of lens is composed of opinion like layers of elongated epithelial cells anchored to each other by interlocking surface ridges, grooves, and protuberances. These elongated fibers contain no nucleus and few cytoplasmic organelles, relying almost entirely on anaerobic glycolysis of energy. Since lens cannot shed aging fibers like skin or intestine, these cells are compacted into the oldest central part of the lens, the nucleus. The continuous accumulation of these old desiccated fibers with altered crystalline protein results in the common but visually insginficant aging change of the nuclear sclerosis.

Optical clarity of lens rests is high percentage of cytoplasmic soluble crystalline protein. The lens consists of about 35% protein, the highest of any tissue and over 90% of it is soluble crystalline variety. Opacity is associated with decreasing concentration of crystalline and increasing albuminoid protien, the latter insoluble in water and is optically opaque. Degneration of lens is due to its decreased nutrition. Since the lens is avascular in postnatal life it depends on the aqueous for the delivery of nutrients and removal metabolic waste products. Glaucoma, ocular inflammation, metabolic disorders and various toxins share the common feature of altering the amount or quality of lenticular nutrition by altering the flow or composition of the aqueous humor.

Diseases of lens

Dislocation of lens which is congenital or acquired. It may be spontaneous which is having a genetic tendency or due to secondary due to rupture. The dislocation may be partial than the subluxation or complete luxation. The free lens may damage the cornel endothelium or vitreous causing oedema and liquefaction. Anterior luxation results in glaucoma and is common in middle aged cats.

CATARACT

This is the most important disorder of lens Cataract means lenticular opacity. The histology of cataract involves germinal epithelial hyperplasia, metaplasia, hydropic changes, fiber necrosis and occasional calcium salts deposition.

Cataract may be congenital or acquired. It maybe complete involving lens completely, partial, progressive, stationary, senile, diabetic, toxic, capsular, cortical, pyramidal, lamellar, perinuclear, nuclear, calcerous, immature, mature and completely opaque types.

Epithelial hyperplasia or metaplasia is seen following foal trauma or adherence of the iris or of persistent papillary membranes to the anterior surface of the lens. The resultant epithelial plaque lays to the anterio lens capsule. Degeneration and resultant fragmentation or liquefaction of lens fibers is the most common lesion of cataract. Degenerated fibers break into pieces. As fiber fragmentation progresses the fragment liquefy and assume a spherical shape. Abortive efforts at new fiber formation by lens epithelium results in the formation of large foamy nucleated cells called balder cells, pathognomonic of cataract.

Cataract may result from exposure the lens to a wide variety of physical and chemical insults, such as solar or other irradiation, cold, increased intraocular pressure, toxins, nutritional excesses and deficiencies, near by inflammation and direct trauma. Diabetic cataract is common in aging dogs. The opacity is bilateral. This is due to excessive presence of glucose. When the rate limiting enzyme of hexose phosphate shunt pathway is saturated the glucose is a shifted to alternative metabolic pathways, chief among these is the sorbitol pathway, activated in the rabbit lens by glucose concentration of greater than 90 mg/dl. In this pathway

the excess glucose's converted to by an aldolase reductase to alcohol, sorbitol which is then slowly reduced to a ketose. Sorbitol accumulates in high concentration in lens with resultant high concentration of osmotic instability with in lens and this attracts water and even to the points of hydrops and cell ruptures.

Cataract is opacity of lens due to lamellar structures of lens fibers. The principal location of cataracts include subcapsular epithelium, cortex and nucleus of lens. Subcapsular cataract is the anteriorpolar cataract or posterior polar cataract. Following damage to the anterior or posterior lens, water may enter that leads further contributing to the opacity (in tumescent cataract). Cortical cataracts occur due to disorganization of lens fibers. Nuclear cataracts are changes in the transparency of oldest lens fibers. Thus cataracts are mostly due to traumatic injuries or due to metabolic disorders.

Aphakia- absence of lens

Microphakia- presence of small lens

Eyelids

Eyelids have cutaneous and conjunctival surfaces and contain both tear and sebaceous glands that is meibomian glands. Any lesion of the skin may involve the cutaneous part of the eyelid.

