General Veterinary pathology

Pathology

- study of disease (pathos = suffering or disease + logos = study).
- study of structure and function of the body in disease
- structural and functional changes in cells, tissues, and organs that underlie disease
- Disease is that condition in which the individual suffers from discomfort (dis = not + ease, i.e., not at ease).
- General pathology is concerned with the basic reactions of cells and tissues to injurious stimuli.

- Pathology covers five aspects of a disease process:

(1) its cause (aetiology)

(2) the mechanisms of its development (pathogenesis)

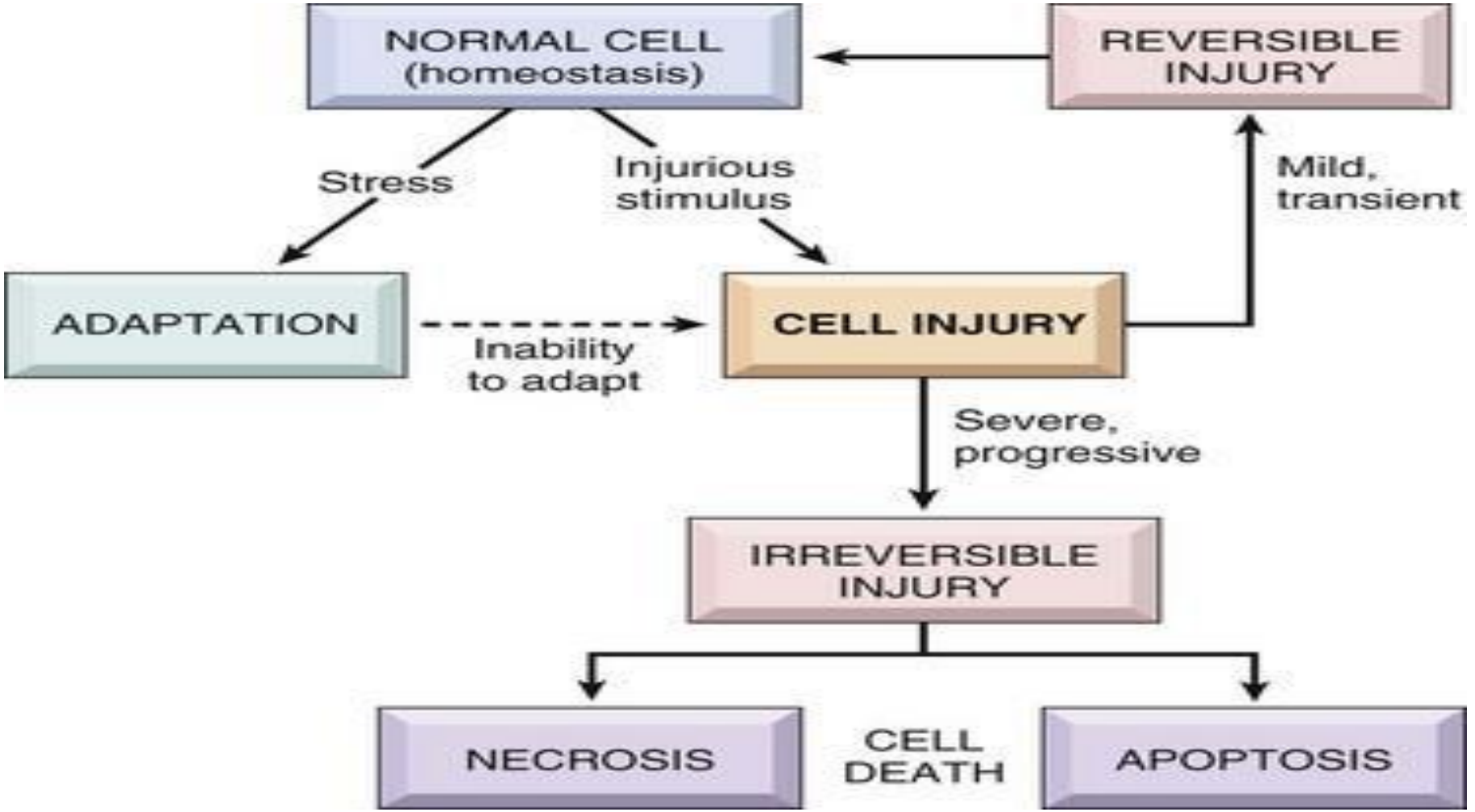
(3) structural changes produced in cells and organs (morphological changes)

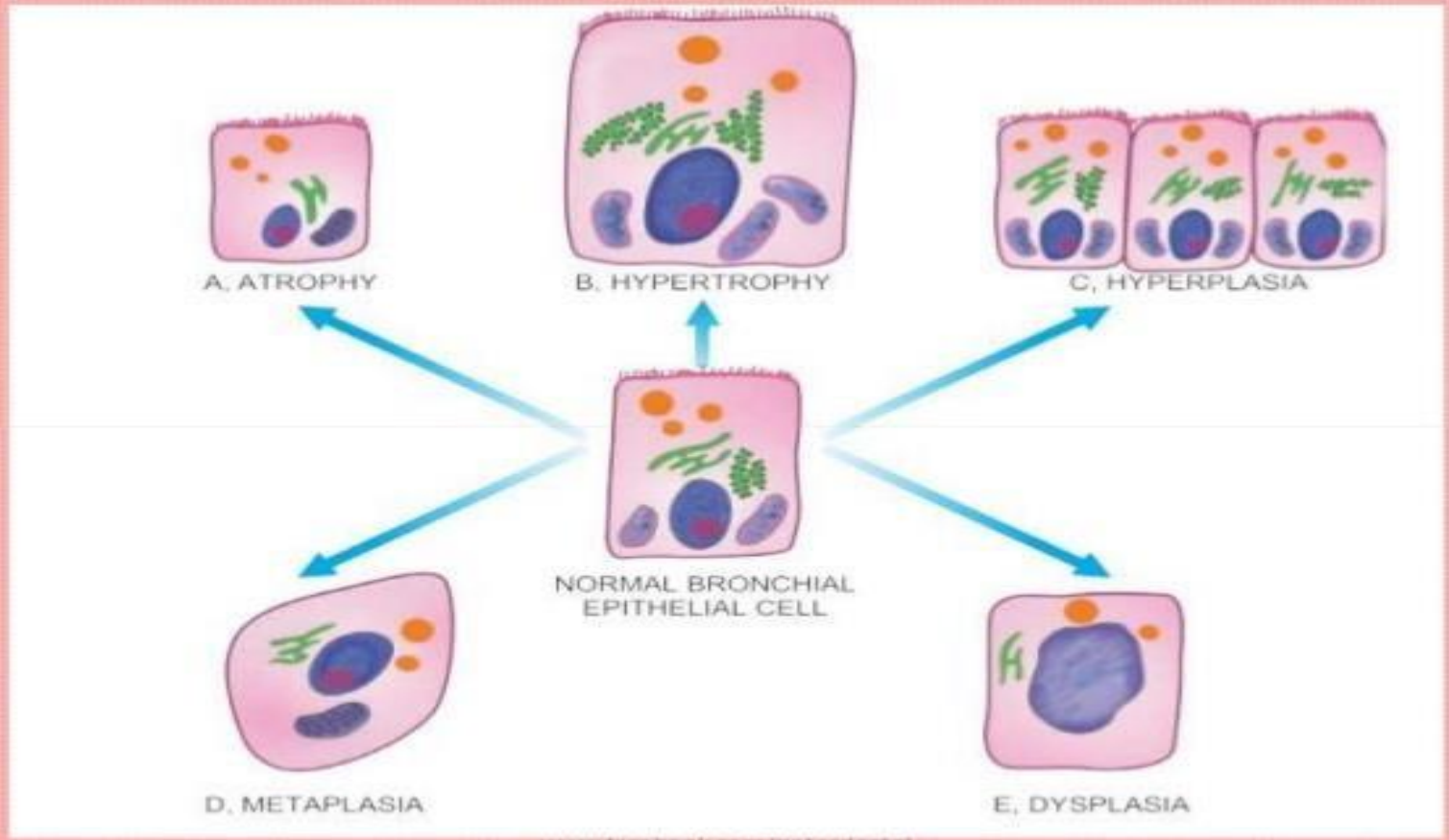
(4) the functional consequences of the morphological changes (clinical significance)

(5) result or termination.

Cell Injury and Cell Death

- Rudolph Virchow: Father of Cellular Pathology
- If the adaptive capability is exceeded, or in certain cases when adaptation is not possible, a sequence of regressive changes occurs, collectively known as cell injury


NORMAL CELL
(homeostasis)
REVERSIBLE
INJURY
Stress
Injurious
stimulus
Mild,
transient
ADAPTATION
Inability
to adapt
CELL INJURY
Severe,
progressive
IRREVERSIBLE
INJURY
NECROSIS
CELL
DEATH
APOPTOSIS


A. ATROPHY
B. HYPERTROPHY
C. HYPERPLASIA
NORMAL BRONCHIAL EPITHELIAL CELL
D. METAPLASIA
E. DYSPLASIA
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Causes of Cell Injury

- Hypoxia: Hypoxia (loss of oxygen supply) is an extremely important and common cause of cell injury and cell death. It affects cells aerobic oxidative respiration.

- Physical agents: Physical agents include mechanical trauma, extremes of temperatures (burns and deep cold), radiation, electric shock and sudden changes in atmospheric pressure.

- Chemical agents and drugs: Virtually any chemical substance or drug can cause cell injury.

- Infectious agents: bacteria, fungi, rickettsiae, chlamydiae, mycoplasma, protozoa, parasites.
- Immunological reactions: immune reactions may also cause cell injury. Examples include anaphylactic reaction to a foreign protein or a drug, and autoimmune diseases.
- Nutritional imbalances: Nutritional deficiencies such as avitaminoses and others are important causes of cell injury. Ironically, excesses of nutrition are also important causes of morbidity and mortality.
- Genetic defects: Genetic defects may cause cell injury.

Hypoxia:

- Reduced blood flow [ischemia]
- Inadequate oxygenation of the blood due to cardiorespiratory failure
- Decreased oxygen carrying capacity of the blood as in anemia and CO poisoning
- Severe blood loss

Physical and Chemical agents

Infections And Immunological causes

CELL INJURY ?

Genetics

Iatrogenic

Nutritional deficiency

General Considerations of Cell Injury

1. The morphological changes of cell injury become noticeable only after some critical biochemical system within the cell has been deranged. Thus, the first lesion to develop is biochemical (molecular) in nature. This, in turn, causes structural changes first at an electron microscopical level (ultrastructural lesion), then light microscopic lesions develop, and these, when extensive, produce gross lesions.

2. The cellular response to injurious stimuli depends on the type of injury, its duration, and its severity.

3. The results of an injurious stimulus depend on the type, status, adaptability, and genetic make-up of the injured cell. The same injury has different result depending on the cell type.

4. Although the exact biochemical site of action for many injurious agents is difficult to determine, four intracellular systems are particularly exposed to attack:

(1) Cell membrane: It is on the maintenance of the integrity of cell membrane that the ionic and osmotic homeostasis of the cell and its organelles depends,

(2) Oxidative phosphorylation and production of adenosine triphosphate (ATP)

(3)Synthesis of enzymatic and structural proteins

(4)Preservation of the integrity of genetic apparatus of the cell.

Cell Injury

- ATP DEPLETION
- Lack of oxygen or generation of oxygen-derived free radicals
- Loss of calcium homeostasis
- Defects in membrane permeability
- Mitochondrial damage

Reversible and Irreversible Cell Injury

- The sequence of events in reversible and irreversible cell injury will be discussed by two model systems:

(1) ischaemic and hypoxic injury, and

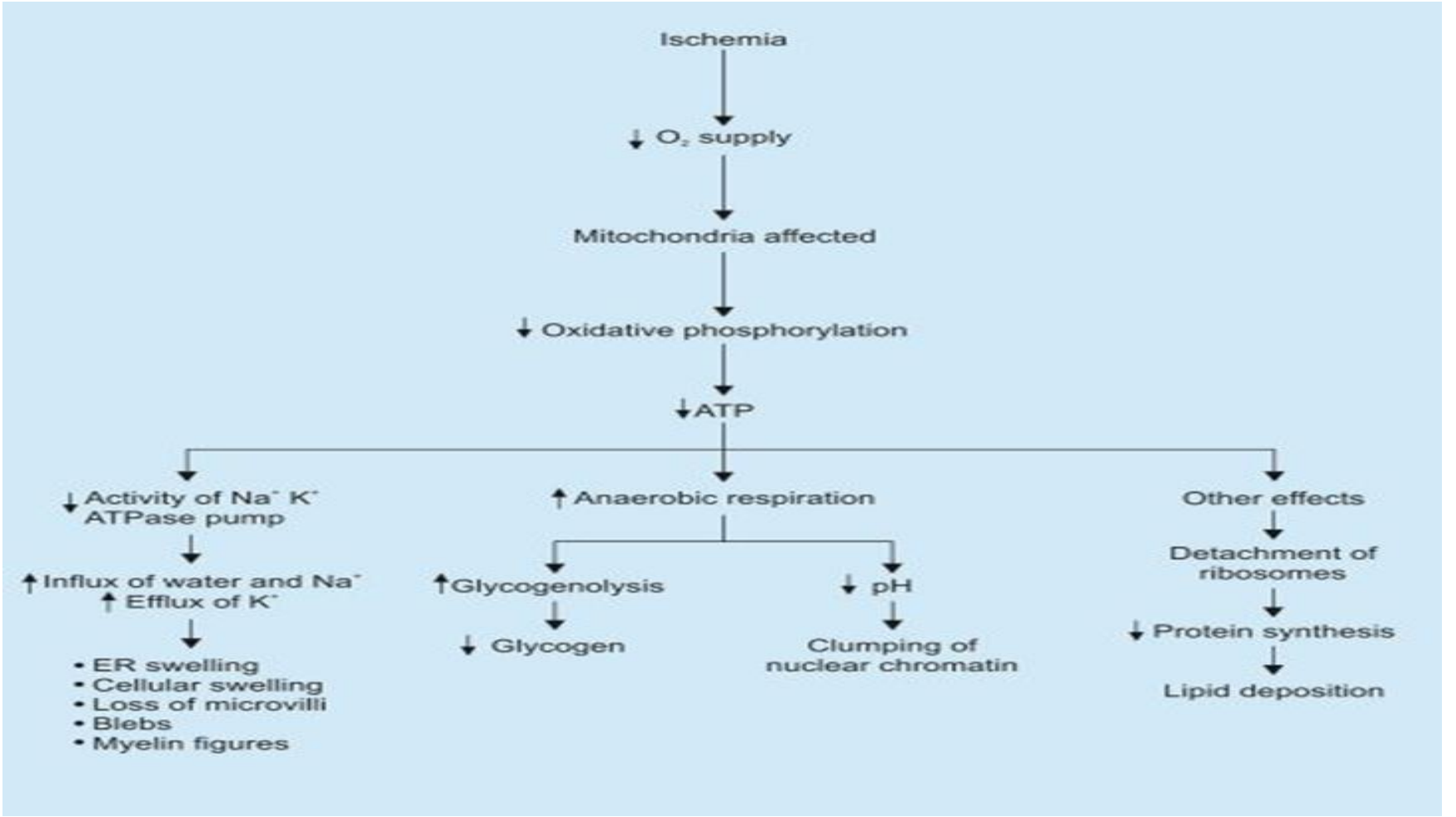
(2) free radical-induced cell injury.

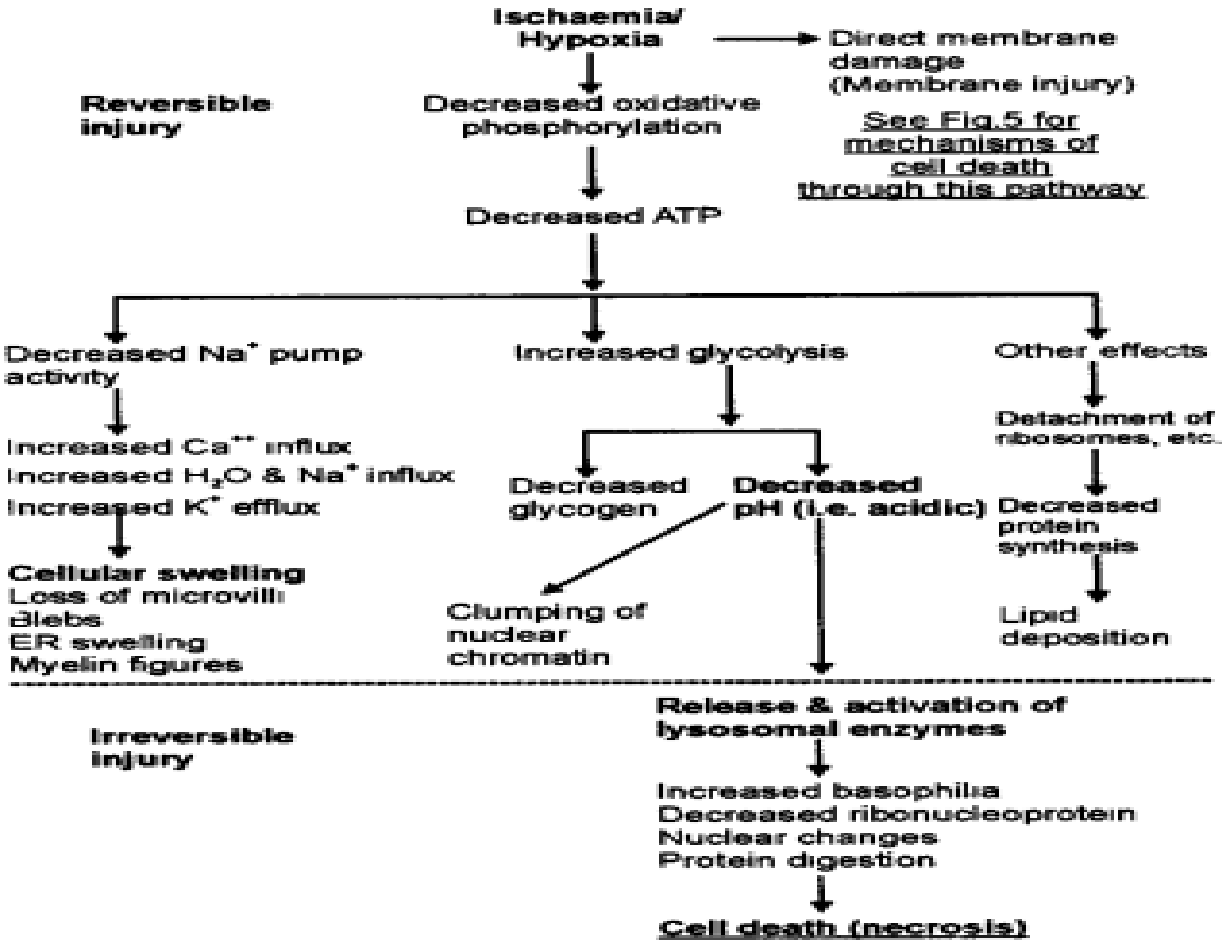
Hypoxia V/s Ischemia

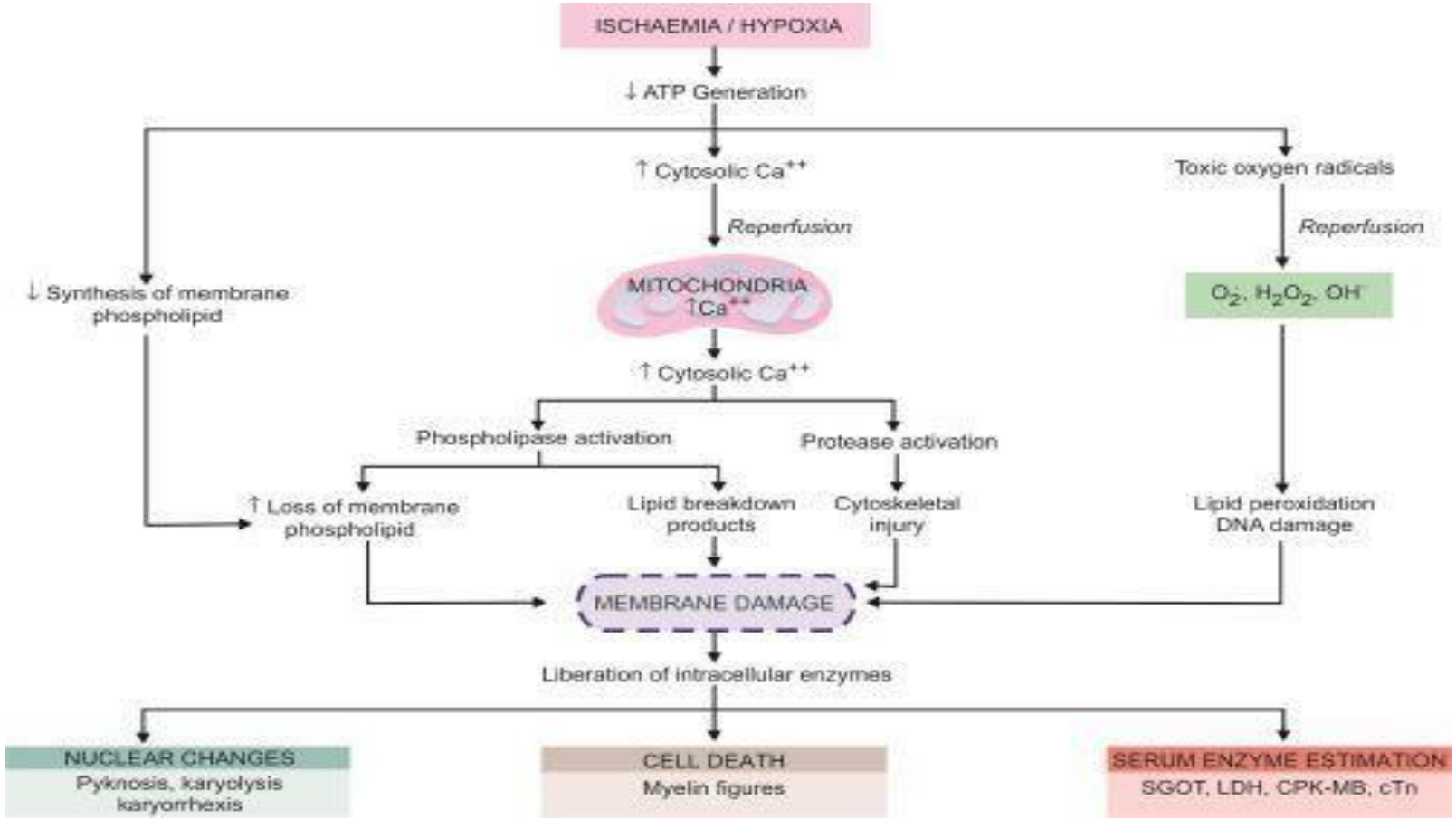
- Hypoxia - loss of oxygen supply
- Ischemia - loss of blood supply.
- In hypoxia, glycolytic energy production can continue (although less efficiently than by oxidative pathways)
- Ischemia affects the delivery of substrates for glycolysis (e.g., glucose) supplied by the flowing blood.
- Therefore, in ischaemic tissues, anaerobic energy generation will stop after glycolytic substrates are exhausted. For this reason, ischaemia injures tissues faster than hypoxia.