The causes of conjunctivitis include every class of noxious stimuli, including allergy and desiccation.

Congenital inward turning of eyelids is known as entropion may lead to conjunctivitis and keratitis due to abrasion of cornea and sclera by the pair of inverted eyelids.

Outward eversion of the eyelids, ectropion and is inherited.

A douberow of eye lashes-distichiasis may also cause conjunctivitis.

Nictitating membrane is well developed in most domestic animlas, but is vestigeal in humans. This is supplied with simple and compound tubular glands.

Inflammation of larcimal glands is called dacroadenitis. It may result from involvement in orbital cellulitis or orbital trauma, spread from severe intraocular inflammation, incident involvement in systemic diseases such as like canine distemper or apparently specific immunologic insult.

In most species an accessory lacrimal glands (harderian gland) exits at the base of third eyelid.

Infectious keratoconjunctivitis or Pink eye is common sheep, goats and cattle and results in diffuse inflammation of cornea, producing temporary blindness. The causative bacteria are *Moraxella bovies, Rickettsia conjunctivae and Chlamydial organisms.*

Keratoconjunctivitis sicca is due to defective production or functions of tears leads

to excessive dryness of corneal surface. Pigmentary keratitis and vascularisation of cornea is common.

It may be due to nutritional deficiencies like B_2 deficiency, as well amino acid deficiency tryptophan.

Vascularisation of cornea either superficial or deep vascularisation is common with inflammatory lesions.

Corneal dermoid: Congenital lesions are observed this in newborn animals.

Anterior synchia is a term used to designated adhesion between the anterior surface of iris and posterior corneal surface.

Posterior synchia is the adhesions between posterior surface of iris and anterior lens capsule.

Iridocyclitis: Inflammation of iris and ciliary apparatus (anterior uveitis)

Anterior uveitis: Inflammation of iris and ciliary body

Inflammation of ciliary body and choroid is posterior uveitis.

Chorioretinitis is inflammation of choroid and underlying retina.

Endopthalmitis is inflammation of most of internal portion of eye when all structures of eye are involved called as panopthalmitis.

Equine periodic opthalmia is a recurrent iridocyclitis seen in horses and causes the blindness.

Hemeralopia: day blindness

Defective organogenesis; failure of eye to attain even the stage of optic cup. Failure of formation of the primary vesicle or its early and complete regression is true an ophthalmic and is very rare. Failure of optic vesicle invagination gives rise to the very rare congenital cystic eye. Incomplete invagination results in congenital retinal nonattachment.

Failure of division of the optic primoridum as it grows from the tlelencephalon results in Cyclopia, or synopthalmos, a single dysplastic midline globe.

Anopthalima, total absence of ocular tissue.

Cyclopia and synopthlamus: Damage to the prosencephalon prior to the outgrowth of the optic vessels may result in improper separation of paired cranial mid line structures including eyes.

Dacroadenitis: Inflammation of lacrimal gland

Blepharitis: Inflammation of eyelids.

Trichiasis and districhiasis: In Trichiasis the eye lashes are directly slightly

inwards, so that they irritate the cornea.

Districhiasis is a congenital condition in which two rows of eye lashes are noticed on each lid and the inner row causes irritation to the cornea.

Ptosis (Blephaoptosis): Dropping of upper eyelid due to inability to rise. Paralysis of the seventh cranial nerve as well this condition it is congenital defect also.

Lagophthalmos (Lagos: hare) wherein the eye cannot be completely closed.

Blepharospasms; Partial or complete closure of eyelids due to irritation of cornea. Keratitis and conjunctivitis are responsible for this.

Exopthalmus: Abnormal protrusion of eye ball maybe retrobulbar abscesses, due to haematomas or inflammation. Hydropthalmos, glaucoma or goiters are responsible for this.

Enaopthaloms (pig eye): abnormal retraction of eye ball into the orbit.

Hyphema: Heaemorrhages into anterior chamber.

Hydropthalmos: Enlargement of eye ball associated with increase in quantity of aqueous humor. This is due to interference with drainage of aqueous humor. Rickets may predispose to Hydropthalmos.

Strabismus (Squint): Where abnormal deviation in the position of eye ball.