Ischaemic and Hypoxic Injury

- The first point of attack of hypoxia is the cell's aerobic respiration, that is, oxidative phosphorylation by mitochondria.
- As the oxygen tension within the cell decreases, there is loss of oxidative phosphorylation and decreased generation of adenosine triphosphate (ATP).
- Sodium is maintained at a higher concentration outside the cell than inside by an energy-dependent (ATP-driven) "sodium pump", that is, by Na+ and K+-adenosine triphosphatase (ATPase) enzyme.
- This pump also keeps concentration of potassium significantly higher inside the cell than outside.
- The decreased ATP concentration, following acute hypoxia, reduces activity of the plasma membrane "sodium pump“.


Ischemia
↓ O_2 supply
Mitochondria affected
↓ Oxidative phosphorylation
↓ATP
↓ Activity of Na^+ K^+ ATPase pump
↑ Influx of water and Na^+
↑ Efflux of K^+
• ER swelling
• Cellular swelling
• Loss of microvilli
• Blebs
• Myelin figures
↑ Anaerobic respiration
↑Glycogenolysis
↓ Glycogen
↓ pH
Clumping of nuclear chromatin
Other effects
Detachment of ribosomes
↓ Protein synthesis
Lipid deposition


Ischaemia/ Hypoxia
Direct membrane damage (Membrane injury)
See Fig.5 for mechanisms of cell death through this pathway
Reversible injury
Decreased oxidative phosphorylation
Decreased ATP
Decreased Na+ pump activity
Increased glycolysis
Other effects
Increased Ca++ influx
Increased H2O & Na+ influx
Increased K+ efflux
Cellular swelling
Loss of microvilli
Blebs
ER swelling
Myelin figures
Decreased glycogen
Decreased pH (i.e. acidic)
Clumping of nuclear chromatin
Detachment of ribosomes, etc.
Decreased protein synthesis
Lipid deposition
Irreversible injury
Release & activation of lysosomal enzymes
Increased basophilia
Decreased ribonucleoprotein
Nuclear changes
Protein digestion
Cell death (necrosis)


ISCHAEMIA / HYPOXIA
↓ ATP Generation
↑ Cytosolic Ca++
Reperfusion
MITOCHONDRIA
↑Ca++
↑ Cytosolic Ca++
Toxic oxygen radicals
Reperfusion
O2, H2O2, OH
↓ Synthesis of membrane phospholipid
Phospholipase activation
Protease activation
↑ Loss of membrane phospholipid
Lipid breakdown products
Cytoskeletal injury
Lipid peroxidation DNA damage
MEMBRANE DAMAGE
Liberation of intracellular enzymes
NUCLEAR CHANGES
Pyknosis, karyolysis karyorrhexis
CELL DEATH
Myelin figures
SERUM ENZYME ESTIMATION
SGOT, LDH, CPK-MB, cTn

Irreversible cell Injury

- Irreversible injury is associated morphologically with severe swelling of mitochondria, extensive damage to plasma membranes, and swelling of lysosomes.
- Extracellular calcium enters into the cell. Large, amorphous, calcium-rich densities accumulate in the mitochondrial matrix.
- After this, there is continued loss of proteins, essential coenzymes, and ribonucleic acids from the hyperpermeable plasma membrane.
- The cells may also leak metabolites, which are vital for the reconstitution of ATP, thus further depleting net intracellular high- energy phosphates.

- The falling pH (due to accumulation of lactic acid and inorganic phosphates) causes injury to the lysosomal membranes.
- Leakage of their lysosomal enzymes into the cytoplasm and activation of acid hydrolases.
- Lysosomes contain Rnases, Dnases, proteases, phosphatases, glucosidases, and cathepsins.
- Enzymatic digestion of cytoplasmic and nuclear components.
- Finally, the dead cell may become replaced by large masses composed of phospholipids called myelin figures.
- These are then either phagocytosed by other cells, or degraded further into fatty acids.
- Calcification of such fatty acid residues may occur with the formation of calcium soaps.

Mechanisms of Irreversible Injury

- Two phenomena consistently characterize irreversibility.

i. The first is the inability to reverse mitochondrial dysfunction (lack of oxidative phosphorylation and ATP generation) even after correction of the original injury (e.g., restoration of blood flow), and

ii. The second is the development of profound disturbances in membrane function.

Cell Membrane Damage

- It is now clear that cell membrane damage is a central factor in the pathogenesis of irreversible cell injury.
- There are several biochemical mechanisms that cause membrane damage:

1. Progressive loss of membrane phospholipids

- Oxygen deprivation (hypoxia) releases sequestered calcium from mitochondria and endoplasmic reticulum, thus raising cytosolic calcium.
- The increased cytosolic calcium concentration induced by ischaemia, following acute hypoxic injury, activates endogenous enzymes.

2. Mitochondrial dysfunction: loss of membrane integrity causes further influx of calcium from the extracellular space, where it is present in high concentration, into the cells. Calcium is taken up greedily by mitochondria.

- Here it activates mitochondrial phospholipases and results in accumulation of free fatty acids.
- Phospholipases and free fatty acids together cause changes in the permeability of the inner mitochondrial membrane.

3. Cytoskeletal abnormalities: Activation of proteases by increased intracellular calcium may cause damage to cytoskeleton. In the presence of cell swelling, this damage results in detachment of the cell membrane from the cytoskeleton, exposing it to stretching and rupture.
4. Toxic oxygen radicals: Partially reduced oxygen free radicals are highly toxic molecules that cause injury to cell membranes and other cellular constituents.

Cellular swelling

- Cellular swelling (previously known as cloudy swelling, parenchymatous, or albuminous degeneration)
- disturbance of cellular metabolism in which cells swell and cytoplasm of the cell becomes more granular than normal.
- Cellular swelling is the most common disturbance of cell metabolism and is the first reaction of a cell to injury.
- It is caused by the mildest irritants and results from the shift of extracellular water into the cell.

- Aetiology: Since cellular swelling is caused by the mildest irritants, it can be produced by any factor that interferes with cellular metabolism. The causes include:

(1) bacterial toxins (the most common cause). Cellular swelling occurs in infectious diseases.

(2) a rise in body temperature (fever)

(3) metabolic diseases (diabetes and acetonaemia)

(4) organic or inorganic poisons (lead, arsenic, chloroform, and alcohol)

(5) circulatory disturbances (anaemia, infarction, passive hyperaemia, and haemorrhage) when insufficient oxygen is brought to the cell.

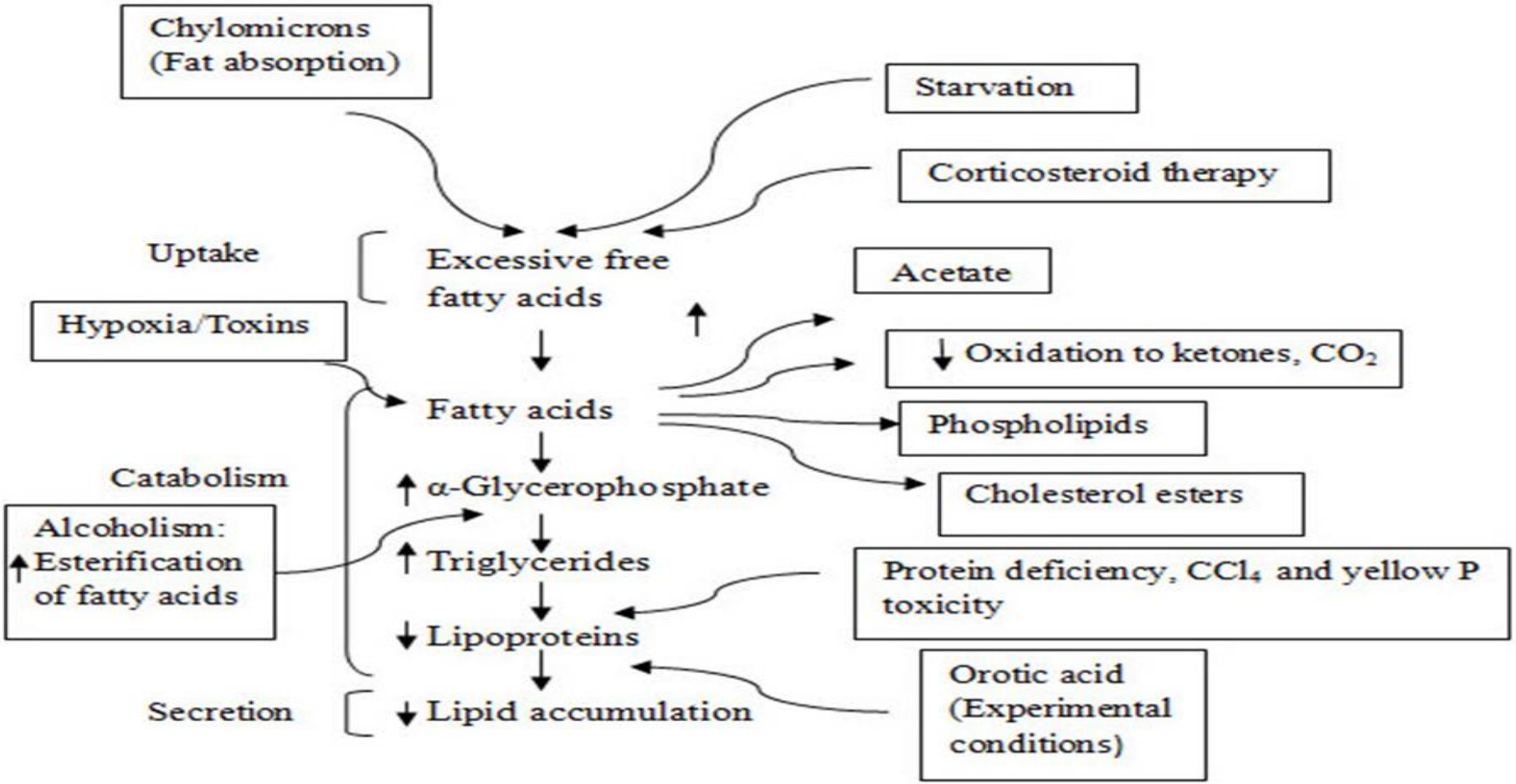
- Macroscopically, the affected organ (liver, kidney) is slightly enlarged, the edges are slightly rounded, and there is an increase in weight.
- Microscopically, cellular swelling is best observed in the liver, the convoluted tubules of the kidney, or in skeletal and cardiac muscle.
- Due to accumulation of fluid within the cells, the cells become swollen, and their edges become rounded. The cytoplasm stains slightly more intense with eosin. The internal structures of the cell are slightly hazy. The cytoplasm of the cell is more granular than normal.

Fatty Change/Hepatic lipidosis

It is the accumulation of triglycerides or true fats and cholesterol in the cytoplasm of parenchymatous cells. Lipidosis is more common than other conditions.

- Mobilization of free fatty acids from the gut (Chylomicrons) or adipose tissue
- Mitochondrial injury leading to decreases in β-oxidation of fatty acids to ketones etc. (Hypoxia, toxins)
- Decreased apo lipoprotein synthesis e.g. CCl_4 poisoning and aflatoxicosis
- Failure to form lipoproteins
- Failure to release lipoproteins from hepatocytes

MECHANISM


Chylomicrons
(Fat absorption)
Starvation
Corticosteroid therapy
Uptake
Excessive free
fatty acids
Acetate
Hypoxia/Toxins
↓ Oxidation to ketones, CO_2
Fatty acids
Phospholipids
Catabolism
α-Glycerophosphate
Cholesterol esters
Alcoholism:
↑ Esterification
of fatty acids
↑ Triglycerides
Protein deficiency, CCl_4 and yellow P
toxicity
↓ Lipoproteins
Orotic acid
(Experimental
conditions)
Secretion
↓ Lipid accumulation

Grossly :

- Enlarged, pale to yellow, soft and friable liver is found in moderate to higher grade fatty changes.

- Enlarged with rounded borders.

-Upon incision, fat droplets are seen on the blades of knife.

-Tissue may float in the fixatives.

- **Microscopically,** hepatocytes show vacuolations which may be small, clear to variable sized and may also form a single large vacuole, pushing the nucleus to a side.
- During the processing of fat tissue with xylol clearing, the fat will be dissolved by the xylol and gives vacuolated appearance in the Haematoxylin and eosin stained sections.
- Special stans for fats are sudan III, sudan black, scarlech red and Oil Red O.
- Oil Red O stains fat red and while it is PAS negative, sudan III and sudan black imparts black colour and scarlech red imparts red colour

Hydropic degeneration

- A variant of cell swelling with excessive accumulation of fluid leading to even bursting of cells. It is caused by more severe irritant.
- Grossly, blisters are seen onskin. Fluid escapes on incision and blister collapses consequent.
- Microscopically, cells are swollen. Cytoplasm shows vacuoles which represent distended and sequestrated segments of endoplasmic reticulum. Cells may enlarge with coalition of fluid and may burst showing blisters and vesicles. Prickle cell layer is affected. Eosin stains pink depending on protein content. Using negative method of staining i.e. staining of fat or glycogen, vacuoles with water are identified.

Mucinous or mucous degeneration

- **Mucinous or mucous degeneration:** excessive accumulation of mucin in degenerating epithelium cell. Mucin is glassy, viscid, stringy, slimy glycoprotein normally produced by epithelium cell lining mucous membranes.
- Mucus is mucin mixed with water.
- It is caused by mild irritant, Mechanical or chemical injury (Disinfectant or soap), Thermal injury by heat or cold, Infectious diseases – Canine distemper, bovine viral diarrhoea
- **Mucoid or myxomatous degeneration**: Mucoid is a glycoprotein similar to mucin in connective tissue found in foetus but not in adult tissue.

- Grossly, mucous covering is seen as clear transparent material on mucous membrane which is stringy and slimy inconsistency. e.g. common cold. Mucosa is hyperaemic.
- Microscopically, cytoplasm shows small droplets of mucous which may coalesce forming large droplets displacing nucleus to side and compressing the nuclei.
- As the mucin accumulation continues the cell ruptures and desquamated. Haematoxylin stains the mucin blue. Mucicarmine and PAS stains the mucin red.

Hyaline degeneration (Hyaline change)

- hyaline – glassy
- Affected tissue appears homogenous glassy and pink in H & E staining. It may be found in different conditions.
- Keratohyaline: normally found in stratum corneum.
- Cellular hyaline
- Connective tissue hyaline

- **Cellular hyaline:** The dead cells are kneaded together forming homogenous mass resembling sand; since it stains with iodine it is called corpora amylacea (Starch-like). They are commonly seen in prostate.
- They are observed in lungs in pneumonia, pulmonary infarction, mammary glands of cows which are dried off quickly, in brain as brain sand, in islets of Langerhans in diabetes and in renal nephritis as the renal tubular epithelium gets desquamated and forms hyaline cast with albumin.
- **Connective tissue hyaline**: This is found in old scars, degenerating stroma of tumours, lymph nodes in chronic inflammation and arteriosclerosis. This is permanent change persisting for life.

AMYLOIDOSIS

- immunological disorder in which homogeneous, translucent amyloid substance is deposited between capillary endothelium and adjacent cells.
- The main event occurring in amyloidosis is the deposition of amyloid fibrils due to abnormality of protein processing.
- The sources of amyloid may be acute phase proteins, immunoglobulins and endocrine secretes.
- Amyloid (Amylon - STARCH) means starch-like. Amyloid is a pathologic glycoprotein deposited in the extracellular spaces and forms fibrils on polymerization.

Primary amyloidosis

- It results from antigen-antibody reaction and deposition of its precipitates.
- The condition is not associated with any diseases e.g. repeated exposure to antigens as in antisera and antitoxin production in horses and B cell dyscrasia (plasmacytoma) in humans in which immunoglobin light chain deposition occurs.
- The soluble immunoglobulin becomes insoluble with defective degradation.

Secondary amyloidosis

- The condition may be associated with chronic diseases like tuberculosis, septic conditions and neoplasia.
- This occurs in two phases.
- In the initial preamyloid phase, there is accumulation of reticular cells and macrophages in the spleen and other lymphoid tissue with consequent rise in plasma serum amyloid associated protein (SAA). and globulins.
- During the second phase, known as amyloid phase, PAS staining cells, amyloid deposition and fall in the SAAs level are found.

- **Grossly**, the amyloid deposition may be diffuse or focal.
- The amyloid is deposited around the central artery of splenic follicles and it forms sheet like deposits which is referred as **bacon spleen** and it may protrude resembling like a grain of sago known as **sago spleen**.
- The organ is waxy in consistency and the cut surface is grayish.
- Splenic corpuscles become large, gray and translucent.
- Liver is enlarged with rounded edges, doughy in consistency, pits on pressure and ruptures easily because of its friable nature.
- Renal amyloidosis - occurs in the glomeruli, the organ is swollen, mottled, pale and yellow to orange in colour
- Amyloidosis of the pancreas occurs in islets of Langerhans. The amyloid is deposited between the capillaries and the islet cells. The destruction of the islet cells causes diabetes.

Effects of amyloidosis

- Hypovolumic or haemorrhagic shock may occur following hepatic rupture. Fatal hepatic rupture is usually observed in the horse.
- Hepatocellular atrophy occurs from pressure and nutritional deficiency.
- In renal amyloidosis, interfere with glomerular filtration.
- The enlargement and ischaemic anoxia leads to tubular epithelial degeneration and necrosis, marked proteinuria, nephrotic syndrome, uremia and death
- In pancreatic amyloidosis, leads to islet cell destruction and development of Diabetes mellitus.
- Blindness may be encountered in horses in with conjuctival amyloid deposition.

Disturbances of Pigment metabolism

- Abnormal deposition of colored substances of diverse origin, in the cells or tissues is called pathological pigmentation.
- The pigments may be formed within the body, in which they are called endogenous of the pigments come from outside the body, such as minerals, medicines, plants etc., They are called exogenous.

EXOGENOUSPIGMENTS

1. **Pneumoconiosis** – Dusts of various kinds: coal dust, iron dust, stone dust, asbestos dust – may be inhaled by animals. These dusts, besides importing a color, cause fibrosis of the lungs.
2. **Anthracosis** –accumulation of carbon particles in the lungs. Usually it is coal dust that accumulates.
3. **Silicosis** – In this condition stone dust is inhaled. It is more common in man than animals. Person working in iron, gold and diamond mines, stone quarries, glazing and enamel industries are frequently affected.
4. **Plumbism** – Plumbism is pigmentation of tissue resulting from the presence of both lead and hydrogen-sulphide. It occurs when lead is ingested in the form of paint or when water or food containing lead is consumed. The lead in the tissue combines with hydrogen-sulphide to form lead sulphide which is a black pigment.

- **Argyrosis** – This is condition that is notice in long continued therapy with silver salts.
- **Byssinosis**: by inhalation of cotton dust.
- Tetracycline – Gets deposited in the bones if it is used for prolonged treatment. The drug gives yellowish discolorations to the bones which gives yellowish greenish autoflourescence under fluorescence microscopy of sections of bones.

Endogenous Pigments

- Melanin – Melanin is a brown-black pigment formed from amino-acid Tyrosine. Melanin protects the skin against harmful rays in sunlight.
- Micro - Melanin appears as very minutes, uniformly regular dirty brown, spherical granules.
- Pathological amount of melanin is called melanosis and is frequently observed in association with:-

- The tumour melanoma : there is a high incidence of the these tumours in grey horses and heavily pigmented breeds of dogs.
- Addison disease:- When there is bilateral destruction of the adrenals due to tuberculosis, atrophy or neoplasm
- Melanosis coli - Is a condition in which rectum and color contain melanin in their mucosa, giving them brownish color.
- Acanthosis nigrans – In dog suffering from a sertoli-cell tumor in which there is estrogen production, raised, rough black patches of skin are found in the axilla, groin, under the belly and ventral thoracic region.

- Condition with deficient production of melanin:-

  1)Albinism- Congenital, complete absence of melanin pigment.

  2)Leucoderma- Local loss of pigment . Such area become inflammed when exposed to sunlight.

  3)Vitilego- Partial or complete loss of melanocytes in the epidermis.
- **Lipofuscin:-** Lipofuscin is an insoluble brown pigment. It is also known as lipochrome, wear and tear or aging pigment.
- yellowish brown, finely granular intracytoplasmic pigment. Its presence is a sign of free radical injury and lipid peroxidation. It is seen in cells undergoing slow, regressive changes, and is prominent in the liver and heart of ageing patients.

- Hemoglobin :- Itself may be visible if released from RBCs in large quantities. It will appear microscopically as a distinctive reddish orange color in renal tubules if it crosses the glomerulus- the kidney is usually almost black in color and is indicative of an acute hemolytic crisis. Chromic copper poisoning in sheep or cattle is a classic example.
- Hemosiderin :- This pigment is brown, contains iron and is usually present in macrophages of the reticulo–endothelial system.
- It is a common finding and if quite prominent as a lesion, the term hemosiderosis is used.
- Hematin: - results from the action of acid or alkali on hemoglobin.

- Porphyra:- This refers to a group of uncommon inborn or acquired disturbances of porphyrin in metabolism.
- Porphyrins are pigments normally present in hemoglobin, myoglobin and cytochromes. The porphyrins collect in teeth and bones and result in pink-tooth of cattle.
- Sometimes porphyrins accumulate and react with sunlight resulting in edema and inflammation on non-pigmented areas of the body, exposed to light.

Hematodin :- In places where hemorrhages occur, hematodin may be liberated and it is this pigment that the color of a bruise or contusion is due. Hematodin is first converted into bilirubin and so the bruise is green. Subsequently the color changes to yellow when bilirubin is converted to bilirubin. It is extra-cellular. (outside the cells)

- Bilirubin:- Is derived from hemoglobin but contains no iron. It is the major pigment of blue, when bilirubin is evented in the blood and deposited in tissue, it results in the common clinical disorder known as jaundice.