Glaucoma is a disease condition where there is an increase in intra-ocular pressure.

Conjunctivitis is the inflammation of the conjunctiva.

Epiphora is a symptom characterized by excessive flow of tears.

Symblepharon: Bulbar conjunctiva is adherent to palepebral conjunctiva.

Ankyloblepharon: Adhesion of eye lids

Dermoid cysts: Misplaced embryonic tissue having different type of tissues, like teeth, hair, glands etc.

Keratitis: Inflammation of cornea.

Luxation lens: Displacement of lens

Cataract: Opacity of cornea

Coloboma of iris: Congenital condition where in portion of iris is absent. Pupil is an irregular shape.

Aniridia: Iris is completely absent.

Iritis: Inflammation of iris.

Cyclitic: Inflammation of ciliary body.

Chroiditis: Inflammation of choroid

Uveitis: Inflammation of iris, cilairybody and choroid

Hyalitis: Inflammation of vitreous body

Retinitis: Inflammation of retina

Anterior synechiae: Attachment of iris to cornea

Posterior synechiae: Attachment of iris to lens

Perioptic opthalmitis. The: Repeated iridocyclitis

Amauarosis: Blindness without any apparent lesion in eye. This may be temporary or permanent.

Emmetropia: Normal sight

Hypermetropia: Long sight

Myopia: short sight

Astigmatism: Refraction through several meridians.

A lens which has the principal focal distance of 1 metre (40") is 1 diopter (1D). 2 D presents foal length of 0.5 meters.

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Plate 1.1.Truantic reticulopericarditis, observe binding wire penetrated the bovine heart

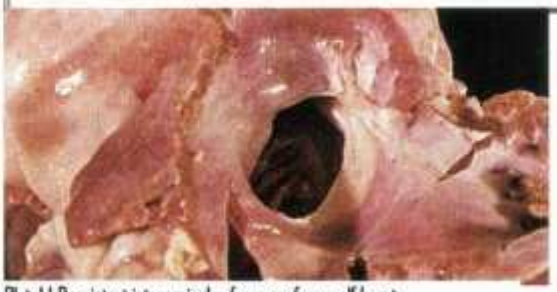


Plate1.1.Persistent interauricular foramen-from calf heart

Plate 1.1.Diseases of Cardiovascular System

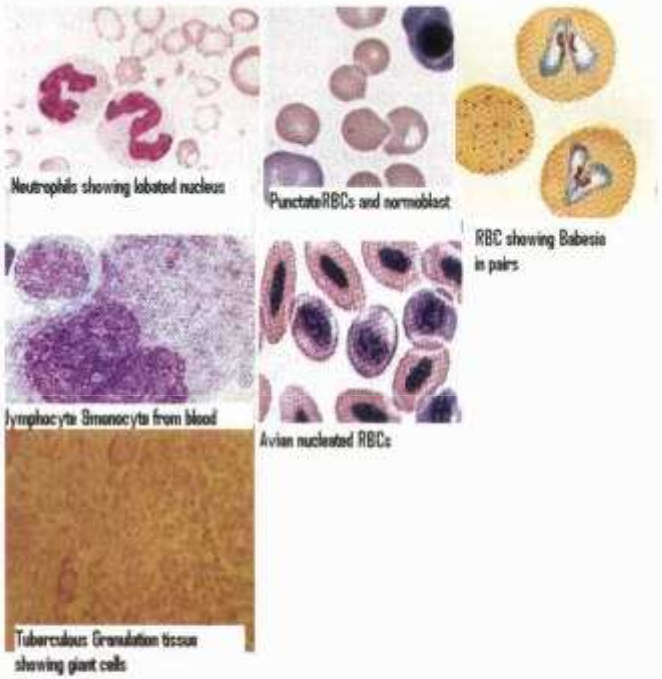


Plate 2. Diseases of Haemopoietic System

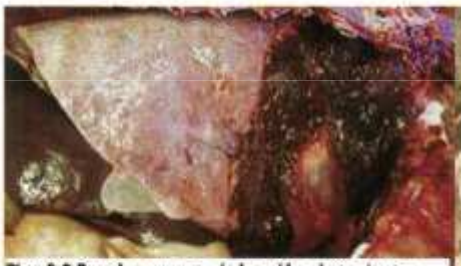


Plate.3.2.Bronchopneumonia-darkened lung lesion-bovine

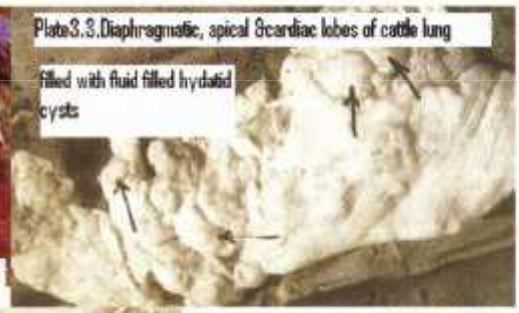


Plate3.3.Diaphragmatic, apical &cardiac lobes of cattle lung filled with fluid filled hydatid cysts

Plate.3.4.A large fluid filled hydatid cyst recovered from cattle lung

Plate.3.5. Histological section of hydatid cyst(degenerating) of cattle showing granulomatous reaction withgerminal membrane(1), granulomatous reaction with foreign body giant cells(2),other mononuclear reaction(3) and fibrous tissue proliferation

Plate3.6.Gross photo of cattle lung, diaphragmatic lobe with interstitial emphysa

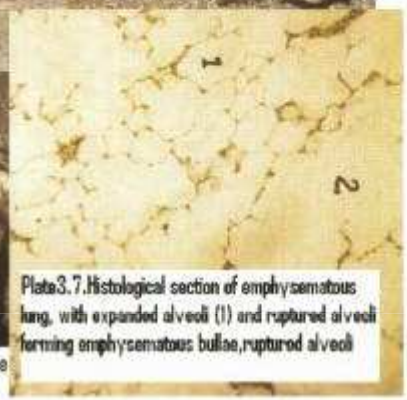
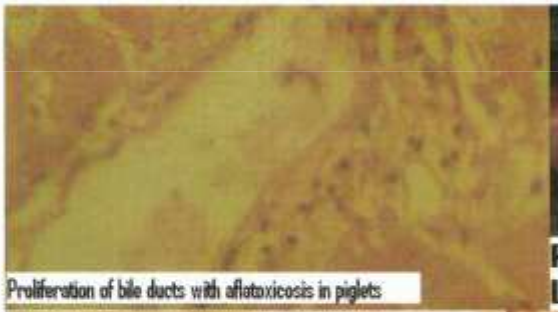


Plate3.7.Histological section of emphysematous lung, with expanded alveoli (1) and ruptured alveoli forming emphysematous bullae,ruptured alveoli

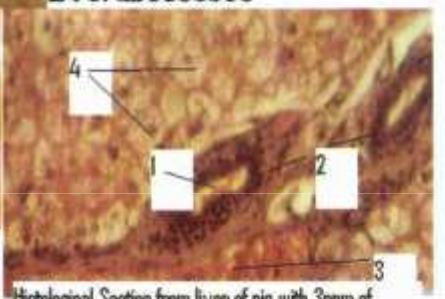
Plate.3.2.. Diseases of Respiratory System



Proliferation of bile ducts with aflatoxicosis in piglets

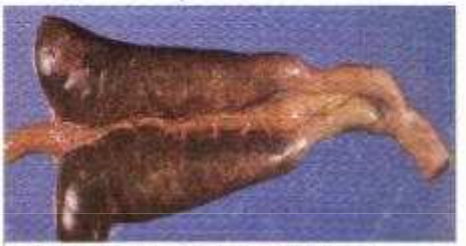
Plate4.1.3
Liverabscesses

Tapeworms-Moneizia recovered from Goat intesines



Histological Section from liver of pig with 3ppm of aflatoxin for 127 days in feed .H&E×50. 1,2-Proliferated bile ducts, 3.Portal veins, 4.liver cells showing hydropic degeneration

Evaginated scolex with rostellum and hooks recovered from hydatid cysts



coccidial typhlitis from a bird,note blood filled caeca

Plate..4.1.Diseases of Digestive System

Plate4.1.2 Nut meg liver due to cirrhosis

Plate4.1.3 Liverabscesses

Plate.4.1.4.Proliferated bile ducts from the liver of pig fed 1ppm of aflatoxin for 120days.