NECROSIS

- Necrosis is death of cells and tissues in the living animal.
- **Focal/ Multifocal necrosis**- terms used for one or more, small, clearly defined areas of necrosis.
- **Diffuse necrosis-** term used when necrosis affects a large area or the entire tissue or organ.
- Grossly, necrotic tissue is pale, grayish white, dull and depressed surrounded by hyperaemic zone.
- Microscopically, nuclear changes are characteristic. These are
- Eosinophilia: The cytoplasm stains darker red in colour.
- Swelling and vacuolation: The cells are swollen and contain different types of vacuoles.
- Pyknosis: Shrinkage or condensation of nucleus
- Karyorrhexis: Fragmentation of nucleus.
- Karyolysis: Dissolution or disappearance of nucleus

Necrosis V/s Autolysis

Autolysis: Autolysis is death of cells and tissues after the death of the animal (somatic death) and it should be distinguished from necrosis.

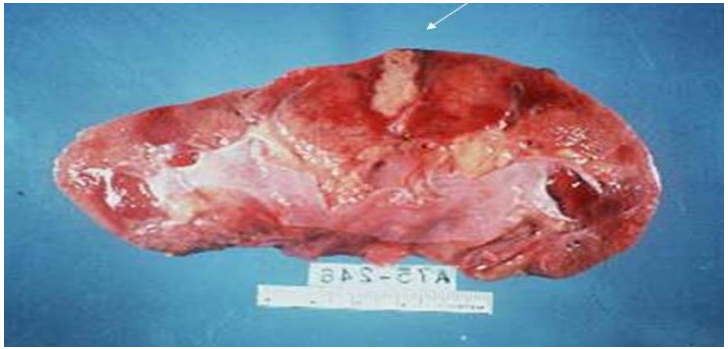
1. The enzymatic digestion of cells by enzymes present within them. The cells most susceptible to autolysis tend to be dying or dead cells.
2. No sharp line of demarcation between affected and healthy tissue.
3. Circulatory changes like congestion and haemorrhage are not present.

Types of necrosis

- Different types of necrosis are recognized according to the causes, pathogenesis and the tissue involved.
- These include
  - Coagulative
  - Liquefactive
  - Caseous
  - fat necrosis.

Coagulative necrosis:

- Most common type of necrosis.
- Architectural outlines persist but structural/ cellular details are lost.
- Type of tissue can be recognized.
- Denaturation (coagulation) of structural and enzymic proteins blocks proteolysis.
- Kidney



Causes of Coagulative Necrosis

- ✓ Ischemia due to thrombosis/ embolism as in infarcts.
- ✓ Bacterial toxins e.g. Fusobacterium necrophorum in livers in cattle.
- ✓ Muscular dystrophy due to deficiency of selenium and Vit.-E in cattle and sheep.
- ✓ Necrosis of renal epithelium due to poisoning from mercuric salts.

- **Gross appearance:**
  - Necrotic area is firm, opaque with cooked meat appearance.
  - It is sharply demarcated from the healthy areas.

- **Microscopic appearance:** Architectural outlines are present; cellular details are lacking. The cellular shape is preserved and nuclear details are lost (Nuclei show pyknosis, karyorrhexis and karyolysis).

- **Result:** Dead tissues remain in the body for a long period, ultimately removed by macrophages.
- This type of necrosis is characteristically found in parenchymatous organs like kidney, liver and muscle except the brain

Liquefactive necrosis

- There is digestion and liquefaction of necrotic tissue. Necrotic tissue is liquid in consistency.
- It is especially seen in the central nervous system (malacia) and any infection with pyogenic bacteria leading to pus formation (Abscess). The former is due to severe hypoxic or toxic injury with focal dissolution of the neuropil. The later is due to autolysis or heterolysis from enzymes of neutrophils leading to collection of pus containing necrotic tissue, microorganisms and dead neutrophils (Suppuration)
- **Causes:**
  1. Pyogenic bacterial infections attract neutrophils. Bacterial and leukocytic enzymes liquefy dead cells and tissues.
  2. Some chemicals like turpentine oil also attract neutrophils and cause pus formation and results into liquefaction of the tissue.
  3. The necrosis in the nervous tissue is mostly liquefactive due to high content of lipids and water.

Gross Appearance of Liquefactive Necrosis

The necrotic tissue is liquefied and filled with semisolid creamy liquid called pus.

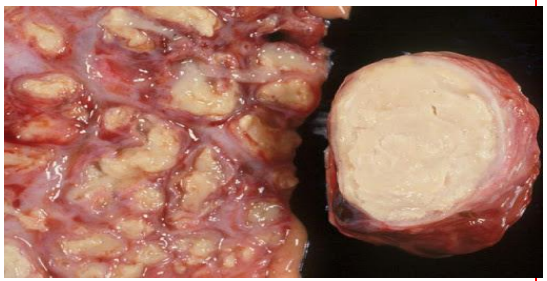
1. **Pus:** It is a thick, white or yellow, creamy liquid consisting of exudate of leukocytes, tissue debris and microorganisms. Proteolytic enzymes released from neutrophils cause liquefaction of dead cells.
2. **Abscess**: It is a localized collection of pus, surrounded by fibrous capsule.
3. **Empyema**: It is accumulation of pus in a body cavity.

Microscopic appearance of Liquefactive Necrosis

- No architectural or cellular details are visible in the area of necrosis
- The necrotic area usually appears as a cavity containing a mass of necrotic neutrophils, bacteria and tissue debris.
- The entire necrotic mass is surrounded by a fibrous connective tissue capsule..

Caseous necrosis

- Dead tissue is converted into a homogenous, granular mass resembling cottage cheese. The architectural and cellular details are lost. This is more chronic type of lesion often associated with poorly degraded lipid materials of bacterial origin.
- **Cause:**
  - Associated with lesions of Mycobacterium tuberculosis and Arcanobacterium ovis, the cause of caseous lymphadenitis.



- **Gross appearance**:
  - The area of necrosis is amorphous, granular, friable, white-gray resembling cottage cheese.
  - The caseous mass is enclosed within a connective tissue capsule.
- **Microscopic appearance**:
  - No architectural or cellular details are seen. Calcification commonly occurs in the necrotic areas.
  - The necrotic tissue is amorphous, granular mass enclosed inside a zone of granulomatous inflammation, containing macrophages.

Fat necrosis

- It is death of adipose tissue in a living animal.
- **Enzymatic fat necrosis:** It is commonly found in steatitis (Inflammation of fat) and other inflammatory lesions affecting adipose tissue, e.g. Pancreatic fat
- Pathogenesis - In acute pancreatic necrosis and pancreatitis, the lipase released from acinar cells gets activated and saponification occurs by digestion of triglycerides into glycerol and fatty acids. Glycerol being water soluble, is absorbed. The released fatty acids when combine with calcium results in the presence of chalky white flakes.
- Grossly, hard, white, opaque masses resembling that of soap flakes are seen. The fat loses yellow translucent nature.
- Microscopically, necrotic adipocytes may show eosinophilic shadow outlines, become basophilic due to dystrophic calcification and surrounded by inflammatory reactions along the area due to acute to chronic injury. Fat solvents do not remove necrotic fat.

- Traumatic fat necrosis It results from mechanical injury to adipose tissue.
- Causes : working, biting, parturition (perivaginal fat in cattle, subcutaneous and intramuscular fat in recumbent cattle)
- Grossly, firm, opaque, chalky masses found in the area with acute to chronic inflammatory reaction. Example: Surgical injury to subcutaneous fat, injury to vagina during dystocia and abdominal fat necrosis in cattle Mesenteric, omental and retroperitoneal fat show necrosis containing large masses. Stenosis of intestine may occur in extreme cases.

- Nutritional fat necrosis: This is the result of necrotic alteration in fat associated with extreme emaciation. e.g. Tuberculosis and Johne’s disease in cattle and sheep.
- Grossly, necrotic fat is opaque, foamy and chalky white and may be calcified.
- Microscopically, necrotic adipocytes are pale pink (eosinophilic) and show numerous clubs (fatty acids) and crystals. The derivatives of fat, glycerol dissolves in body fluids, and fatty acid crystals dissolve in fat solvents leaving clefts. Calcified area is basophilic, surrounded by chronic inflammatory cells.

APOPTOSIS

- Programmed cell death in which there is death of individual cells without inciting inflmmatory processes.
- A pathway of cell death induced by a tightly regulated suicidal programme

Often called Programmed cell death which helps in:

- Deletion of un-needed cells during embryogenesis
- Normal involution
- Regression of hyperplasia /tumour
- Removal of viruses
- Immunity

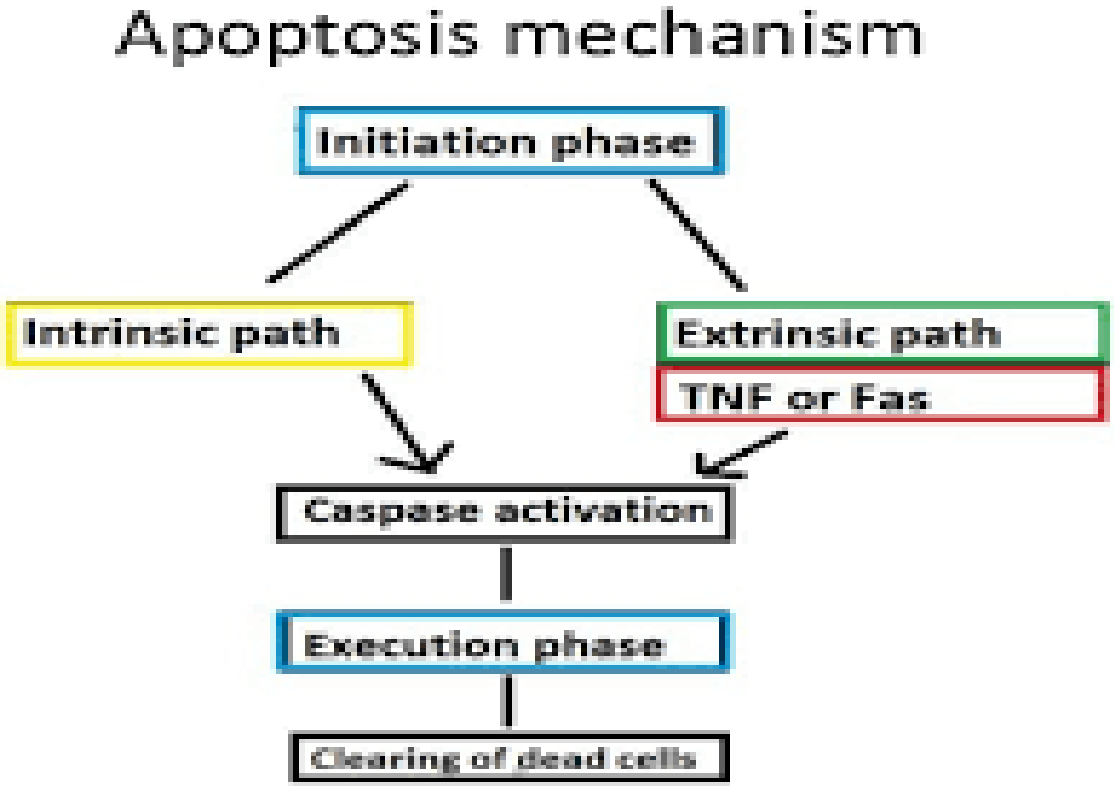
Caspases

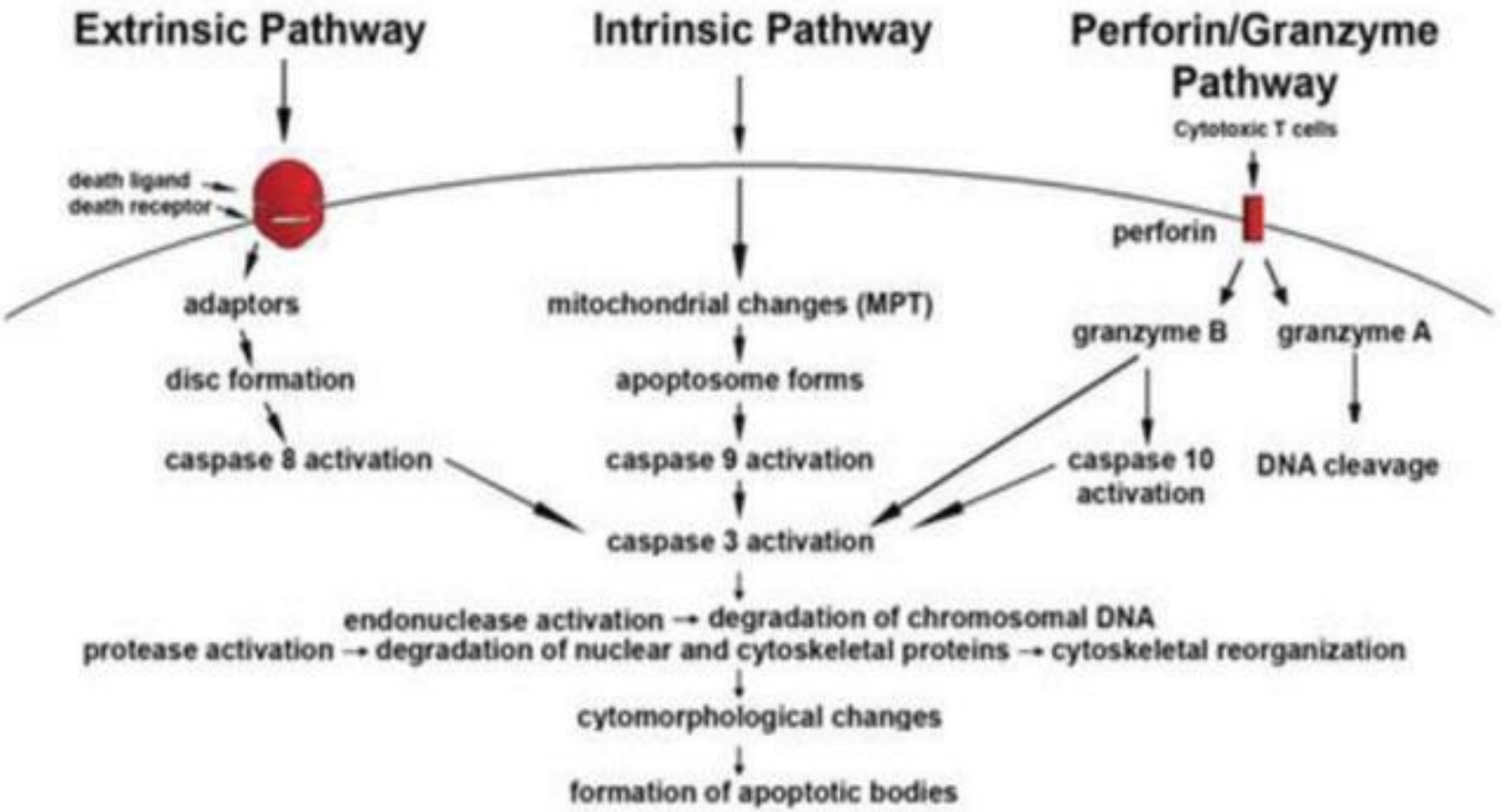
KEY PLAYER

- Cysteine dependent
- aspartate directed
- Proteases

- Mechanism of Apoptosis: There are two processes:
- Initiation phase mediated by caspases:
  - Extrinsic receptor initiated pathway
  - Intrinsic mitochondrial pathway
- Execution phase in which enzymatic degradation leads to cell death

Mechanism


Apoptosis mechanism
Initiation phase
Intrinsic path
Extrinsic path
TNF or Fas
Caspase activation
Execution phase
Clearing of dead cells


Extrinsic Pathway
Intrinsic Pathway
Perforin/Granzyme Pathway
Cytotoxic T cells
death ligand
death receptor
perforin
adaptors
mitochondrial changes (MPT)
granzyme B
granzyme A
disc formation
apoptosome forms
caspase 8 activation
caspase 9 activation
caspase 10 activation
DNA cleavage
caspase 3 activation
endonuclease activation → degradation of chromosomal DNA
protease activation → degradation of nuclear and cytoskeletal proteins → cytoskeletal reorganization
cytomorphological changes
formation of apoptotic bodies

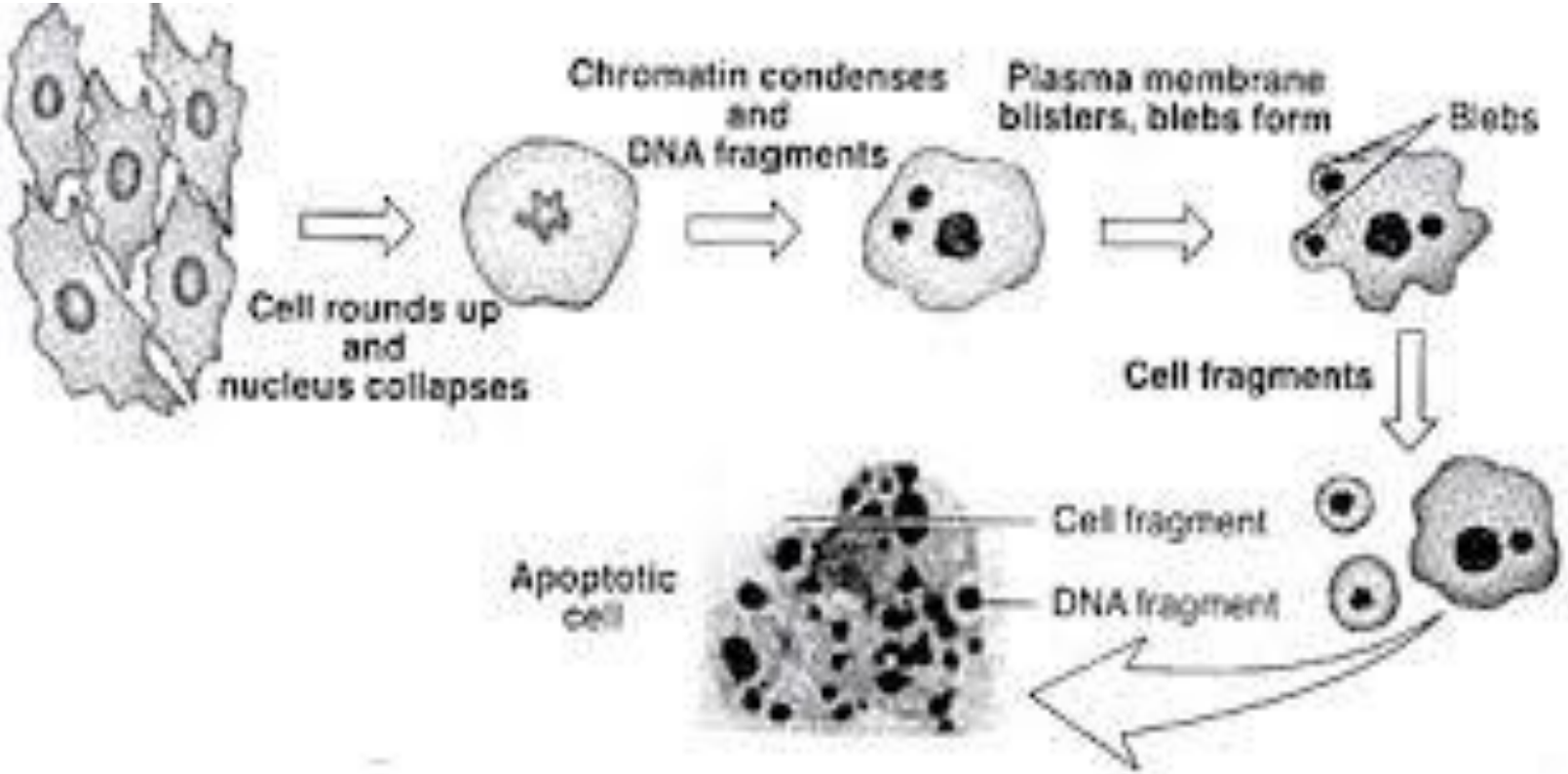
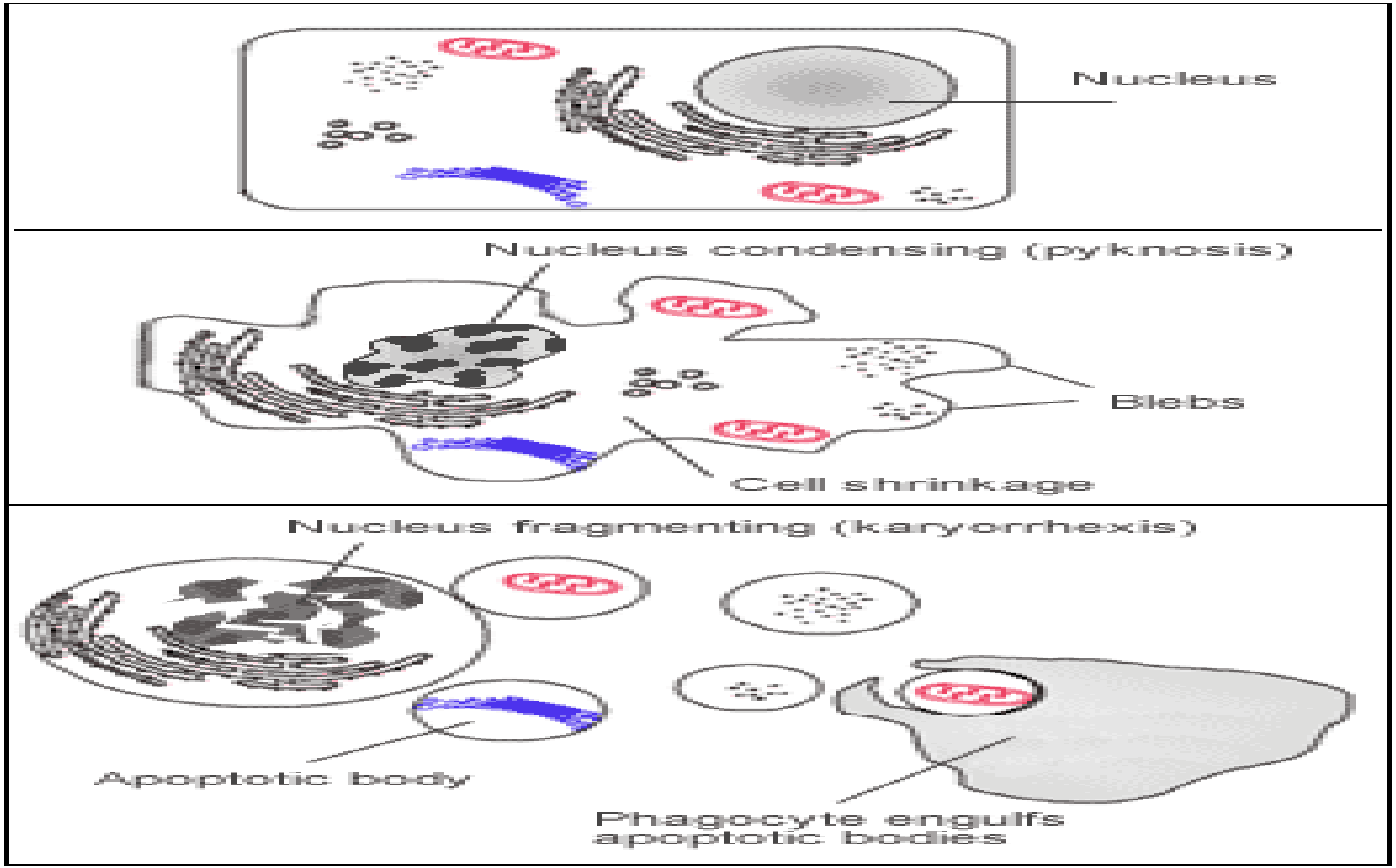


Fig. 5.33A: Sequence of cellular events during apoptosis


Nucleus
Nucleus condensing (pyknosis)
Blebs
Cell shrinkage
Nucleus fragmenting (karyorrhexis)
Apoptotic body
Phagocyte engulfs
apoptotic bodies

Microscopic changes

- Shrinkage of individual cells: cells-size smaller, cytoplasm is dense and organelles are tightly packed.
- Condensation of chromatins: Most characteristic in apoptosis. Aggregation of chromatins under nuclear membrane with variable shape and size (Semilunar shape)
- Cytoplasmic fragmentation
- Cytoplasmic buds containing fragments of nucleus: Cytoplasm shows excessive surface budding and formation of membrane bound fragments (Apoptotic bodies) containing cytoplasm and tightly packed organelles with or without nuclear fragments. Nucleus itself may break up into two or more fragments
- Presence of apoptotic bodies in the adjacent cells and phagocytes
- Inflammation is absent

PM CHANGES AND GANGRENE

- Somatic death: Somatic death is the death of the body as a whole. When respiration and cardiac action have stopped, the animal is said to have undergone somatic death
- Putrefaction: Decomposition of tissues brought about by the protein splitting anaerobic saprophytic organisms, results in the formation of gas and variety of foul smelling substances- ammonia, hydrogen sulphide, indol, skatol and putrescent amines-like “putriscience and cadaverine”.
- The tissue turns black or dark-green as a result of formation of iron sulphide from break down haemoglobin. The common putrefactive organisms are Clostridium spp. normally present in faeces

PM changes

1. Algor mortis
2. Rigor mortis
3. Livor mortis- hypostatic congestion
4. PM clotting of blood
5. Imbibition of hemoglobin
6. Imbibition of bile
7. PM desquamation
8. PM softening
9. PM discoloration
10. PM distention
11. PM displacement
12. PM rupture of organ and tissue

- Algor mortis is cooling of the body. It commences at or before the stoppage of blood flow.
- Rigor mortis is contraction of muscles after death. Usually, rigor mortis appears in 1 to 8 hrs after death and may disappear from 20-30 hours.
- Rigor mortis develops first in those muscles that are very active. e.g heart, palpebral muscles, muscles of the head and neck. Gradually other muscles of the forelimbs, the trunk and the hind limbs, are affected in that order.

- Livor mortis: Hypostatic congestion is, due to gravity, accumulation of blood in vessels of organs that are found on the lower side of the recumbent animal.
- PM clot is the coagulation of blood in the vessels after death.
- Imbibition of hemoglobin: PM staining is pinkish discolouration of endothelium of larger vessels due to haemoglobin (liberated from lysed erythrocytes) after death.
- PM imbibition of bile is the yellow pigmentation of the tissue occurring in the vicinity of gall bladder.

- PM softening is softening of tissues, after death, by the action of autolytic enzymes of the cells and the proteolytic ferments of the saprophytes and infecting bacteria.
- PM discoloration: Pseudomelanosis coli is staining (blackish / greenish discolouration) of intestines due to formation of iron sulphide (H2s + Fe from Hb = Iron sulphide) after death of animals.
- PM bloat / PM emphysema is accumulation of gas in the rumen and intestines due to fermentation of food after death.
- PM displacement of organs: This may occur following handling of carcass by rolling etc.
- PM rupture of organ and tissue: This may be attributed to softening and handling but devoid of any inflammatory reaction

Gangrene

- Gangrene is a necrotic area invaded by saprophytic organisms leading to putrefaction.
- There are three types of gangrene
- Dry gangrene
- Moist gangrene
- Gas gangrene

Dry Gangrene

- Dry gangrene: Dry gangrene represents an area of coagulation necrosis resulting from infarction followed by mummification. The extremities of the body like tail, ears, legs and udder are affected
- Affected part is dry (dehydration due to exposure to environment) and brown to black (due to formation of iron sulphide: iron from haemoglobin degradation, sulphide from putrefaction), proliferation of bacteria due to unfavourable environment, temperature and moisture.
- However, at the junction of living and dead tissue, there is a line of demarcation due to active inflammatory reaction
- Causes
  - Toxins (phytotoxins and ergotoxins
  - Fescue poisoning
  - Cold (Frost bite)

Moist gangrene

- Causes: Intestine displacements, Intussusceptions, volvulus, incarceration
- Gross pathology: The affected parts are soft, moist and reddish brown to black, foul smelling or putrid odour due to hydrogen sulphide, ammonia and mercaptanes. The environment is conducive for rapid growth of bacteria. There is no line of demarcation between live and dead tissue.
- Histopathology : Initial coagulation necrosis with a few bacterial multiplications. Later liquified due to rapid proliferation of bacteria and infiltrating neutrophils.

Gas gangrene

- Anaerobic bacterial proliferation producing toxin and damaging the tissues. Examples: Clostridium perfringens, Clostridium septicum introduced by penetrating wounds.
- The clostridia proliferate in necrotic tissue under anaerobic environment and produce toxins which cause tissue damage. The Clostridia chauvoei spreads haematogenously from the intestine and lodges in muscle which requires some injury and necrosis for the spores to germinate and bacteria to proliferate.
- Gross pathology: Affected parts are dark red to black, contain gas bubbles, serosanguineous exudates and foul smelling.
- Histopathology: Coagulative necrosis of muscle, bacteria, serosanguineous exudates and gas bubbles are see

Shock

Failure of the circulatory system to adequately perfuse vital organs.

- **Cardiogenic shock**
- **Hypovolemic shock**
- **Septic/Endotoxic shock**
- **Neurogenic shock**
- **Anaphylactic shock**

CARDIOGENIC SHOCK

- Results from cardiac pump failure

Cause:

- **Myocarditis**- Septicaemia or viral infection
- **Myocardial degeneration**-Vita E/Se def, infarcts
- **Cardiac temponade**- Haemopericardium
- **Electrolyte imbalance**-Hyperkalemia in uremic animals

Mechanism

Inadequate cardiac output

Hypotension

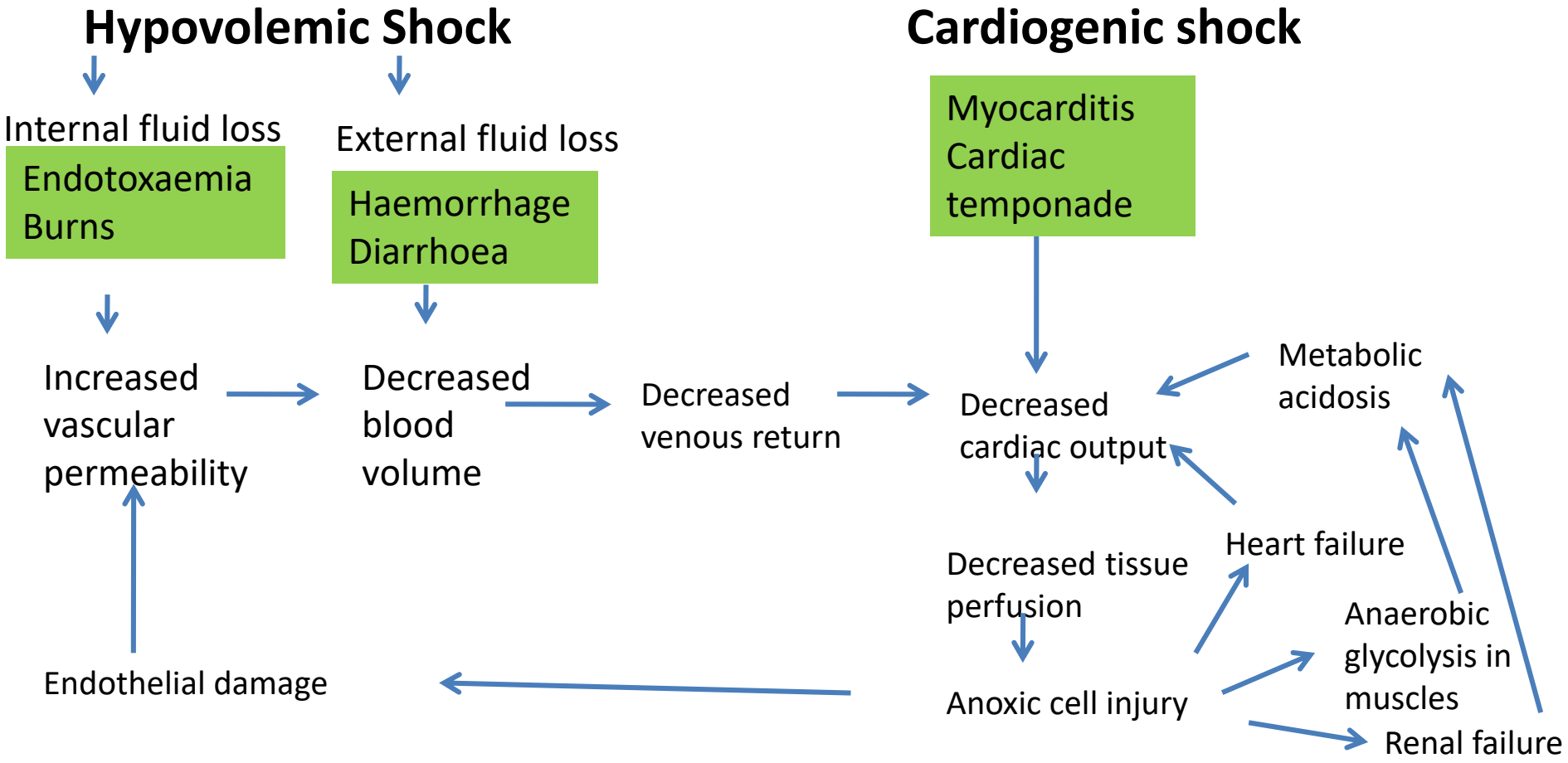
Impaired tissue perfusion

Cellular hypoxia

Hypovolemic Shock

Sudden severe loss of blood volume

- Acute haemorrhage->1/4th to 1/3rd
- Loss of fluid: vomiting, diarrhoea etc.
- Increased vascular permeability
- Loss of intravascular fluid & proteins


Hypovolemic Shock
Cardiogenic shock
Internal fluid loss
Endotoxaemia
Burns
External fluid loss
Haemorrhage
Diarrhoea
Myocarditis
Cardiac
temponade
Increased
vascular
permeability
Decreased
blood
volume
Decreased
venous return
Decreased
cardiac output
Metabolic
acidosis
Heart failure
Decreased tissue
perfusion
Anaerobic
glycolysis in
muscles
Endothelial damage
Anoxic cell injury
Renal failure

SEPTIC/ENDOTOXIC SHOCK

- Results from bacterial infection in which large quantities of endotoxins are released into circulation.
- Endotoxins are complex components of cell wall of gram -ve bacteria (LPS)
- Endotoxins bind to serum proteins
- Resulting complex bind to Macrophage/monocyte
- TNF alpha, IL-1 secreted into circulation
- Marked capillary dilation
- Severe pooling of venocapillary blood
- Decreased cardiac venous return
- Cardiovascular collapse

Anaphylactic shock

- Systemic manifestation of an acute allergic response
- Exposure to allergens
- Activation of mast cells or other effector cells
- Release of histamine and other chemical mediators
- Marked venocapillary dilation
- Increased vascular permeability
- Loss of intravascular fluid
- Decreased cardiac venous return
- Cardiovascular collapse

NEUROGENIC SHOCK

- Severe trauma, anaesthetic accident, spinal cord injury.
- There is disruption of vasomotor control, loss of vascular tone, vasodilation and peripheral pooling of blood.

CLINICAL CONSEQUENCES OF SHOCK

Decreased tissue perfusion causes anoxic injury

Anoxic injury to endothelial cells

↓

Increased vascular permeability

↓

Loss of intravascular fluid

Insufficient renal & muscular perfusion

↓

metabolic acidosis

↓

Suppress cardiac output

Insufficient myocardial perfusion → Anoxic injury to myocytes

↓

Decreased cardiac output

INFLAMMATION

- Reaction of vascularised living tissue to local injury caused by microbes or necrotic tissue.
- Reaction of blood vessels leading to accumulation of fluid and leukocytes in extravascular tissues.
- Inflammation serves to destroy, dilute, or otherwise neutralize harmful agents (microbes, toxins), and repair the damaged tissues. It is basically a protective response
- The inflammatory response is closely interwoven with the process of repair. Repair begins during the early phase of inflammation. Healing, which is the end result of inflammation, is a part of the dynamic process and not a separate entity.

- Beneficial Effects of Inflammation
  - To destroy / dilute the injurious agent (microbes; toxins)
  - Cell injury
- Harmful Effects of Inflammation
  - Chronic inflammatory reactions e.g. rheumatoid arthritis
  - Atherosclerosis
  - Pulmonary fibrosis
  - Hypersensitivity reactions
- Repair produces scars that causes mechanical obstruction and loss of functions

- **5 Cardinal Signs** of inflammation

1) **Heat** (Calor)
2) **Redness** (Rubor)
3) **Swelling** (Tumor)
4) **Pain** (Dolor)
5) **Loss of Function** (Functio laesa)

First four by Cornelius Celsus

Fifth one by Rudolph Virchow.

Stimuli of inflammation

- Infections (bacterial, viral, fungal, parasitic)
- Microbial or other toxins; xenobiotics
- Trauma (blunt or penetrating)
- Physical or chemical agents (thermal, irradiation, caustics)
- Tissue necrosis
- Foreign bodies
- Immune (hypersensitivity reactions)
- Nutritional imbalance

- Inflammation is of two types: acute and chronic.
- Acute inflammation is of relatively short duration lasting for a few minutes, several hours, or a few days; and its main characteristics are the exudation of fluid and plasma proteins (oedema) and the emigration of leukocytes, mainly neutrophils.
- Chronic inflammation, on the other hand, is of longer duration and is associated histologically with the presence of lymphocytes and macrophages, and with the proliferation of blood vessels, fibrosis, and tissue necrosis.

Acute Inflammation

- Aetiology (causes) Acute inflammation can be provoked by any noxious stimulus - called an irritant.

1. Infectious agents: bacteria, viruses, fungi, chlamydiae, rickettsiae, mycoplasma, protozoa, helminths, and even arthropods (insects).
2. Chemical agents: toxins, acids, alkalies, and other caustic substances.
3. Physical agents: These include burns, electricity, radiation, excessive cold, and trauma.
4. Immunological reactions: antigen-antibody interactions that occur under certain circumstances. These include various hypersensitivity reactions and autoimmune diseases.
5. Nutritional imbalances: These include deficiencies in specific vitamins.
6. Necrotic tissue: Certain stimuli, such as toxins, bacteria, and ischaemia, cause cell necrosis directly, and the necrotic tissue, in turn, can trigger the release of inflammatory mediators.

Cardinal signs

1. Redness (L. rubor): This is due to a great increase of blood in the inflamed area as a result of hyperaemia.
2. Swelling (L. tumor): due to hyperaemia and outpouring of protein-rich fluid containing blood cells into the extravascular tissues (called 'exudate,).
3. Heat (L. calor): increased blood flow through the area that carries warmth to the periphery from the higher interior temperature of the body. Also, as the rate of metabolism is increased at the inflamed site, there is greater production of heat.
4. Pain (L. dolor): Pain occurs partly from increased pressure on sensory nerve endings, and by stretching of tissues from accumulation of exudate. Also, chemical mediators like 5-hydroxytryptamine (serotonin), kinins (bradykinin), and prostaglandins.
5. Loss of function (L. functio-Iaesa): This is due to a combination of pain, swelling and destruction of tissues.

Tissue alterations

- Tissue Alterations In Acute Inflammation: vascular changes and the cellular events.
- Vascular changes: Julius Cohnheim (1839-1884) was the first to describe vascular changes in 1877.

1. Changes in blood vessels following injury (tissue damage, microbial virulence factors, etc)

- Momentary vasoconstriction
- Vasodilation (arteriolar dilatation – nerve stimuli from axonal reflex also)
- Increased blood flow
- Opening of new capillary beds
- Brought about by substances - Histamine − chemical mediators of inflammation

2. Changes in the rate of flow

- Increased vascular permeability (Vascular leakage): A characteristic feature of acute inflammation is the striking increase in permeability of the vessels to proteins resulting in inflammatory oedema

3. Changes in the Bloodstream: redistribution of the cellular elements of the bloodstream.

Margination: leukocyte adhesion at the periphery of vessels

Rolling: process of brief, loose sticking of leukocytes to the endothelium

Adhesion: firm sticking of leukocytes to the endothelium

Pavementing: endothelium is virtually lined by white cells

4. Exudation of Plasma Following increased vascular permeability, fluid part of the blood escapes into the inflamed area. This is known as exudation. The accumulated plasma outside the vessel is known as an inflammatory exudate.
5. Emigration of Leukocytes: This is the process by which leukocytes come out of the blood vessels into the extravascular space.
6. Diapedesis of Erythrocytes: Red cells may also leave the intact blood vessels.

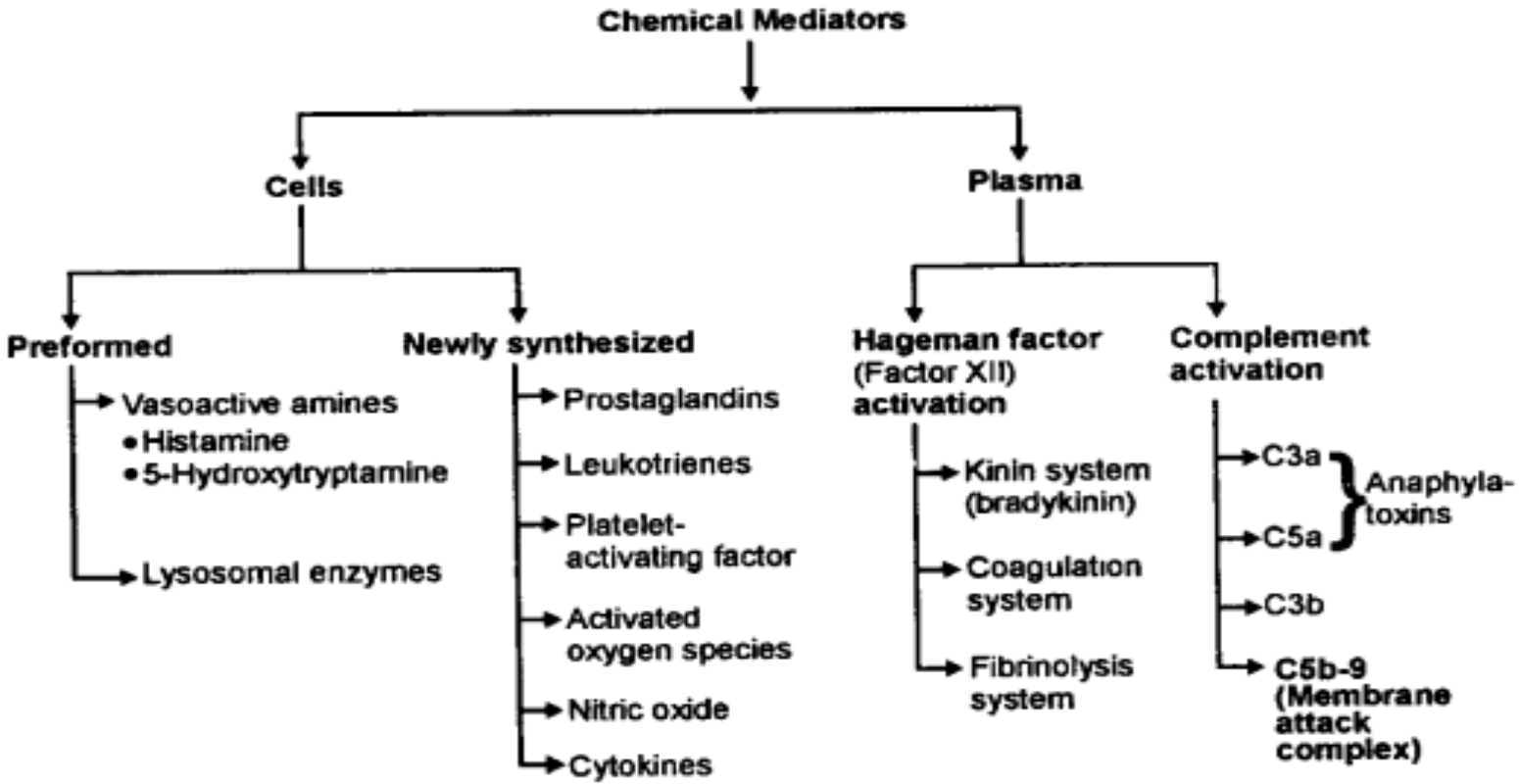


Fig. 16. Chemical mediators of inflammation

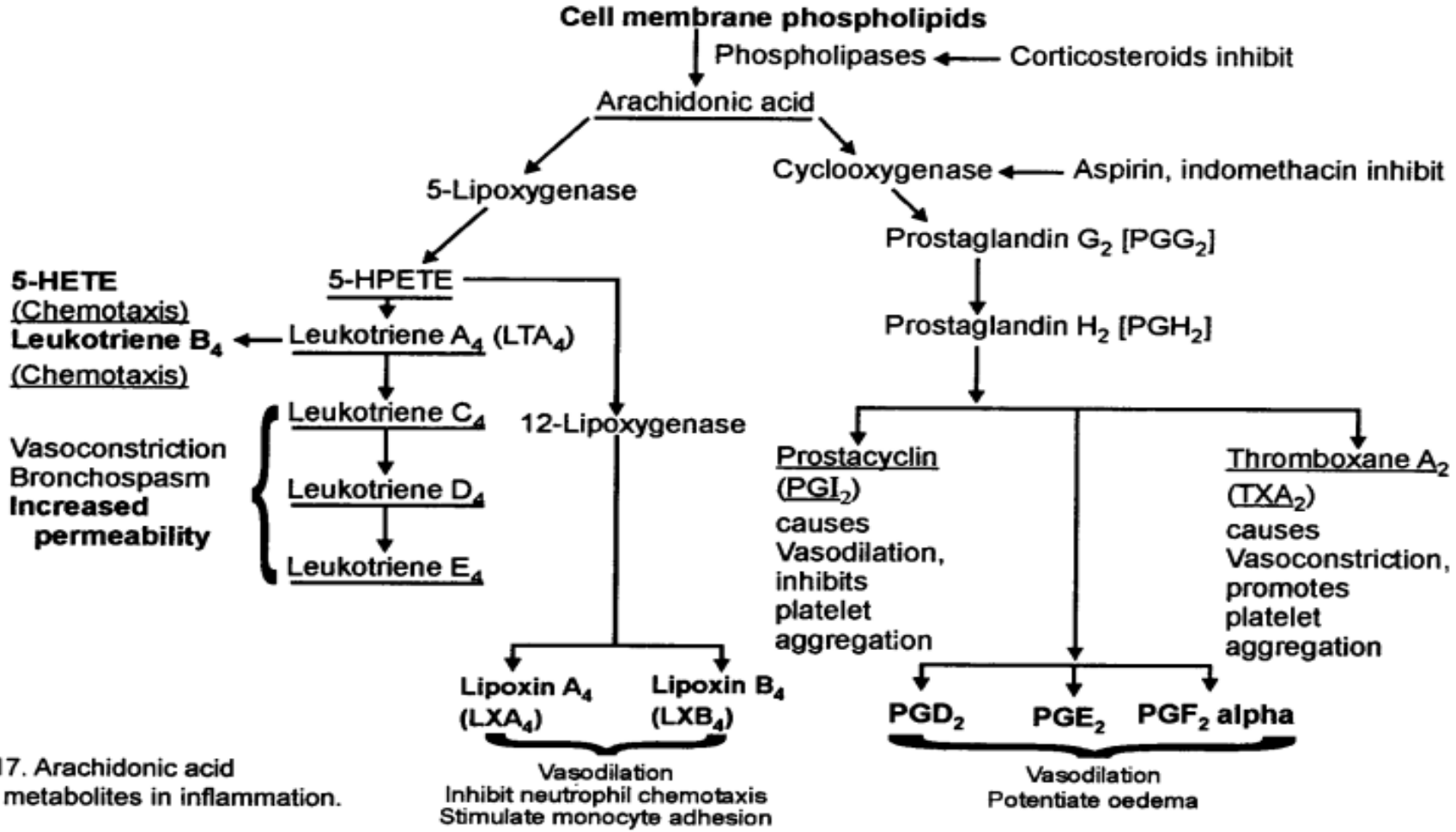


Fig. 17. Arachidonic acid metabolites in inflammation.