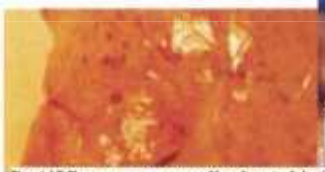


Plate.4.1.5.Observe gross appearance of liver from pigs fed with aflatoxin at 2ppm for 120 days showing haemorrhages on the surface of liver parenchyma under Glisson's capsule

Plate.4.1.7 Observe caecal mucosa of intestine of sheep suffering with Johne's disease and are positive for acid fast bacilli

Plate4.1.6 observe the caecal mucosa of cattle with corrugated appearance and positive for Johne's disease, where mucosa showed acidfast bacilli

Plate4.1.8 Observe lumen of cat intestine filled with Ascaris vitulorus worms

Plate.4.1.2.Diseases of Digestive System

Plate4.2.1. Mesentric Lymphnode of sheep cut open to show black pigment masses that are common with Johne's disease strains in sheep

plate.4.2.3. Intestines : of sheep with pimply gut nodules (larvae of oesophagostomu, lunder serosa.

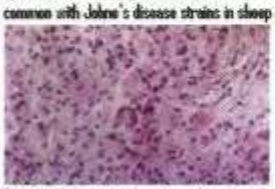


Plate4.2.2.Histological reaction of lymph nodes from sheep in Johne's disease showing histiocytes and syncitial giant cells

Plate4.2.4Histological Section of sheep intestine with pimply gut nodules showing amorphous mass and granulomatous reaction.

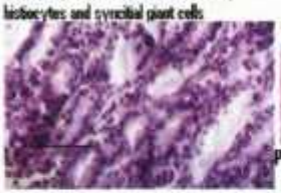


Plate4.2.5.Intestinal reaction with coccidiosis in sheep.coccidial oocysts and schizontes(arrows)

Plate4.2.6 Intestinal reaction with coccidiosis in sheep.coccidial oocysts and schizontes(arrows)

Plate4-2-1.Diseases of Digestive System

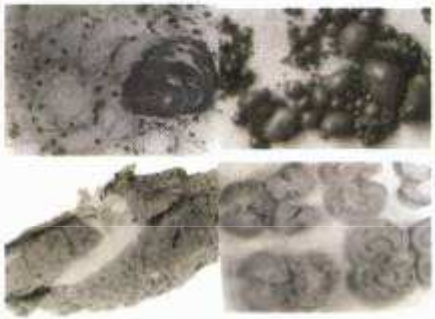


Plate.5.Diseases of Urinary System

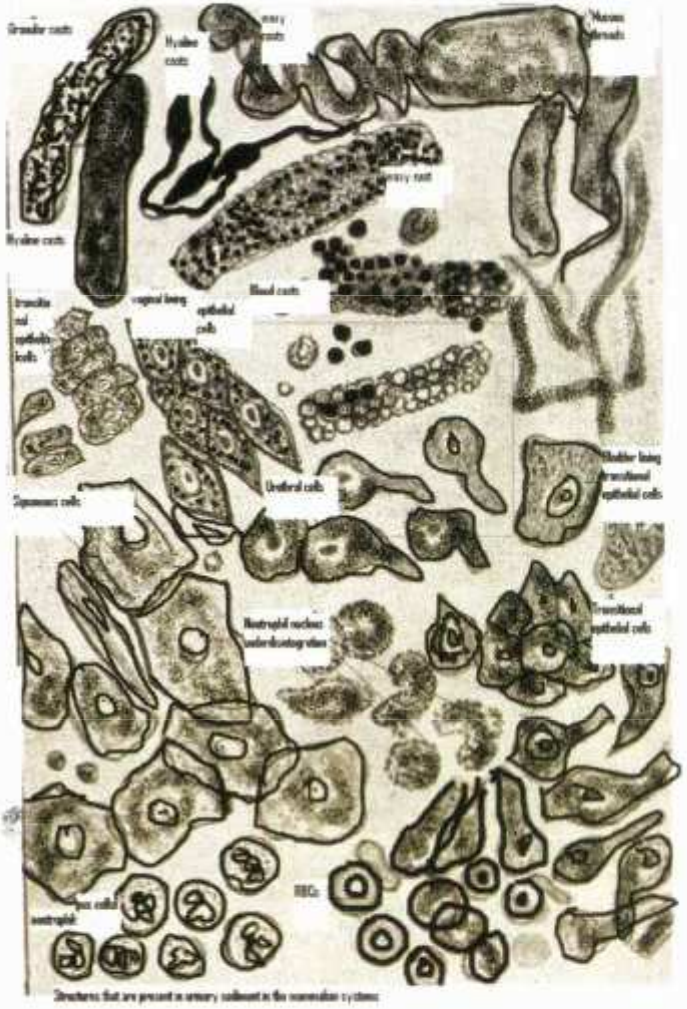
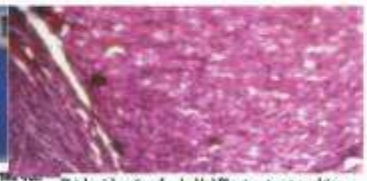