Table 4. Most likely mediators in inflammation

Vasodilation
Prostaglandins
Nitric oxide
Increased vascular permeability
Vasoactive amines (histamine, 5-hydroxytryptamine)
C3a and C5a (by causing release of vasoactive amines)
Bradykinin
Leukotrienes C_4, D_4, E_4
Platelet-activating factor
Chemotaxis, leukocyte activation
C5a
Leukotriene B_4
Bacterial products
Chemokines (interleukin-8)
Fever
IL-1, IL-6, tumour necrosis factor
Prostaglandins
Pain
Prostaglandins
Bradykinin
Tissue damage
Neutrophil and macrophage lysosomal enzymes
Oxygen metabolites
Nitric oxide

CELLULAR EVENTS

- Elie Metchnikoff, in 1884.
- most important function of inflammation is delivery of leukocytes, particularly neutrophils and monocytes, to the site of injury
- The sequence of events in the journey of leukocytes from the lumen of blood vessels into the extravascular space is called extravasation. These events can be divided into:

(1) margination (2) adhesion, (3) emigration (transmigration), (4) phagocytosis (5) release of leukocyte products.

- Chemotaxis: Unidirectional migration of cells towards a chemical attractant. It is the force that attracts leucocytes into the inflamed tissue
- Chemotactic agents
- Exogenous: Bacterial products
- Endogenous Chemical mediators:
- C5a (complement)
- Leukotriene B4
- Cytokines (interleukins)

- The process of taking particulate matter in the cytoplasm by cells is known as phagocytosis, and that of the fluid as pinocytosis.
- (i) first is recognition and attachment of the particle to the surface of the neutrophil
- (ii) second is its engulfment with subsequent formation of a phagocytic vacuole
- (iii) third is killing and degradation of the ingested material.

1. Recognition and Attachment: Micro-orgranisms are not recognized by neutrophils and macrophages until they are coated by naturally occurring serum proteins
2. Engulfment: During degranulation leakage of hydrolytic enzymes, metabolic products (H 2 O 2) and lysozymes from neutrophil into outside medium cause tissue damage. Kinins released cause vascular dilatation and nerve stimulation. Proteases liberated induce tissue damage, platelets aggregate and release PAF4 which is chemotactic to neutrophils and Coagulation factors causing polmerization of fibrin. PDGF stimulates fibrinogenesis and angiogenesis. Monocytes transform into macrophages to release collagenase, antimicrobial proteases, elastases, complements, IL-1 and TNF. Activation of systemic response leads to release of acute phase proteins (complement, fibrinogen, etc) from the liver and leucocytes and increased haematopoiesis in bone marrow and lymphopoiesis in lymph node and spleen.

3. Killing and Degradation: Brought about by reactive oxygen species like hydrogen peroxide(H 2 O 2) and Myeloperoxidase enzyme present in lysosome of neutrophils

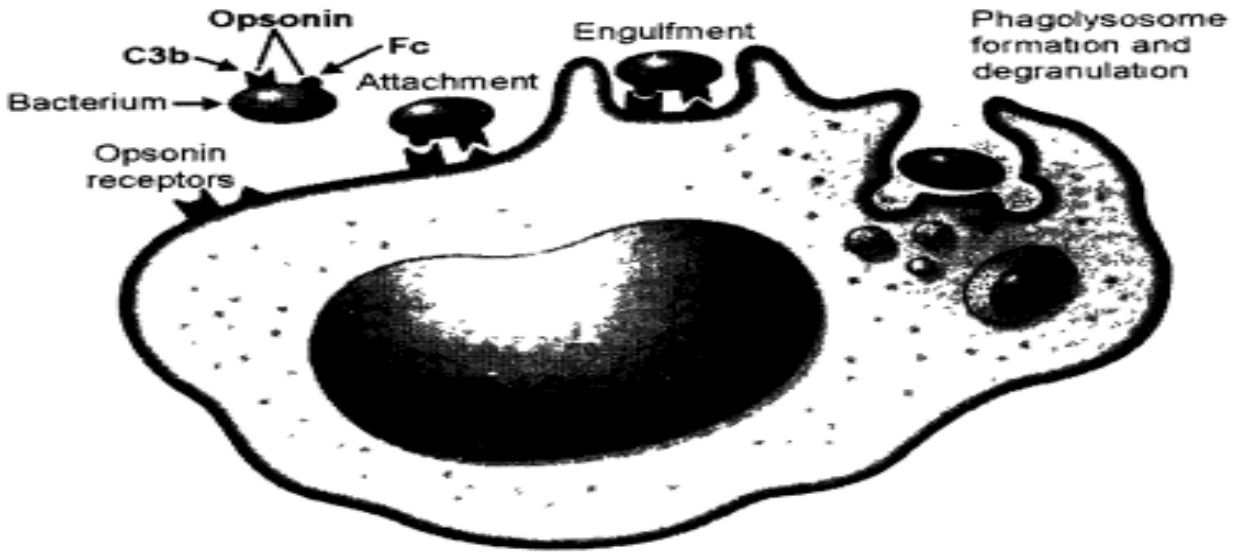


Fig. 24. Phagocytosis of a bacterium. It involves: (1) attachment and binding of opsonins (C3b, Fc) to receptors on the leukocyte surface, followed by (2) engulfment, and (3) fusion of the phagocytic vacuole with granules (lysosomes) and degranulation.

- Release of leukocyte products and leukocyte-induced tissue injury: (i) lysosomal enzymes, present in the granules; (ii) oxygen-derived active metabolites (i. e., free radicals), and (iii) products of arachidonic acid metabolism

Cells of Acute Inflammation

- 1. Neutrophils These are also known as polymorphs, polymorphonuclear leukocytes, and granulocytes. The term heterophil is used to describe functional counterpart of the neutrophil in certain species such as rabbit, guinea pigs, and the domestic fowl (chicken),
- first line of cellular defence
- Neutrophils are the characteristic feature of acute inflammation, and are the main component of the purulent exudate (pus).
- An increase in the number of leukocytes in blood is known as leukocytosis; if neutrophils, then as neutrophilia. Schilling index helps in determining the immature (juvenile) forms of neutrophils in the blood, and an increase in their number is known as 'shift to the left'

2. Eosinophils are characteristic of inflammations associated with parasitic infestations and immune reactions mediated by IgE, typically those of allergies. The finding of an increased number of eosinophils in the blood (eosinophilia) is an indication of parasitism or allergy.

3.Basophils: involved in Type 1 hypersensitivity and release histamine

4. Lymphocytes, Monocytes (Macrophages), Plasma Cells These cells appear late in inflammation and are the important cells of chronic inflammation

- The acute inflammation, which is always accompanied by exudate formation, is further classified as follows, based on the main component of the exudate.

Catarrhal or Mucous Inflammation

- Inflammation of a mucosal surface which is predominantly characterized by **hypersecretion of mucus**
- Mucus is a clear, transparent, glistening slimy material containing water and mucin.
- Mucus stains blue with haematoxylin.
- Irritants that are mild in nature, such as formalin, phenol, detergents, irritating foods in the digestive tract, inhaled dust, cold air, bacterial and viral infections of low virulence in respiratory tract.

Serous

- main component of exudate is plasma derived from blood, or a clear watery fluid derived from secretions of the mesothelial cells lining the peritoneal, pleural, and pericardial cavities.
- moderately severe irritants.
- stains pink with eosin;
- rubbing nature and second-degree burns also form blisters on the skin. Certain viruses (foot-and-mouth, vascular stomatitis)

Fibrinous

- Protein-rich exudate with adequate vascular permeability such that fibrinogen escapes the vessels and polymerizes in the tissue or on a surface to form fibrin
- more violent type of injury.
- Fibrinous inflammation commonly occurs in body cavities, such as pleural and peritoneal sac. In fibrinous pericarditis, the space may become filled with large masses of rubbery fibrin loosely gluing the parietal and visceral epithelium ('bread and butter' pericarditis).
- Stains dirty pink with eosin.
- Gross appearance of fibrin : White to yellow, easily broken down, usually adherent mat of exudate on a serous or mucosal surface.
- Infectious feline enteritis, malignant catarrhal fever, *Corynebacterium diphtheriae*, various salmonella, or *Fusobacterium necrophorum*
- Masses of fibrin on epithelial surface may either form a pseudomembrane (croupous membrane) when it is easily peeled away, or a diphtheritic membrane when it is quite firmly attached.
- If the necrotic, denuded epithelial cells are also included in the mass, it is a 'true membrane', otherwise, without epithelial cells it is called a 'false membrane'.
- Calf diphtheria, and intestinal tract in swine fever.

Suppurative/ Purulent

- Neutrophils are the principle component of pus, along with dead cell, serum, etc.
- Any irritant causing positive chemotaxis and necrosis will produce suppuration.
- Usually associated with acute inflammation, but may be seen in subacute to chronic inflammation.
- The main causes of suppurative inflammation are:

1. Pyogenic bacteria: Ex. staphylococci, streptococci, and members of the Coli group.

2. Specific organisms like *C. pyogenes*, *P. mallei*, *A. bovis*, etc.

3. Chemicals - turpentine, mercuric chloride, croton oil etc.

- Streptococci and staphylococci produce white or yellow pus.
- Corynebacteria, particularly in cattle, produce greenish pus;
- bluegreen colour comes from the pigment-forming pyocyaneus bacillus.
- Canine pus is thin and watery due to extremely proteolytic neutrophilic enzymes.
- Bovine pus is rather viscid.
- Avian pus has a dry, caseous consistency due to the presence of antienzymes.
- The rabbit serum is particularly rich in the anti enzyme and poor in leukocytes, and therefore it is not common to see suppurative conditions in this animal

Term

- Abscesses are localized accumulations of pus & are frequently surrounded by a connective tissue capsule.
- Cellulitis (phlegmon) is a diffusely spreading suppurative inflammation of connective tissue caused by streptococci, and has red raised margins.
- Empyema – accumulation of pus in a natural cavity.
- Sinus: It is a tract in the tissues communicating with an epithelial surface, discharging pus from an abscess.
- Fistula is a tract that connects two epithelial surfaces - skin and mucous membrane, for the discharge of pus from an abscess.
- Boil (furuncle): This is a small suppurative inflammation in the skin that involves a hair follicle or a sebaceous gland, and is caused by *Staphylococcus aureus*.
- Pustule: It is a circumscribed cavity in the epidermis containing pus.

Hemorrhagic

- Hemorrhagic exudate refers to an inflammatory process in which hemorrhage is the primary sign
- Vascular damage allows the Red Blood Cells to leak into the injured area

Lymphocytic (lymphoplasmacytic)

- Characterized by a **nearly pure** infiltrating population of **lymphocytes** &/or **plasma cells**
- often no gross lesions
- Seen most commonly with immune mediated disease & some viral disease**s**
- **Immune mediated diseases**: interface dermatitis
- **Viral diseases**: lymphocytic thyroiditis, ovine lymphocytic intersttial pneumonia
- *Ex*. German Shorthair Pointer with **lupus erythematosis**& **pemphigus**

Table 7. Terminology of inflammation

Time	Extent	Exudate	Position in organ	Anatomy	Suffix
Acute	Focal	Serous	Parenchymatous	Nephr-	-itis
Chronic	Diffuse	Fibrinous	Interstitial	Hepat-	-itis
		Catarrhal		Rhin-	-itis
		Suppurative		Periton-	-itis
		Haemorrhagic		Enter-	-itis

CHRONIC INFLAMMATION

- Chronic inflammation is an inflammation of prolonged duration (weeks, months, or even years) in which active inflammation, tissue destruction, and healing proceed simultaneously.
- In contrast to acute inflammation, which is characterized by vascular changes, oedema and neutrophilic infiltration, chronic infiltration is characterized by infiltration with mononuclear cells, tissue destruction and repair, involving new vessel proliferation and fibrosis.
- Causes of chronic inflammation
- Bacteria – Pasteurella aviseptica, Erysipelothrix rhusiopathiae
- Phytotoxins – Crotalaria, senecio
- Foreign bodies – sharp objects, dust, worms, inert objects
- Constant & repeated mechanical irritation e.g.: kennel granuloma, calluses

- characteristic microscopic features of chronic inflammation are

(1) infiltration with mononuclear cells (chronic inflammatory cells). These include macrophages, lymphocytes, and plasma cells. Their presence indicates persistent reaction to injury.

(2) tissue destruction. This is mainly caused by the inflammatory cells.

(3) Repair. This is achieved by proliferation of small vessels (angiogenesis) and, in particular, fibrosis. Fibrosis involves proliferation of fibroblasts and deposition of extracellular matrix by these cells.

macrophage is the central figure in chronic inflammation . Other types of cells present in chronic inflammation are lymphocytes, plasma cells, eosinophils, mast cells, and giant cells.

- Acute Chronic Inflammation :
- Although neutrophils are characteristic of acute inflammation, many forms of chronic inflammation show large numbers of neutrophils (and even pus), caused by either, persistent bacteria or by the mediators produced by macrophages or necrotic cells.
- Examples include actinomycosis and chronic osteomyelitis.
- In actinomycosis, centre of the lesion remains full of neutrophils months or years after the initial infection. This, then, is an example where chronic and acute responses co-exist.
- This is sometimes called 'acute chronic infammation'.

- **Granulomatous /** Also called —**histiocytic inflammation**

- Characterized by macrophage infiltration

-These can further differentiate into epithelioid cells (activated macrophages that assume an epithelial cell-like appearance) & merge to form multinucleate giant cells

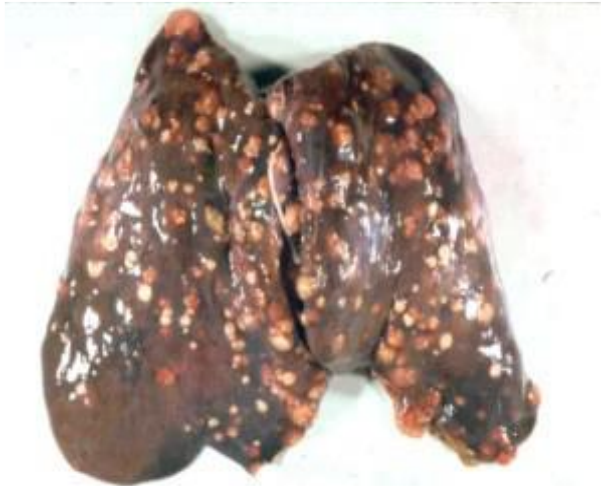
-Lymphocytes & plasma cells are nearly always present too.

An accumulation of epithelioid cells, surrounded by a collar (rim) of lymphocytes, is called a granuloma.

- Granulomas are localized accumulations of macrophages and epithelioid cells usually centered around the causative agent or necrotic debris or a caseous center

- Usually accompanied by fibrosis around or within the reaction

- Characteristic of persistent infectious organisms such as *Mycobacterium spp*., fungi, parasites & protozoa also indigestible foreign material



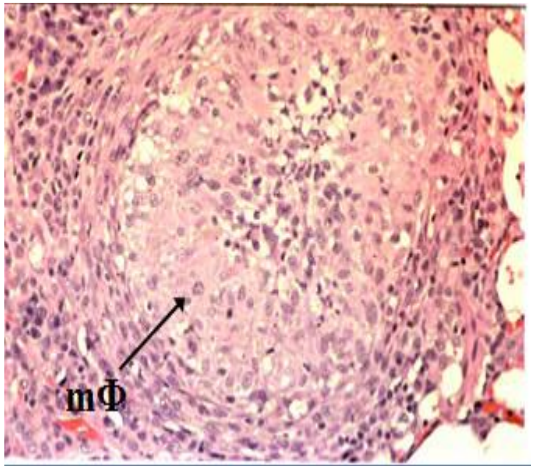

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Table 8. Comparison of acute and chronic inflammation

Acute inflammation	Chronic inflammation
1. Short duration	1. Long duration
2. Irritant is severe	2. Irritant is of low intensity
3. Marked vascular changes	3. Vascular changes are less prominent
4. Profuse exudation	4. Exudation scanty
5. Soft consistency	5. Firm consistency
6. No, or only slight, proliferation of connective tissue, blood vessels, and epithelium	6. Proliferation of connective tissue, blood vessels, and epithelium

Combination of Types

To describe combination of exudate, the least important component of the exudate is placed first.

- For example, the term serofibrinous would mean that fibrin is the main component.
- The term mucopurulent would mean more pus in the exudate than mucus.

- fibrinosuppurative

– pyogranulomatous

- Result of chronic inflammation
- Delayed healing
- Permanent change or scar formation
- Distortion / Disfigurement of the organ / tissue (Inflammatory cells displace, replace or obliterate the tissue)
- Impairs mobility
- Epithelial surface – hyperplasia – Metaplasia – Neoplasia
- Increase intracranial pressure - destruction neurons and glia

Peracute	Acute	Subacute	Chronic
Min to hours after initiation *Hallmarks* - **Edema** (pus filled) - **Hyperemia** (red) - Minimal cellular infiltration - Example: hives, urticaria	hours to 3-5 days after initiation *Hallmarks* - **Edema** - **Extensive vascular engorgement** - Fibrin exudation then neutrophils - Lymphatic dilation leading to swollen regional lymph nodes - 5 cardinal signs are very evident	several (3-5) to many (7-14) days *Hallmarks* - **Minimal edema** (pus reabsorbed) - **Decreased vascular changes** - Change of infiltrating leukocytes from neutrophils to lymphocytes, macrophages, & plasma cells	7-14 days until resolution or death *Hallmarks* - Angiogenesis - Fibroplasia - **Regeneration** - Inflammatory cells are predominantly macrophages - Possible formation of epitheloid cells & multinucleate giant cells - Also infiltration of lymphocytes & plasma cells

Sr. No.	Name of the organ	Term for its inflammation
I.CENTRAL NERVOUS SYSTEM:		
1	Brain (of nervous tissue and vessel wall)	Encephalitis
2	Spinal cord	Myelitis
3	Brain and spinal cord	Encephalomyelitis
4	Choroid plexus	Choroiditis
5	Meninges	Meningitis
6	Meninges of spinal cord	Spinal meningitis
7	When pia arachonoid involved	Leptomeningitis
8	When Dura arachonoid involved	Pachymeningitis
9	Nerve	Neuritis
10	Ependyma	Ependymitis

II. MUSCULO SKELETAL SYSTEM

a) Bone and related structures

1	Bone / part of bone	Osteitis
2	When begining with periosteum	Periosteitis
3	Bone marrow	Osteomyelitis
4	Joint	Arthritis
5	Bursa	Bursitis
6	Bone and joint	Osteoarthritis
7	Synovial space / sheath	Synovitis
8	Tendon	Tendonitis
9	Tendon and its sheath	Tendovaginitis
10	Bone morrow	Osteomyelitis
11	Vertebrae	Spondylitis
12	Hip joint	Coxitis
13	Stifle joint	Gonitis
14	Periosteum of metacarpal and metatarsal region	Sore shins
15	Sessamoids	Sesamoiditis
16	Inner aspect of left tibia	Track leg
17	Sinus of leg joint	Sinuvitis
18	Inflammation of bursa between ligamentum nuchae and atlas and axis	Polevil
19	Inflammation between ligamentum nuchae and the thoracic spines	Fistulus withers
20	Bursitis and arthritis involving distal sessemoid or navicular bone	Navicular disease
21	Sensitive laminae of hoof	Laminitis (founder)

1	Muscle	Myositis
III. SENSORY ORGANS		
a) Eye and allied structures		
1	Eye	Opthalmitis
2	Cornea	Keratitis
3	Uvea (vascular tunic)	Uveitis
4	Iris and ciliary body	Anterior uveitis / Iridocyclitis
5	Ciliary body and chorid	Posterior uveitis
6	Diffuse uveitis	Panuveitis
7	Choroids and retina	Chorioretinitis
8	Uveary retina and ocular cavities	Endoophthalmitis
9	All ocular structure and sclera	Panophthalmitis
10	Retina	Retinitis
11	Eyelids	Blephritis
12	Conjunctiva (covering mucosa of the eye including the orbit and inner surface of eyelid)	Conjunctivitis
13	Cornea and conjunctiva (layers below conjunctiva)cs	Kerato conjunctivitis
14	Orbit	Orbital cellulitis
15	Lacrimal sac	Dacryocystitis
16	Lacrimal gland	Dacryoadenitis
17	Optic nerve	Optic neuritis
18	Sclera	Scleritis

b) Ear		
1	Inner ear	Otitis interna
2	Middle ear	Otitis media
3	External ear	Otitis externa
c) Skin and appendages		
1	Adipose tissue	Stealitis
2	Dermis and epidermis	Dermatitis
3	Subcutaneous tissue (suppurative infla.)	Cellulitis
4	Hair follicles	Folliculitis
5	Vessels	Vasculitis
6	Follicules	Folliculitis / panniculitis
7	Muscle and skin	Dermatomyositis

1	Mouth / oral cavity (mucosa)	Stomatitis
2	Teeth	Odontitis
3	Dental pulp	Pulpitis
4	Gum	Gingivitis
5	Lips	Chielitis
6	Periodontium	Periodontitis
7	Tongue	Glossitis
8	Parotid gland (salivary gland)	Parotiditis
9	Any of the salivary gland	Parotitis
10	Pharynx	Pharyngitis
11	Tonsil	Tonsillitis
12	Both palates	Palatitis
13	Soft palate	Angina
14	Hard palate	Lampas
15	Salivary gland	Sialoadenitis

16	Oesophagus	Oesophagitis
17	Crop (bird)	Ingluvitis
18	Peritoneum	Peritonitis
19	Omental bursa	Omental bursitis
20	Rumen	Rumenitis
21	Reticulum	Reticulitis
22	Omasum	Omasitis
23	Stomach (monogastric stomach)	Gastritis
24	Abomasum (ruminant stomach)	Abomasitis
25	Intestine	Enteritis
26	Both stomach and intestine	Gastro enteritis
27	Duodenum	Duodenitis
28	Jejunum	Jejunitis
29	Ileum	Ileitis
30	Caecum	Typhilitis
31	Colon	Colitis
32	Rectum	Proctitis

33	Anus	Anitis
34	Liver	Hepatitis
35	Cronic inflmation of liver	Cirrhosis
36	Gall bladder	Cholecystitis
37	Bile duct	Cholangitis
38	Cholangioles	Cholongiolitis
39	Pancreas	Pancreatitis
40	Retroperitonium	Retroperitonitis
V. URINARY SYSTEM		
1	Kidney	Nephritis
2	Kidney and pelvis	Pyelonephritis
3	Ureter	Ureteritis
4	Urinary bladder	Cystitis
5	Urethra	Urethritis
6	Pelvis	Pyelitis

VI. RESPIRATORY SYSTEM		
1	Pleura	Pleuritis / pleurisy
2	Air sac	Air saculitis
3	Nose / nasal cavity	Rhinitis / coryza
4	Sinuses	Sinusitis
5	Larynx	Laryngitis
6	Trachea	Tracheitis
7	Bronchi	Bronchitis
8	Bronchioles	Bronchiolitis
9	Lung / alveoli	Pneumonia / pneumonitis
10	Pleura and lung	Pleuropneumonia
VII. REPRODUCTIVE SYSTEM		
1	Ovary	Oophoritis /Ovaritis
2	Ovarian capsule	Perioophoritis
3	Bursa (ovarian)	Bursitis
4	Oviduct	Salpingitis
5	Uterus	Metritis

6	Perimetrium (serosa)	Perimetritis
7	Perimetrium along with broad ligament	parametritis
8	Endometrium	Endometritis
9	whole thickness of uterine wall	metritis
10	Cervix	Cervicitis
11	Vagina	Vaginitis
12	Vulva	Vulvitis
13	Mammary gland	Mastitis / mammitis
14	Nipples	Thelitis
15	Testes	Orchitis
16	Epididymis	Epididymitis
17	Seminal vesicles	Seminal vesiculitis
18	Spermatic cord	Funiculitis
20	Prepuce	Posthitis
21	Glans penis	Balanitis
22	Prepuce and glans penis	Balanoposthitis

VIII. CARDIOVASCULAR SYSTEM		
1	Pericardium	Pericarditis
2	Epicardium	Epicarditis
3	Myocardium	Myocarditis
4	Endocardium	Endocarditis
5	Valves	Valvulitis
6	Aorta	Aortitis
7	Artery	Arteritis
8	Vein	Phlebitis
9	Umbilical vein (only distal part or may extend from the umbilicus to the liver)	Omphalo- phlebitis
10	External aspects of umbilicus	Omphalitis
11	Umbilical artery (less common)	omphaloarteritis
12	Lymph vessel	Lymphangitis
13	Lymph gland	Lymphadenitis
14	Spleen	Splenitis

Disturbances in Growth

- APLASIA/AGENESIS: absence of any organ.
- HYPOPLASIA: failure of an organ/ tissue to attain its full size.
- Macroscopic and microscopic features:
  - Organ size, weight, volume reduced
  - Reduced size of cells
  - Reduced number of cells
  - Connective tissue and fat is more

- ATROPHY: decrease in size of an organ that have reached their full size.
- HYPERTROPHY: increase in size of cells leading to increase in size of organ/ tissue without increase in the number of cells.
- HYPERPLASIA: increase in number of cells leading to increase in size of organ/ tissue.
- METAPLASIA: transformation of one type of cells to another type of cells.
- Presence of nodular glands on oesophageal mucous membrane due to vitamin A deficiency in chickens also known as "Nutritional roup".

- ANAPLASIA: reversion of cells to a more embryonic and less differentiated type. It is a feature in neoplasia.
- DYSPLASIA: Abnormal development of cells/ tissues which are improperly arranged. It is the malformation of tissue during maturation.

Disturbances in Circulation

- HYPEREMIA: increased amount of blood in circulatory system.
- It is of two types, active and passive.
- In active hyperemia blood accumulates in arteries while in passive hyperemia the amount of blood increases in veins which is also known as congestion.

HAEMORRHAGE

- It is the escape of all constituents of blood from blood vessel.
- **Two types**
- Haemorrhage by rhexis : When there is rupture of a blood vessel
- Haemorrhage by diapedesis : When blood leaves through intact blood vessels

Site of haemorrhage

Epistaxis	**Bleeding from nose**
Haematemesis	Blood in vomit
Haemoptysis	Blood in sputum
Metrorrhagia	Bleeding from uterus
Enterrohagia	Bleeding from intestine
Melena	Blood in stools
Haematuria	Blood in urine
Haemothorax	Blood in thoracic cavity
Haematocoel	**Bleeding into tunica vaginalis**
Hemosalphinx	Bleeding in oviducts
Hematoma	Tumour-like accumulation of blood
Apoplexy	Haemorrhage into brain

- Petechiae: Pinpoint haemorrhage of about one mm diameter or pinhead size
- Ecchymoses: More than one to 10 mm diameter haemorrhage
- Extravasation: Larger area
- Suffusions: Irregular, diffuse and flat areas of haemorrhage on mucosal or serosal surfaces
- Linear hemorrhage: Haemorrhage appear in line in crests or folds on mucous membrane.
- Hematoma = collection of blood in an organ or tissue.
- When there is increased amount of blood in pericardial sac, it causes heart failure and is known as cardiac tamponade.

THROMBOSIS

- Formation of clot of blood in vascular system in the wall of blood vessel.
- It occurs due to endothelial injury leading to accumulation of thrombocytes, fibrinogen, erythrocytes and leucocytes.
- Occlusive thrombus totally occlude blood vessels.
- Mural thrombus is on the wall of heart.
- Valvular thrombus is on valves of heart.
- Cardiac thrombus is in heart.
- Saddle thrombus is at the bifurcation of blood vessel just like saddle on back of horse.
- Septic thrombus contains bacteria.
- Red thrombi: Contain red blood cells and less fibrin.
- White thrombi: Contain platelets and are rich in fibrin.

- EMBOLISM: Presence of foreign body in circulatory system which may cause obstruction in blood vessel.
- Thromboembolism: is a condition in which a blood clot (thrombus) breaks off from its original site and travels through the bloodstream (as an embolus)
- Caisson disease/Decompression sickness (DCS) / Bends(pain) : is a condition that occurs when divers come back to the surface too quickly after being deep under water.
  - It is caused by the formation of nitrogen bubbles in the blood stream and, in the worst cases, can cause death.
- ISCHEMIA: deficiency of arterial blood in any part of an organ. It is also known as local anemia.

- INFARCTION: Local area of necrosis resulting from ischemia.
  - Red Infarct or hemorrhagic • Venous infarction (no drainage)
  - White infarcts or Pale/anaemic • Arterial occlusions • In solid organs with end-arterial circulations (e.g., heart and kidney)

EDEMA

- Accumulation of excessive fluid in intercellular spaces and/ or in body cavity.
- Etiology:
  - Deficiency of protein.
  - Passive hyperemia.
  - Increased permeability of capillaries.
  - Obstruction of lymphatics.

Etiology

- **Decreased plasma oncotic pressure**
- **Increased hydrostatic pressure**
- **Increased capillary permeability**
- **Obstruction to lymphatic flow**

1. *Decreased plasma oncotic pressure*

- Hypoalbuminemia or hypoproteinemia
- Most common cause of generalized symmetric edema

2. Increased hydrostatic pressure in capillaries and veins

- caused by chronic (congestive) heart failure or obstruction to venous return
- symmetric pulmonary edema in acute heart failure

3. Increased capillary permeability

- Endotoxemia or Part of the allergic response
- Vasculitis or Damage to the vascular endothelium

4. Obstruction to lymphatic flow

- Tumors or inflammatory swelling
- Congenital in inherited lymphatic obstruction edema in Ayrshire and Hereford calves

PATHOPHYSIOLOGY

Hydrostatic vs. Osmotic Pressure

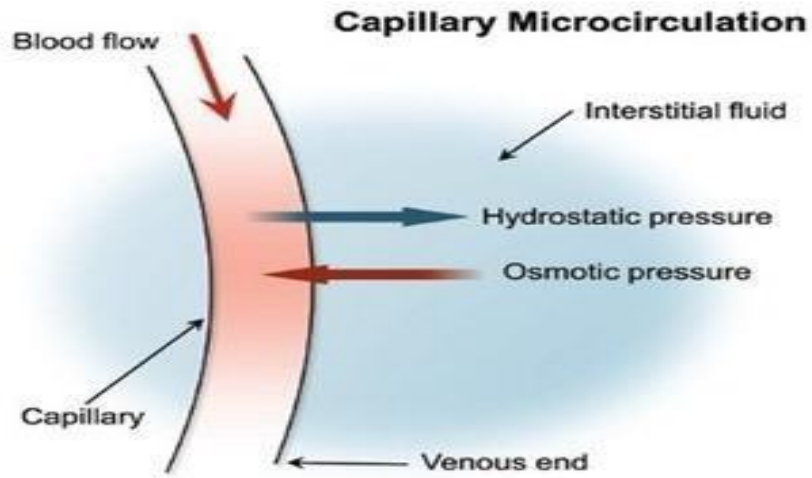
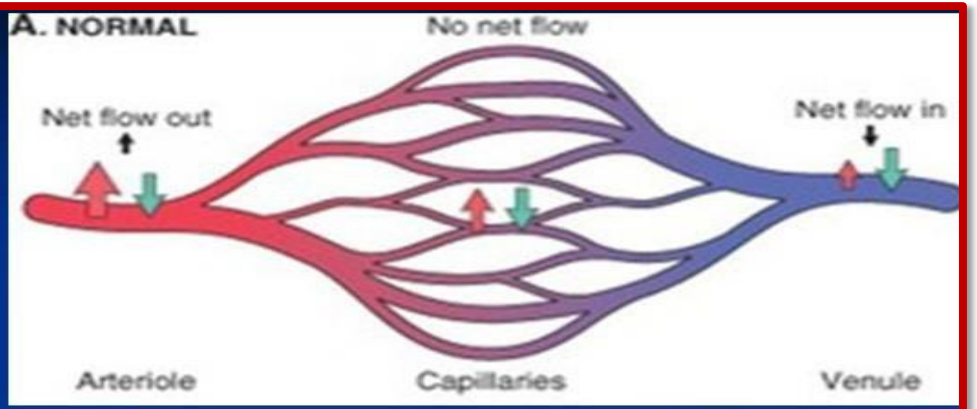
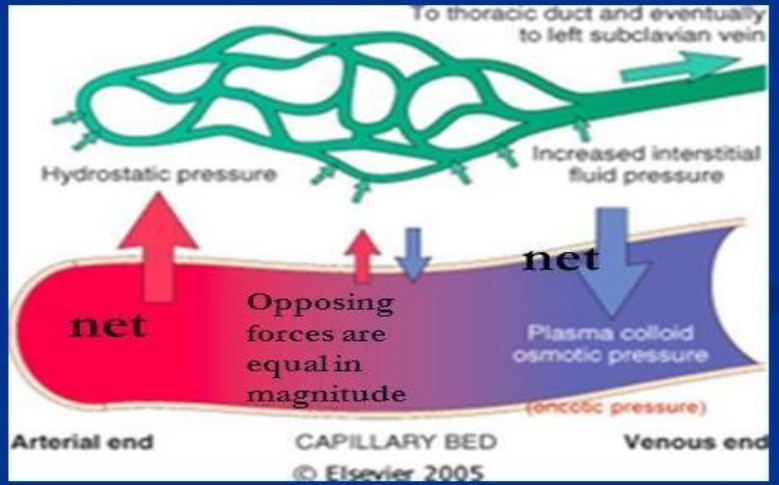


Figure 2. *Fluid exchange occurs across capillaries according to hydrostatic and colloid osmotic pressures maintained between the extracellular and intravascular compartments.*

- **Hydrostatic** pressure is water being pushed out by some force. If there is a lot of water in the blood vessel, it will get pushed out, causing edema in the tissues.
- **Osmotic** pressure is water moving from its area of high concentration to its area of low concentration. If there are too many particles in the plasma, water will be sucked into the blood vessel, causing the blood pressure to elevate.

- ***Hydrostatic* pressure** and ***oncotic* pressure** are opposing forces in blood vessels.
- Under normal conditions, **hydrostatic pressure** tends to "push" fluid out of the capillary (filtration) whereas oncotic pressure tends to "pull" fluid into the capillary (reabsorption)
- The "net force" determines whether *filtration* or *reabsorption* occurs at any single location along the capillary microvasculature





- Ascites: accumulation of fluid in peritoneum. It is also known as hydroperitonium.
- Hydropericardium: fluid accumulation in pericardial sac.
- Hydrocele: fluid accumulation in tunica vaginalis of the testicles.
- Anasarca: generalized edema of body.
- Hydrocephalus: accumulation of fluid in brain.
- Hydrothorax: accumulation of fluid in thoracic cavity.

- Anasarca in large animals is usually confined to the *ventral wall of the abdomen and thorax*, *the brisket*

- Edema of the limbs is uncommon in cattle, sheep, & pigs but is **quite common in horses** when the venous return is obstructed or there is a lack of muscular movement

- Local edema of the head in the horse is a common lesion in African horse sickness and purpurea hemorrhagica

- Muffled heart & respiratory sounds
- Presence of fluid may be ascertained by percussion and thoracocentesis or pericardiocentesis
- Pulmonary edema is accompanied by respiratory distress; outpouring of froth from the nose
- Cerebral edema- severe nervous signs of altered mentation

- Shock is a circulatory disturbance characterized by reduction in total blood volume, blood flow and by hemconcentration.
- SLUDGED BLOOD: agglutination of erythrocytes in the vascular system of an animal.

Disturbances in Calcification

- CALCIFICATION: deposition of calcium phosphates and calcium carbonates in soft tissues other than bones and teeth. It may be classified as dystrophic and metastatic calcification.
- Dystrophic or Local Calcification: When the deposition occurs in dead (necrotic) or dying tissues.
- It occurs in a focal area of the body.
- Dystrophic calcification may occur despite normal serum levels of calcium, and in the absence of derangements in calcium metabolism.

- Metastatic or General Calcification: deposition of calcium salts in many tissues throughout the body.
- In contrast to dystrophic calcification, deposition of calcium salts can occur in normal tissue, and it almost always indicates some derangernent of calcium metabolism,
- deposition of calcium salts rnay occur in organs throughout the body, especially in those that secrete or excrete acid substances such as the stomach (hydrochloric acid), kidney (hippuric acid, and lungs (carbon dioxide).

GOUT

- Gout is a disorder of uric acid metabolism characterized by deposition of urate crystals in tissues.
- Deposition is due to an increase in the concentration of uric acid in blood (hyperuricaemia) and body fluids.
- Gout is mainly a disease of humans and birds

Gout in Poultry

- Etiology
  - Common in poultry due to deficiency of uricase enzyme.
  - Deficiency of vitamin-A
  - Absence or inadequate amount of uricase
- Macroscopic and microscopic features :
  - White chalky mass of urates and uric acid.
  - Deposition of urates/ uric acid on pericardium, kidneys etc.
  - Dialation of ureter due to excessive accumulation of urates.
  - Presence of sharp crystals in tissue
  - Crystals are surrounded by inflammatory cells including macrophages, giant cells and lymphocytes

CONCRETIONS

- Concretions are solid, compact mass of material endogenous or exogenous in origin found in tissues, body cavities, ducts or in hollow organs.
- Concretions are stone like bodies commonly occur in urinary system, gall bladder and gastrointestinal tract.
- Concretions of endogenous origin are known as calculi while those formed from exogenous material are known as piliconcretion (Hair), phytoconcretion (plant fibers) and polyconcretion (Polythenes).

- Calculi: formed due to deposition of salts around the nucleus/ nidus consisting of either fibrin, mucus, desquamated epithelial cells or clumps of bacteria.
- Calculi formation is more common in urinary system and in gall bladder of man and animals; however, they may also occur in salivary gland, pancreas and intestines.

- URINARY CALCULI: formed in renal tubules, pelvis or in urinary bladder which may carried away through urine and may cause obstruction in ureter or urethra.
- Urinary calculi is also known as urolith and the process of formation of calculi is termed as urolithiasis.
- Horse- Calcium carbonate, calcium phosphate, magnesium carbonate
- Ruminants-Calcium phosphate, magnesium phosphate, aluminium phosphate
- Pigs- Ammonium phosphate, magnesium phosphate, calcium carbonate, magnesium carbonate, magnesium phosphate, magnesium oxalate.
- Dogs-Calcium carbonate, calcium phosphate, sodium urate, ammonium urate.
- Salivary calculi also known as sialolith.
- Enterolith are common in horses, which occur mostly in large intestine 'colon'.
- In dogs bone in diet may provide a nidus and such concretions are known as coproliths.

- Piliconcretions/ Trichobezoars: are hair balls occur due to excessive licking of skin in calves or in adults.
- PHYTOCONCRETIONS/ phytobezoars

IMMUNOPATHOLOGY

- disorders of immune system characterized by increased response or hypersensitivity, response to self antigens (autoimmunity) and decreased responses (Immunodeficiencies).
- HYPERSENSITIVITY It represents an accelerated immune response to an antigen (allergen), which is harmful to body rather than to provide protection or benefit to the body. Such violent reactions may lead to death.
- This condition is also known as allergy or atopy.
- The hypersensitive reactions can be classified into four classical form including anaphylaxis (Type I), cytotoxic hypersensitivity (Type-II), Immune complex mediated hypersensitivity (Type III) and delayed type hypersensitivity (Type-IV) reaction.

ANAPHYLAXIS OR TYPE-I HYPERSENSITIVITY

- Anaphylaxis or type I hypersensitivity reaction is rapidly developing immune response to an antigen characterized by humoral antibodies of IgE type (reagin). These reagins sensitize basophils/ mast cells to release chemical mediators (Histamin, Serotonin, Prostaglandins,) of inflammation leading to acute inflammatory reaction.
- Etiology • Administration of drugs • Administration of serum • Bite of insects, bee etc. • Dust, pollens etc.

- CYTOTOXIC OR TYPE II HYPERSENSITIVITY REACTION: Cytotoxic reactions are characterized by lysis of cells due to antigen- antibody reaction on the surface of cells in the presence of complement.
- Etiology/ Occurrence • Blood transfusion • Hemolytic anemia • Infections such as Equine infectious anemia, rickettsia, parasites (trypanosomiosis, babesiosis) • Thrombocytopenia

- IMMUNE COMPLEX MEDIATED OR TYPE-III HYPERSENSITIVITY REACTION
- Type-III hypersensitivity reaction is characterized by the formation of immune complexes as a result of antigen - antibody reaction and their deposition in body tissues leading to inflammatory reaction.
- Arthus reaction is focal area of inflammation, necrosis at the site of infection.

- DELAYED TYPE HYPERSENSITIVITY (DTH) OR TYPE IV HYPERSENSITIVITY REACTION DTH reaction is mediated by sensitized T-Iymphocytes and is the manifestation of cell- mediated immune response.
- Etiology • Tuberculin reaction • Graft versus host reactions • Granulomatous reaction

PHOTOSENSITIZATION

- activation of photodynamic chemicals on the skin by long wave length UV or occasionally by visible light.
- Necrosis and edema are produced in the exposed areas of skin of animals.
- The cellular damage by photosensitization is due to release of reactive oxygen species leading to mast cell degranulation and production of chemical mediators of inflammation.