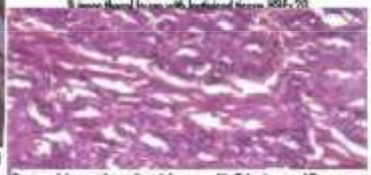
Plate.5.2Urine showing Urinary casts and pigments

Observe multiple cystic cavities in the CL of left ovary.Rt.ovary normal



Histological section of embedded CL,note outer stromal tissue & inner thecal layer with infiltrated tissue.H&E x 20

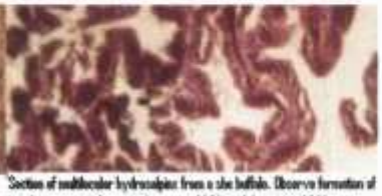
Histological section of embedded CL showing outer stromal tissue & inner thecal layer (Pink colour) with infiltrating blood vessels in luteinized tissue. Vue/Becous 20



Section of dermoid cyst from left ovary of buffalo showing different types of rete tubules with abundant inter tubular connective tissue. H &E x 20

Plate.6.1.Disease of Female genital system

Section of left follicle from left ovary of buffalo .Observe outer thecal layer and a layer of degenerated granulosa cells and inner pinkish follicular fluid. H & E x 20



Section of multilocular hydrocalpinx from a cbe buffalo. Observe formation of irregular cavities in between the mucosal folds and the mucosal folds were reduced in size as thin membranes H & E x 20

Plate.6.1.Abscess of mammary gland and loss of teat-Mastitis

Plate.6.2.Necrotic endometritis, exposed cotyledons with haemorrhages-bovine uterus

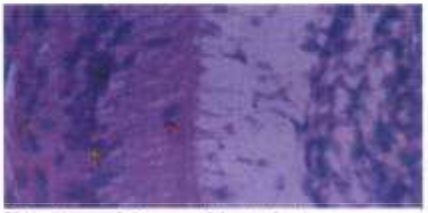
Plate.6.3.Pyocalpinx

Histological section from the uterus of bovine with pyometra showing flattened endometrial folds (a), oedema(b),coiled endometrial glands(c) and macrophages (d)infiltrated into submucosa.H&E x100

Plate 6.2. Diseases of Female Genital System

Histological section from uterus of bovine showing a)folds of endometrium b)increased thickness of lamina propria c)loss of glandular epithelial cells . H&E x100

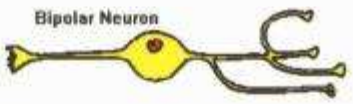
Histologicla section from ovary from cbebuffalo showing degenerated and cystic follicle (a),fibrous connective tissue proliferation (b),degenerted CL(c)and increased number of blood vessels in CL(d). H&E x100