Types

- Type I: Primary photosensitization
- Type II: Abnormal porphyrin metabolism associated photosensitization
- Type III: Hepatogenous photosensitization

Type I: Primary Photosensitization

- Causes
  - Plants containing helianthrones (e.g. hypericine in *Hypericum perforatum*; fagopyrin in *Fagopyrum esculentum*) and furocoumarin pigments (e.g. *Cymopterus watsonii*and *Ammi majus*), tetracyclines and sulphonamides
- Examples
  - Phytotoxins from furocoumarin plants exposed to fungi or other injury may be absorbed into skin which reacts with UV light
  - Phenothiazine is converted into photoreactive compound when bypasses the liver, reaches the skin causing photodermatitis on exposure to sunlight

Type II: Abnormal porphyrin metabolism associated photosensitization

- Due to inherited enzyme deficiency, abnormal porphyrin photodynamic metabolic products like uroporphyrin and protoporphyrin accumulate in blood and tissues.
- The uroporphyrin also causes discolouration of bone known as “osteohaemochromatosis” and teeth called “pink teeth”.
- Examples
  - Bovine congenital porphyria
  - Bovine haematopoetic protoporphyria

Type III: Hepatogenous photosensitization

- Hepatogenous photosensitization is caused by impaired hepatic capacity to excrete phylloerythrin derived from chlorophyll degradation in the alimentary tract, mainly affecting herbivores.
- Causes
  - Hepatocellular damage or injury (Toxic hepatitis due to *Lantana camara*, *Tribulus terrestris*, plants producing pyrrolizidine alkaloids, sporidesmins)
  - Inherited hepatic defects
  - Biliary obstruction
  - Infection: Leptospirosis
  - Chemicals: CCl_4 poisoning

Pathology of Cutaneous System

- Congenital icthyosis is scaly epidermis which resembles with skin of fish and occurs due to a simple autosomal recessive homozygous gene in calves.
- Epitheliogenesis imperfecta is a congenital defect characterized by discontinuity of epithelium on skin leaving patches without squamous epithelium mostly at feet, claws and oral mucosa.
- Congenital alopecia Alopecia or hairlessness on the skin with complete lack of hair follicles has been observed in dog and other animals.
- Congenital albinism Albinism is absence of melanin pigmentation due to deficiency of tyrosinase.

- Congenital cutaneous asthenia The collagen fibers are irregular in size and orientation and become fragmented due to disorganization of fibrils within the fibers. This condition occurs due to a deficiency in procollagen peptidase responsible for formation of collagen.
- ACANTHOSIS NIGRICANS This is increased amount of melanin in skin along with hyperkeratosis. This condition commonly occurs in dogs, at ventral abdomen and medial surface of legs.

- Papule: Focal Hyperplasia of stratum spinosum epithelium leading to hard nodular eruption on skin.
- Vesicle: A cavity in epidermis containing fluid and covered by a thin layer of epidermis elevated from the surface.
- Pustule: A vesicle filled with pus.
- Acanthosis: Thickening of epidermis due to hyperplasia of stratum spinosum/ prickle cell layer.
- Hyperkeratosis: Thickening of keratin layer stratum corneum.
- Parakeratosis: The retention of nucleus in keratin layer.
- Bulla/bleb: Cavitations in epidermis filled with fluid and larger than vesicle.
- Erosion/ Excoriation: Superficial loss of epithelium.
- Fissure: Linear defect in epidermis, which may be crusted at mucocutaneous junctions.

- Abscess: A circumscribed cavity filled with pus.
- Ulcer: A break in the continuity of the epidermis exposing dermis.
- Urticaria: A circumscribed area of swelling/ oedema involving dermis
- Folliculitis: Inflammation of hair follicles.
- Acne: Enlargement of sealed off hair follicles or sebaceous glands and rupture through the epidermis. It leaves a rounded hole in the epidermis and a canal down to the dermis.
- Eczema: Eczema is a form of allergic dermatitis of obscure etiology and characterized by erythema, vesicular rash, serus exudate and pruritus.

Pathology of Musculoskeletal System

- Abrachia – Absence of both fore limbs.
- Amelia – Absence of limbs.
- Apodia – Absence of posterior limbs.
- Micromelia – All parts of limbs are present but are smaller size.
- Perodactyly – Absence of some of the toes.
- Adactylism – Absence of all the toes in limb.
- Brachydactylism – Abnormal shortening of toes.

- Polydactylism – More number of digits, seen in horse & pig.
- Syndactylism – Fusion of toes, seen in cattle & pigs.
- Prognathism – Having a long jaw- pig-mouth in horse.
- Brachygnthism – Having a short jaw- parrot-mouth in horse.
- Kyphosis – Abnormal curvature & dorsal prominence of spine hump-back. This is rare in animals.
- Scoliosis – Abnormal lateral curvature of the spinal column.
- Torticollis – Wry neck – twisting of the neck

EQUINE RHABDOMYOLYSIS

- Azoturia or Monday Morning Disease.
- The disease occurs in well fed horse after a gap of holiday. Suddenly after walking few steps, the horse is unable to move further and feels pain with intense sweating and hardening of muscles.
- Urine is dark brown with myoglobin-myoglobinuria
- Etiology
  - Accumulation of lactic acid in muscles
  - High glycogen storage
  - Lack of oxygen supply

WHITE MUSCLE DISEASE

- Extensive coagulative necrosis of muscles is observed in calves possibly due to deficiency of vitamin E during 6 month of age.
- Etiology
  - Vitamin E deficiency
  - Selenium deficiency
  - Stress

Myositis

- Inflammation of muscles
- Acute
- Chronic
- Hemorrhagic
- Gangrenous

- Fibrous osteodystrophy occurs as excessive action of parathyroid hormone on bones and characterized by bone resorption with replacement by fibrous tissue, increased osteoid formation which does not get sufficient minerals for deposition and formation of cysts.
- Etiology • Hyperparathyroidism • Dietary deficiency of calcium or excess of phosphorus • Vitamin-D deficiency • Excessive bran feeding (Disease in horses of flour millers).

- RICKETS: failure of adequate deposition of calcium in bones of growing animals caused by deficiency of calcium and vitamin D and characterized by bending of limbs, enlargement of ends of long bones and skeletal deformities.
- Rachitic rosary appearance
- Bow legged

- OSTEOMALACIA Osteomalacia is also known as adult rickets. It occurs in bone of adults caused by deficiency of vitamin D and calcium and characterized by softening of bones.
- Osteoporosis is atrophy of bones caused by possibly hormonal imbalance and characterized by inadequate deposition of calcium, brittleness of bones due to its increased porosity.
- Osteopetrosis is enlargement of bone caused by fluorosis or avian leukosis virus and characterized by increase in bony tissue. It is also known as marble bone disease.
- Osteomyelitis is the inflammation of bone with bone marrow caused by trauma and pyogenic bacteria and characterized by destruction, replacement and excessive growth of new bone adjacent to the infected part.

Cardiovascular Malformations

- Anomalies or malformations of the heart and vessels occur with frequency in domestic animals.

1. Auricular Defect

- **Patent foramen ovale**
  - In this condition the foramen ovale which communicates the right auricle with the left during foetal life becomes persistent even after birth.
  - Hence, the blood flows from right auricle to left auricle i.e the unoxygenated blood is pumped through left ventricle through out the body.
  - Patent foramen ovale has been met with in calves.

2. Ventricular Defects

- Interventricular septal defects: In foetal life, there is no partition in ventricles and there is only one chamber which is divided into two right and left by inter ventricular septum. But when interventricular septum does not develop completely and due to defect in formation of complete partition, there is mixing of blood from both chambers. It is responsible for thickening of myocardium, roughening of endocardium and cyanosis.

3. Defects in Blood Vessels

a) Patent ductus arteriosus

- The shunt which connects the pulmonary artery with the aorta should obliterate within a few weeks after birth.
- Sometimes the shunt may be patent and hence blood might enter from aorta in to the pulmonary artery causing increased pressure in the pulmonary artery.
- This leads to hypertrophy of right ventricle. And the animals may be cyanotic.

b) Coarctation of the aorta

- This is narrowing of the lumen of the aorta.
- Because of the narrowing of the aorta there is resistance to the flow of blood. This leads to hypertrophy of the left ventricle.

c) Transposition of the aorta

- In this condition, the aorta arises from right ventricle or from both the ventricle. This is incompatible with life.

4. Multiple Defects in the Heart

- Tetralogy of Fallot
  - This refers to four defects in the heart. (Interventricular septal defect, Dextraposed aorta, Stenosis of pulmonary valves and Hypertrophy of right ventricle)
  - The affected animals are stunted and their mucous membranes are cyanotic.

- Other defects
  - Acardia is a condition in which there is complete absence of heart. This condition is incompatible with life.
  - Diplocardia is a condition in which two hearts are present.
  - Ectopia cardis when the heart is found outside the thorax usually in the neck region or abdominal cavity.
  - Persistent right aortic arch: developmental anomaly of aorta in which the aorta develops from right arch present on right side of trachea and oesophagus.

- CARDIAC FAILURE Cardiac failure is the inability of heart to maintain adequate blood supply leading to death. It can be divided into two types: Acute and chronic heart failure.
- Acute cardiac failure is sudden failure of contraction of heart leading to death within minutes.

- CHRONIC CARDIAC FAILURE Chronic cardiac failure is the inability of heart to maintain balance between its output and venous return of blood. It can be further divided into two left and right sided heart failure.
- LEFT SIDED HEART FAILURE Left sided heart failure is caused by myocardial damage and characterized by congestion and oedema in lungs with hypertrophy of alveolar lining cells.
- Right-sided heart failure is caused by a disease of lungs or pulmonary vasculature and mostly occurs after a left sided heart failure.

- Brisket disease is a condition of slow cardiac failure, which occurs at 2500 meters sea level or above where pressure of air is low.
- MULBERRY HEART DISEASE It is characterized by firm contraction of heart and petechial hemorrhage on pericardium giving the appearance of mulberry.
- Sarcocystis tenella
- Found universally in the myocardium of cattle, sheep and pigs.
- The muscle fibres contain the Miescher’s tubes in which are found the spores called Rainey’s corpuscles.
- Vegetative/ cauliflower like growth on endocardium either in valves (Valvular vegetative endocarditis e.g. Swine erysepelas) or in wall (Mural vegetative endocarditis).

Pericarditis

- Pericarditis refers to inflammation of both the parietal and visceral surfaces of the pericardium.
- A true pericarditis is nearly always infectious with an accumulation of exudate within the sac.
- Based on the lesion or exudates pericarditis is classified as
  - Fibrinous pericarditis
  - Suppurative pericarditis (Purulent Pericarditis)
  - Uric acid pericarditis

✓ Fibrinous pericarditis

- is a characterized by an accumulation of fibrin within the pericardial sac.
- Grossly, the fluid is grayish to yellow, and flecks of blood may be present.
- The deposition of fibrin on the pericardium and into the sac gives the appearance of bread and butter - Such a heart is also called **shaggy heart.**

- In cattle it is commonly a part of blackleg, pasteurellosis, contagious bovine pleuropneumonia, and some forms of neonatal coliform infections.
- In swine, fibrinous pericarditis is frequently associated with Glasser's disease, pasteurellosis, and salmonellosis.
- In the horse, streptococci are usually present.
- In serve infections, adhesions develop with organization of fibrinous exudate and the heart finally fails Occassionally caseation or calcification of the exudates may occur.

✓ Purulent Pericarditis

- is characterized by the accumulation of pus in the pericardial sac **(due to pyogenic bacteria).**
- It occurs most commonly as a result **traumatic pericarditis**.
- Also, in traumatic pericarditis the exudate may be fibrinous or fibrino-purulent in nature.

✓ Traumatic Pericarditis

- This condition occurs in cattle as a result of traumatic perforation of the pericardium by a foreign body originating in the reticulum (**traumatic reticulitis).**

- Ingested foreign bodies enter the reticulum; pierce the wall of the reticulum, overlying peritoneum and diaphragm and enter the thoracic cavity.

- Subsequently the foreign body may enter the pericardial sac **(**as well as the myocardium and endocardium) resulting in an exudative pericarditis).

Pathology of myocardium

1. **Hypertrophy**
   - Hypertrophy of the heart muscle means increase in the size of the individual myocardial fibres.
   - Left side of heart is more often affected and Ventricles suffer more frequently.
   - Physiological hypertrophy due to greater strain on heart as in race horses and grey hounds.
   - Grossly: Heart is enlarged and walls become thicker

- **hyaline changes (and necrosis)** of the myocardium occurs as a part of Vit E deficiency "white muscle disease syndrome“, calcium deficiency and gossypol poisoning.
- Hyaline degeneration is a prenecrotic lesion usually terminating in necrosis and calcification
- Grossly: Heart contains scattered grayish spots and usually focal
- Microscopically: Coagulative necrosis of myocardial fibers will be seen.
  - become hypereosinophilic, lose striations

- Myocardial infarction precipitated by arteriosclerosis of the coronary artery is a burden of aging humans, but is rare in domesticated animals.
- In animals however, acute obstruction of the coronary arteries due to emboli occurs with some frequency, with the development of infarction.
- If the coronary obstruction is chronic, the end result is diffuse scarring of the myocardium and markedly altered function.

- Coagulative necrosis of the myocardium is a lesion commonly associated with vitamin E and selenium deficiency **(white muscle disease)** in lambs, calves, and pigs.

Pathology of endocardium

- Endocarditis refers to inflammation of the endocardium which may be valvular or mural. – Inflammation of valves is common and is called
  - valvular endocarditis
  - Inflammation of septal endocardium is called mural endocarditis

- In domestic animals, valvular endocarditis occurs more frequently than mural.

- The location of endocarditis varies with the animal species involved. In cattle, lesions are most common in the right heart; whereas in the horse. dog, and pig, endocarditis occurs most frequently in the left heart.

- In the dog and horse, *streptococci* and *staphylococci* are most commonly isolated from *valvular lesions*: whereas *Corynebacterium pyogenes* is most frequently recovered in cattle. In swine, streptococci are common.

Valvular endocardiosis

- This condition is also referred to as "**nodular fibrosis**", and it is characterized by fibrous thickening of the heart valves.
- Valvular endocardiosis occurs primarily in dogs and the mitral valve is most frequently and severely affected.
- Valves are thickened due to fibroelastic tissue with abundant mucous ground substance. The valve cusps are shortened and thickened.
- The incidence of valvular endocardiosis increases with age, and may cause congestive heart failure.

1. Inflammation of arteries

- Inflammation of the wall of artery is called arteritis. Inflammation of tunica intima is called endarteritis.
- Based on the course, arteritis is classified as acute (Virus – Equine viral arteritis, equine herpes virus,) and chronic arteritis (Larvae of *Strongylus vulgarisi)*.
- Inflammation of the intima results in the formation of a thrombus at the site called thromboendarteritis .

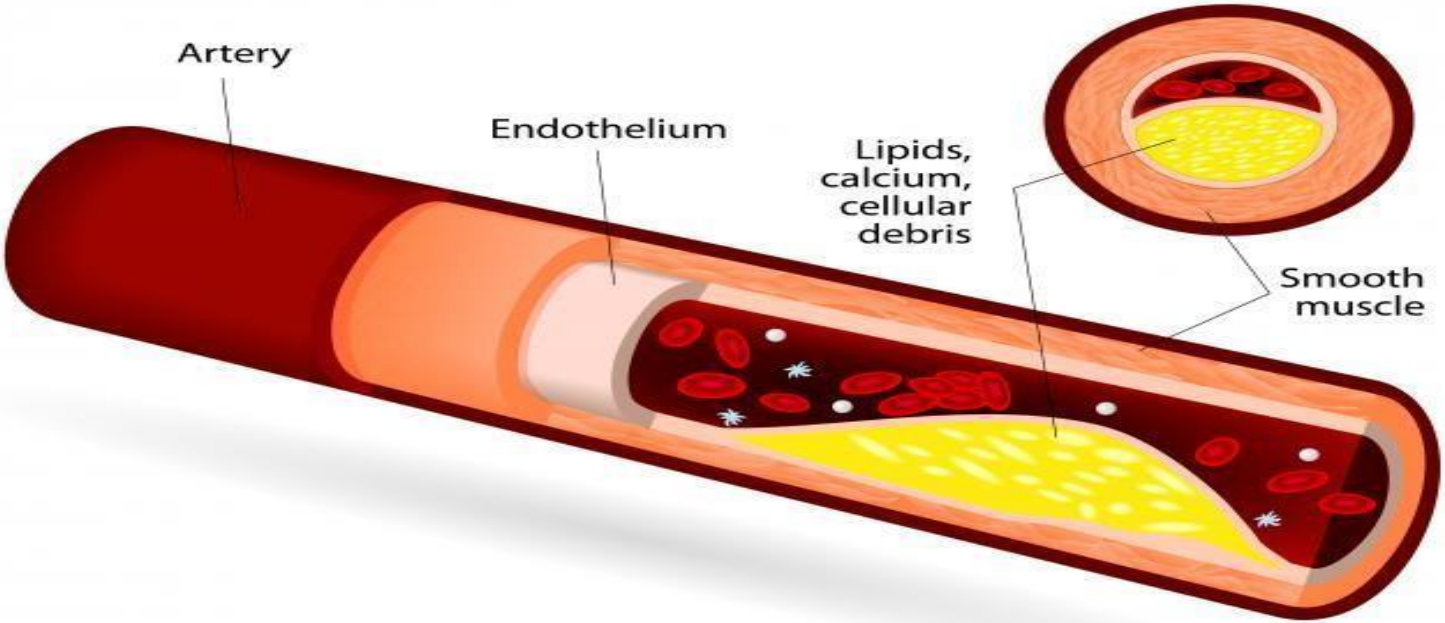
- Aneurysm is Localized circumscribed dilatation of an artery, vein or cardiac chamber.
- The arterial wall is composed of stretched intima and adventitia with only remnants of media. There is a tendency for aneurysms to enlarge progressively and to ultimately rupture.

- Arteriosclerosis is hardening of the arteries.
- It includes those degenerative changes characterized by induration **(fibrous thickening),** loss of elasticity, and narrowing of the lumen.
- The **"hallmark"** of arteriosclerosis is the fibrous plaque which appears as a white, firm, glistening elevation on the luminal surface of arteries.
- It is not common in animals.
- Etiology**:** Johne's disease ,Toxins, Hypertension, Hypothyroidism in old dogs

- Subclassifications within the broad category of arteriosclerosis are atherosclerosis, medial sclerosis, and arteriolosclerosis.

- Atherosclerosis is characterized by the accumulation of lipid in larger arteries in the form of elevated, lipid-filled plaques called atheromas.
- Athere means a soft, mushy, gruel like substance.
- Atherosclerosis is a condition such a substance is deposited in the intima of larger elastic arteries.
- The atheroma begins as an intimal lesion which progressively extends into and affects the media.

ATHEROSCLEROSIS



1. Inflammation of Veins

- Phlebitis is characterized by the presence of inflammatory exudate in the wall of veins. The condition is less common than arteritis.

- Acute phlebitis occurs in **"naval infection" (Omphalophlebitis)** of calves, lambs and foals.

- The resulting bacteremia may lead to acute death or give rise to wide-spread suppurative lesions **(abscesses).**

- Lymphangitis is associated with several specific diseases, including:
  - Anthrax in dogs, pigs and horses **(acute thrombolic lymphangitis),**
  - Mycobacterium infections **(granulomatous lymphadenitis)** and
  - Cutaneous glanders of horses **(ulcerative lymphangitis).**
    - ulcerative lymphangitis**:** of horses is a chronic progressive inflammation of the subcutaneous lymphatics.
    - The condition is caused by Corynebacterium ovis **(C. pseudotuberculosis)** which is the pathogen responsible for caseous lymphadenitis of sheep and goat

1. High altitude Disease of Cattle

- Also referred to as "High Mountain Disease" "Brisket Disease", and "Pulmonary Hypertensive Heart Disease".

- High altitude disease of cattle develops subsequent to chronic hypoxia of a high altitude environment which causes increased pulmonary vascular resistance and increased pulmonary arterial pressure.

- Young cattle are more susceptible than adults and the morbidity rate is highest in animals exposed to high altitudes for the first time.

- 2. Mulberry Heart Disease of Swine
- Also referred to as Dietetic Microangiopathy
- Mulberry heart disease occurs primarily in pigs from 3- 4 months of age and the cause is unknown.
  - – it is widely felt that a deficiency of vitamin E and selenium plays a prime role.

- Parvovirus infection in pups is characterized by a severe non-suppurative myocarditis which causes sudden death in the 4 to 6-week age range. The viral myocarditis is apparently a new disease entity in the dog.

- Grossly, pulmonary edema is the most prominent lesion; the myocardium is grossly normal.

- Microscopically, there is a rather intense infiltration of the myocardium with mononuclear cells. Basophilic intranuclear inclusion bodies are found within cardiac myofibrils in association with the myocarditis.

- ANEURYSM: Localized circumscribed dilatation of an artery, vein or cardiac chamber.
- Fracture or necrosis of medial layer of large blood vessels permitting parallel blood circulation till the next division of blood vessel is called as Dissecting aneurysm or false aneurysm. • Formation of sac in artery due to dilation, also known as True aneurysm.
- ARTERIOSCLEROSIS: Arteriosclerosis is hardening of arteries causing 3 types of diseases in arteries depending on their size and etiological factors viz., Atherosclerosis, medial sclerosis and arteriolosclerosis.
- ATHEROSCLEROSIS: is characterized by hardening and thickening of intimal layer of large arteries and aorta due to proliferation of connective tissue, hyaline degeneration, infiltration of fat/lipids and calcification. These intimal changes may lead to loss of elasticity of artery (Athere means mushy substance).