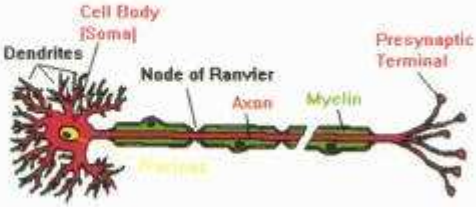


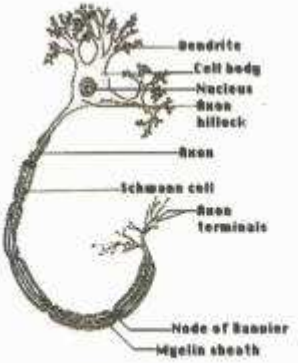
Photomicrograph from empididymis showing pseudo-stratified lining epithelium of tubules. Observe spermatozoa in the lumen. H&Ex1000

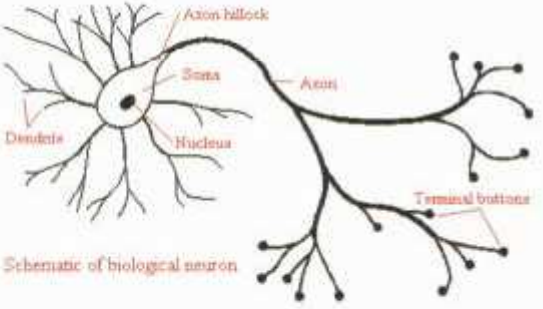
Ddouble tailed and coiled tails of spermatozoa

Plate7.1.Male genital system









Schematic of biological neuron

Cerebellum neuron-purkinjeocell

Plate 8-Nervous System

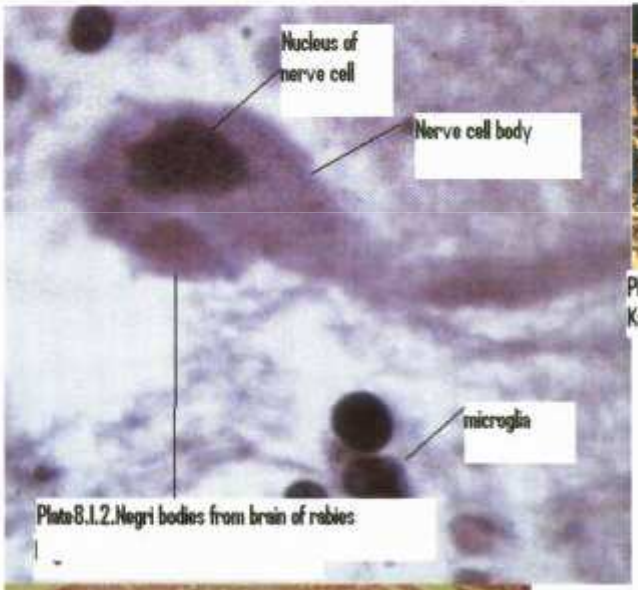


Plate 8.1.2. Negri bodies from brain of rabies

Plate 8-I-3. Purkinjee cells with processes Kajal's Gold stain

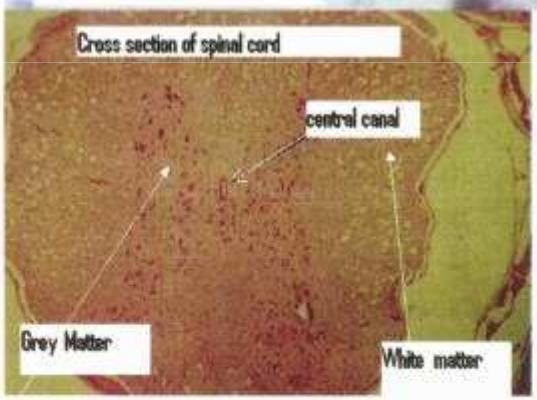


Plate-8.1.2. Diseases of Nervous System

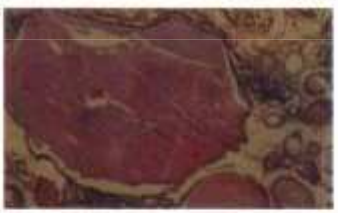


Plate. 9.1.1. Colloidal goitre, observe the follicles are uneven and filled with pinkish colloid material

Plate9.1. Diseases of endocrine system

Plate10. Musculo-skeletal system