- Medial sclerosis involve medium sized muscular arteries and characterized by fatty degeneration and hyalinization of muscular tissue of medial arteries leading to necrosis. This is also known as Monckeberg medial sclerosis.
- Arteriolosclerosis affects arterioles in kidneys, spleen and pancreas and is characterized by hyperplasia of intimal cells of arterioles producing concentric lamellations occluding their lumen.
- Telangiectasis is marked dilation of veins particularly of sinusoidal capillaries in one or more lobules in liver.
- MANCHESTER WASTING DISEASE OF CATTLE: Calcific arteiosclerosis
- POLYARTERITIS NODOSA (PERIARTERITIS NODOSA): It is a collagen disease affecting all layers of the wall of artery

PATHOLOGY OF RESPIRATORY SYSTEM

- PATHOLOGY OF UPPER RESPIRATORY TRACT
  - *Rhinitis* is the inflammation of nasal mucosa of upper respiratory passage
  - Nasal discharge
    - Catarrhal
    - Purulent
    - Fibrinous
  - Infection may extend to lower parts of respiratory tract and reach in lungs

- Rhinitis (porcine atrophic rhinitis): *Bordetella bronchiseptica* in pigs - Mucopurulent exudate - Disappearance of nasal septum - Retarded growth of snout
- *Epistaxis* is bleeding from nasal passage due to trauma, neoplasm and ulcerative lesions as a result of infections
- *Pharyngitis* is the inflammation of pharynix
- *Laryngitis* is the inflammation of larynx

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- *Sinusitis* is the inflammation of sinuses
  - Frontal sinusitis in dehorned cattle
  - Larvae of botfly *Oestrus ovis* enters in nasal passage and migrate upto frontal sinuses and turbinate bones and cause mucopurulent inflammation
  - Leeches (*Dinobdella ferox)* is known to cause nasal cavity inflammation in domestic animals and suck blood
- Nasal polyps are the inflammatory condition of respiratory mucosa resembling neoplastic growth caused by fungus and characterized by formation of new growth simulating benign neoplasm in nasal passage
- Rhinosporidium sceberi, a fungus most commonly prevalent in southern India

- Macroscopic features: Formation of a single polyp in respiratory mucosa, pedunculated, elongated, fills nasal cavity. Cauliflower like growth may cause bleeding

- Microscopic features: Fibrous covering by mucous membrane and heavily infiltrated by neutrophils, lymphocytes, eosinophils, macrophages around fungus

Nasal Granuloma

- Nasal granuloma is the granulomatous inflammation of respiratory mucosa in nasal cavity caused by blood flukes and characterized by the presence of granulomatous growth filling the nasal passage causing obstruction

- Etiology

  - *Schistosoma nasalis*, a blood fluke

  - Type II hypersensitivity reaction of nasal mucosa to plant pollens, fungi, mites etc

- Macroscopic Features: Nasal pruritus. Small tiny nodules on nasal mucosa later becomes cauliflower like growth
- Microscopic features
  - Oedema in lamina propria
  - Infiltration of eosinophils, mast cells, lymphocytes and plasma cells and absence of epithelioid cells
  - Proliferation of fibroblasts
  - Lesion is covered by squamous epithelium
  - Mucous glands may have metaplastic pseudo stratified columnar
  - epithelium

TRACHEITIS

- Tracheitis is the inflammation of trachea
- In canines, it is tracheobronchitis while in poultry it is manifested by laryngo tracheitis
- Etiology
  - Canine tracheobronchitis caused by adenovirus, influenza virus and herpes virus
  - Avian infectious laryngotracheitis (ILT) is caused by herpes virus
- Microscopic features
  - Inclusion bodies in tracheal and bronchial epithelium in canines
  - Haemorrhagic tracheitis, presence of intra nuclear basophilic inclusions in tracheal epithelial cells in infectious laryngo tracheitis

- Bronchitis is the inflammation of bronchi, characterized by catarrhal, suppurative, fibrinous or haemorrhagic exudate.
- Etiology
  - Bacteria *e.g.* Pasteurella
  - Virus *e.g.* Infectious bronchitis in poultry
  - Parasites
  - Allergy/ Inhalation of pollens etc.

PATHOLOGY OF LUNGS

- Atelectasis is the failure of alveoli to open or the alveoli are collapsed and thus do not have air
- Etiology
  - Obstruction in bronchi/ bronchiole
  - Pleuritis
  - Atelectasis neonatorum in new born animals
  - In the absence of respiration, lung alveoli remain closed and thus sink in water indicating still birth

- Macroscopic features
  - Dull red in color, hard area of lung like liver in consistency
  - Atelectic lung sinks in water
- Microscopic features
  - Compressed alveoli
  - Absence of air spaces
  - Collapsed bronchioles
  - In inflammatory condition, exudate compresses alveoli

Emphysema

- Emphysema is the increase in amount of air in lungs characterized by dilation of the alveoli. It may be acute or chronic and focal or generalized
- Etiology
  - Bronchitis
  - Atelectasis in adjoining area of lung
  - Pneumonia
  - Allergy to dust, Pollens etc
  - Pulmonary adenomatosis

PNEUMONIA

- Pneumonia is the inflammation of lungs characterized by congestion and consolidation of lungs
- Various stages of pneumonia
  - Stage of Congestion
  - Red hepatization
  - Grey hepatization
  - Resolution

- Stage of congestion: This stage of lung is characterized by active hyperemia and pulmonary oedema.
- Stage of red hepatization: This stage of lung is characterized by the consolidation of lungs due to accumulation of blood in blood vessels (congestion). The consolidated lungs are firm and looking like liver and hence the name" red hepatization".
- Stage of grey hepatization: The lung remains hard but due to lysis and removal of erythrocytes, it becomes grey or less red in colour.
- Stage of resolution: After a week, the recovery starts in the form of resorption of fluid; autolized cells and debris is removed by phagocytic cells. The causative organism is neutralized or removed from the lungs through immunity of body

- Bronchopneumonia is the inflammation of lungs involving bronchi or bronchioles along with alveoli. It is thought to be spread through bronchogenous route
- Macroscopic features:
- Congestion and consolidation of anterior and ventral parts of lungs (Lobular pneumonia)
- Patchy lesions on one or several lobes and adjacent area shows Emphysema
- Mediastinal lymphnodes are swollen
- Microscopic features
  - Congestion, edema or hemorrhage in lung
  - Infiltration of neutrophils, mononuclear cells in and around bronchioles/ bronchi
  - Catarrhal inflammation of bronchi and Proliferation of bronchiolar epithelium

INTERSTITIAL PNEUMONIA

- Interstitial pneumonia is the inflammation of the lungs characterized by thickening of alveolar septa due to serous/ fibrinous exudate along with infiltration of neutrophils and/or mononuclear cells and proliferation of fibroblasts
- It is also known as lobar pneumonia
- Spread Mainly through hematogenous route

- Macroscopic features
  - Lungs are pale or dark red in colour
  - Oedema, dripping of fluid from cut surface
- Microscopic features
  - Alveoli may have serous or fibrinous exudate
  - Thickening of alveolar septa due to accumulation of exudate, inflammatory cells and in chronic cases, proliferation of fibrous tissue
  - Infiltration of mononuclear cells in alveolar septa

FIBRINOUS PNEUMONIA

- Fibrinous pneumonia is the inflammation of lungs characterized by the presence of fibrin in alveoli or bronchioles and may give rise to hyaline membrane formation over the surface of alveoli or bronchiole

- Macroscopic features
  - Antero-ventral portion of lung is congested and consolidation
  - Colour of lungs become deep red due to congestion
  - Surface of lungs is covered by fibrin sheet
  - Interlobular septa are prominent due to accumulation of plasma and fibrin

- Microscopic features
  - Principal exudate is fibrin, fills alveoli, bronchioles and bronchi
  - Congestion and/or hemorrhages
  - Infiltration of neutrophils, macrophages and giant cells
  - Formation of eosinophilic false membrane of fibrin over the surface of alveoli and bronchiole and then known as *hyaline membrane pneumonia*

Verminous Pneumonia

- Etiology
  - *Metastrongylus apri* in pig
  - *Dictyocaulus filariae* in sheep and goat
  - *D. viviparus* in cattle and buffaloes
  - *Capillaria aerophila* in dogs and cats
  - *D. arnfieldi* in horse and donkeys

- Aspiration pneumonia is caused by faulty medication through drenching which reaches in lungs instead of target place (digestive track) and characterized by necrosis and gangrene of lung paranchyma
- Etiology
  - Drugs, food, foreign body and oil drench which reaches in lungs through trachea
  - Paresis of throat predisposes the animal for aspiration pneumonia

Mycotic pneumonia

- Mycotic pneumonia is caused by a variety of fungi and characterized by the presence of chronic granulomatous lesions in lungs
- Etiology
  - *Aspergillus fumigatus*
  - *Blastomyces* sp.
  - *Coccidioidomyces immitis*
  - *Cryptococcus* sp.

- Macroscopic features
  - Nodules in lungs
  - On cut, cheese like caseative mass comes out from nodules
  - Caseation involves both bronchiole and alveoli
  - Such lesions may also present in trachea, bronchi and air sacs

- Microscopic features
  - Presence of granulomatus lesions *i.e.* caseative necrosis, macrophages, epithelioid cells, lymphocytes, giant cells, fibroblasts etc.
  - Presence of branched hyphae of fungi in the necrosed area

TUBERCULOUS PNEUMONIA

- Tuberculous pneumonia is caused by *Mycobacterium* sp. and characterized by the presence of chronic granulomatous lesions in the lungs
- Etiology
  - *Mycobacterium tuberculosis*
  - *M. bovis*

- Grey, white or light yellowish nodules in lungs
- Nodules are hard, painful and/or calcified
- Animal carcass is cachectic, weak or emaciated
- On cut, the cheesy material come out from the nodules
- Microscopic features
- Tubercle comprises a central necrosed area surrounded by macrophages, epithelioid cells, lymphocytes, giant cells and covered by fibrous covering
- Acid-fast bacilli bacteria may present in necrosed area
- Central area may be calcified

PULMONARY ADENOMATOSIS

- Pulmonary adenomatosis/ OVINE PULMONARY CARCINOMA: is a slow viral disease of sheep and characterized by metaplasia of alveolar squamous epithelium to cuboidal and/or columnar epithelium leading to glandular appearance of alveoli

- Etiology: Retrovirus (Pulmonary adenomatosis virus)

- Pneumoconiosis is the granulomatous inflammation of lungs caused by aerogenous dust particles of sand, silica, beryllium, carbon or asbestos. It is also known as anthracosis.
- Roaring is impaired sound due to laryngeal hemiplegia in horses.

- Air sacculitis is inflammation of air sacs caused by *E. coli*, Mycoplasma, reovirus etc. and characterized by thickening of the wall of air sacs and presence of cheesy exudate
- Pleuritis is the inflammation of pleura characterized by serous, fibrinous or purulent exudate
- It is also known as *pleurisy*

- Presence of air in pleural cavity is termed as *pneumothorax*
- Presence of lymph in pleural cavity is called as *chylothorax*
- Tuberculous pleuritis is characterized by small nodules on pleura and is known as
- *"pearly disease"*
- In chronic cases, development of fibrous tissue causes adhesions and is known as *adhesive pleuritis*

Pathology of Digestive System

- Epitheliogenesis imperfecta of tongue Abnormal smooth surface of tongue due to small filiform papillae. It occurs as a defect in autosomal recessive gene and occurs in Holstein-Friesian cattle. This is also known as smooth tongue.
- Cleft palate: This is most common congenital abnormality occurs due to failure of oral-nasal cavity to divide leaving cleft. It may also extend towards lips producing 'hare lip' condition. Cleft lip (Chelioschisis) and cleft palate (Palatoschisis)
- Mega colon There is distention of colon which abruptly terminate in rectum due to mutant gene in dogs.
- Duplication of colon In dog, the colon is duplicated from caecum to rectum and this defect is associated with malformation in the body of vertebrae T4 and T5·
- Atresia coli In calf, the absence of colon occurs and the intestine terminates in blind caecum.
- Atresia ani This is absence of anal opening.

- Ranula: When the dilatation of the salivary duct and gland occurs as cyst on the floor of the mouth it is called a ranula.
- Sialoliths: Sialoliths are salivary calculi which are common in horses.

PATHOLOGY OF MOUTH CAVITY

- Stomatitis is the inflammation of mucosa of oral cavity. It includes:
- Gingivitis: Inflammation of gums
- Glossitis: Inflammation of tongue
- Cheilitis: Inflammation of lips
- Tonsilitis: Inflammation of tonsil
- Palatitis/Lampas: Inflammation of palates

- Catarrhal stomatitis: Mucous exudation in oral cavity.
- Vesicular stomatitis: Vesicles in oral mucosal e.g. FMD
- Erosive stomatitis: Erosions in oral mucosa e.g. Rinderpest
- Fibrinous stomatitis: False membrane in oral mucosa.
- Ulcerative stomatitis: Presence of ulcers in oral mucosa e.g. mucosal disease.

PHARYNGITIS

- Inflammation of pharynx
- Paroxysmal coughing
- Cattle- Actinobacillus lignieressi, Fusobacterium necrophorum, IBR
- Horse- Strangles, EHV, parainfluenza virus
- Pigs – Anthrax

- **PHARYNGEAL OBSTRUCTION -** stertorous respiration, enlargement of retropharngeal lymph nodes

PHARYNGEAL PARALYSIS

- - inability to swallow
- **Etiology:** Peripheral Nerve injury,
- -Guttural pouch infection in horses,
- -Trauma,
- -Rabies,
- -Botulism,
- -AHS,
- -Central lesion.

Pathogenesis

Inability swallow and regurgitation

↓

Roaring due to laryngeal paralysis

↓

CUD DROPPING due to partial pharyngeal paralysis.

↓

Aspiration pneumonia

- Choke is complete or partial obstruction of esophagus either due to any foreign material or pressure from adjoining areas.
- Etiology • Beets, turnip, carrots, bone • Abscess tumor of neck area

Oesophageal obstruction

- Cattle: choke in cervical region
- Horses: thoracic part of oesophagus
- Barium radiography help in diagnosis

- Esophagitis is the inflammation of esophagus caused by trauma, parasites etc. and characterized by catarrhal inflammation, ulceration or stenosis due to fibrosis.
- Etiology • Trauma due to foreign bodies • Chemicals- Acids, alkalies • Infection- Mucosal disease virus • Parasite- Spirocerca lupi • Nutritional- Vit. A deficiency

- INGLUVITIS: inflammation of crop caused by fungi and characterized by ulcerative or diphtheritic lesions.
- Etiology • Candida albicans • Monilia albicans
- Turkish towel like appearance in crop mucosa.

Ruminal Tympany (Bloat)

- Normally, the bulk of this gas is eliminated by eructation or belching
- Bloat is the overdistension of the rumen and reticulum with gases derived from fermentation.

Frothy bloat (primary tympany)

fermentation gases are trapped in a stable, persistent foam which is not readily eructated. This type of bloat occurs most commonly in two settings:

- Animals on pasture, particularly those containing alfalfa or clover (pasture bloat). These legumes are rapidly digested in the rumen, which seems to results in a high concentration of fine particles that trap gas bubbles. Additionally, some of the soluble proteins from such plants may serve as foaming agents.
- Animals feed high levels of grain, especially when it is finely ground (feedlot bloat). Again, rapid digestion and an abundance of small particles appear to trap gas in bubbles.
- Pasture bloat: The vital factor is the frothiness of ruminal contents. The stable dispersion of feed particles are responsible for the frothiness.
- Feedlot bloat: Feedlot bloat is due to feeding finely ground grain. High carbohydrate content increases encapsulated bacteria that produce slimes. The slime entraps the gases of fermentation. Maximum stability of foam occurs at pH of about 6.

- Excessive green or legumes intake →Chloroplast released from the legume leaf forms monomolecular foams that trap gas bubbles → Frothy bloat (Pasture bloat)
- Saponin, pectin, hemicellulose – help in production of foam in rumen
- **Pectin methyl estrase** present in leaf hydrolyse pectin to polygalactouronic acid and acid pectin which possess gel formation property.
- Foam may block cardia and hence eructation

Free gas bloat (secondary tympany)

- occurs when the animal is unable to eructate free gas in the rumen.
- partial obstruction the esophagus (foreign bodies, abscesses, tumors) or interfere with rumenoreticular motility (i.e. reticular adhesions, damage to innervation of the rumen)
- A ruminant cannot eructate when lying on its back, and if a cow falls into a ditch and is unable to right itself, she will bloat rapidly.

- Saliva has **Antifoaming property due to mucin** which prevent froth formation by reducing surface tension. If volume, composition or rate of secretion of saliva is altered → possibility of **gel formation.**

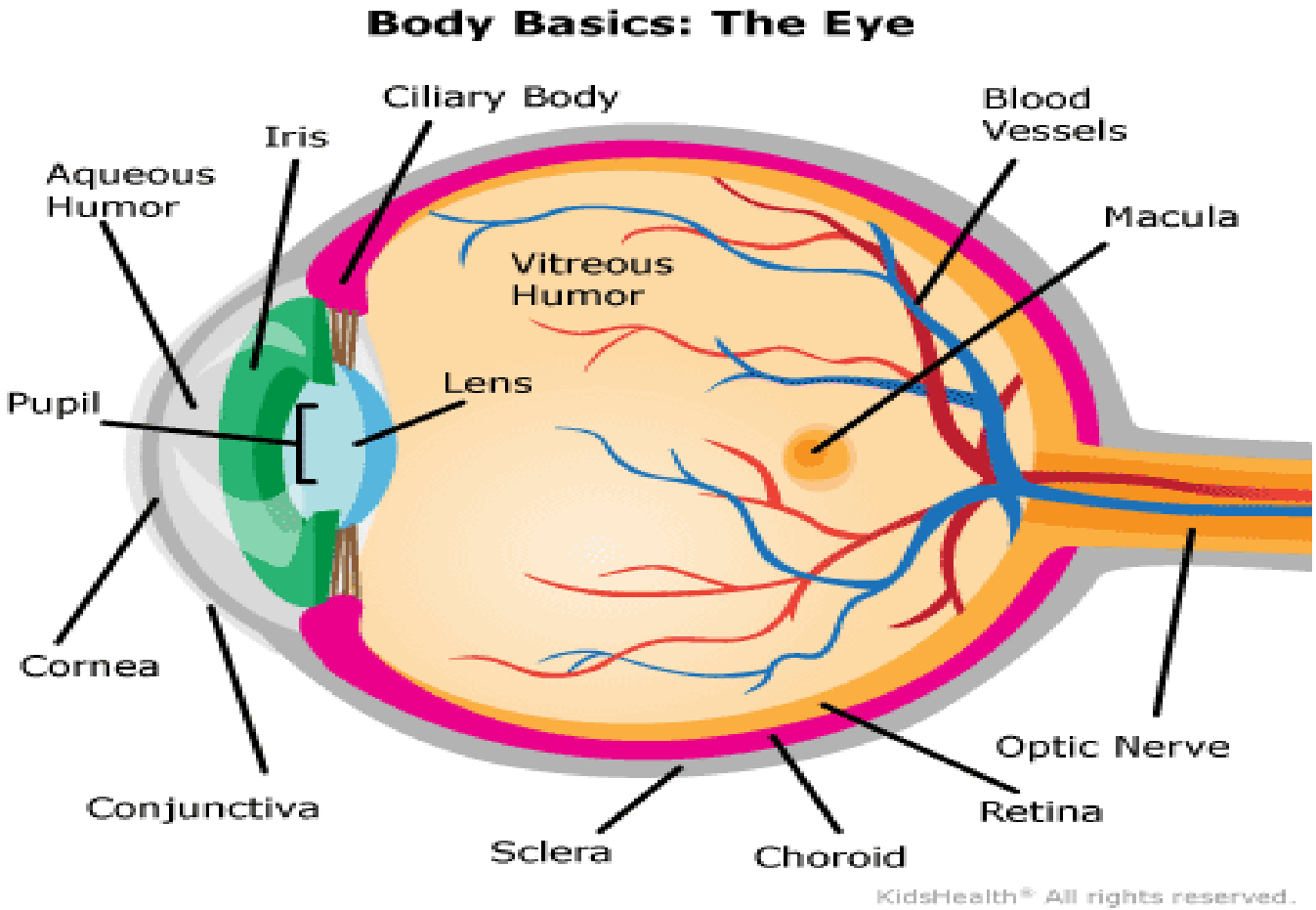
- Low pH due to excessive CHO feeding help mucinolytic bacteria proliferation →bacteria also produce **insoluble slime due to mucopolysaccharide** which increase viscosity →froth formation

- distention of the rumen compresses thoracic and abdominal organs. Blood flow in abdominal organs is compromised, and pressure on the diaphragm interferes with lung function.
- The cause of death is usually hypoxia due to pulmonary failure.
- Anorexia, overdistension of the left flank
- Protrusion of the paralumbar fossa above the ventral column and enlarged abdomen
- Signs of abdominal pain – kicking at belly, looking at flank, rolling on ground, grinding of teeth
- Dyspnea and grunting
- Dyspnea manifested by open mouth breathing, protrusion of the tongue, and extension of the head

- antifoaming agents have been used to relieve frothy bloat.
- vegetable oils (corn, peanut) or mineral oil, which are administered in 100-300 ml volumes to cattle.
- A number of effective commercial products are available that include such agents as polaxalene (a surfactant) or alcohol ethoxylate (a detergent).

AFFECTIONS OF EYE

Structure of eye



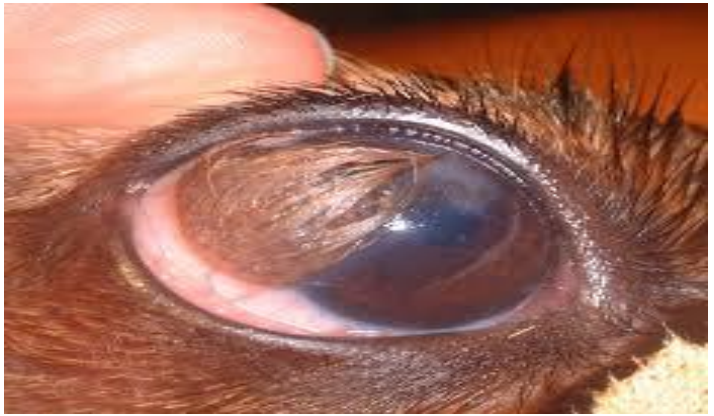
- The eye ball is located the orbit. It is protected by eyelids, which have stratified squamous epithelium (the conjunctiva) lining the surface that comes into contact with the eyeball.
- Just behind the eyelashes are a row of tiny sebaceous glands, the meibomian glands, the secretion of which serves to lubricate the eyelashes, preventing their adhesion.
- The lens is a peculiar structure composed entirely of epithelium. It has neither stroma nor vascular tissue. In front it is bathed by the aqueous humor and is nourished by it.
- Actually the anterior surface of the lens forms the posterior boundary of the anterior chamber. Its anterior surface is in contact partly with the iris.
- Its posterior surface fits into the depression of the vitrous- the hyaloid fossa.
- Usually, the conjunctival mucosa is free of bacteria either due to the flushing action of the tears or to the bacteriostatic property of the lysozyme.

CONGENITAL ANAMOLIES

Anophthalmia congenitus	Complete absence of one or both eyes.
Microphthalmia	One or both eyes are small.
Cyclops	There is only one eye due to fusion of the orbits.
Ankyloblepharon	Both the eyelids are fused together
Starbismus (Squint)	In animals this condition is bilateral with the two eye globules tuning inwards.
Entropion	Turning in of the eyelids
Ectropion	Turning out of eyelids. Usually the lower eyelid is affected.
Coloboma	Failure of the closure of embryonic

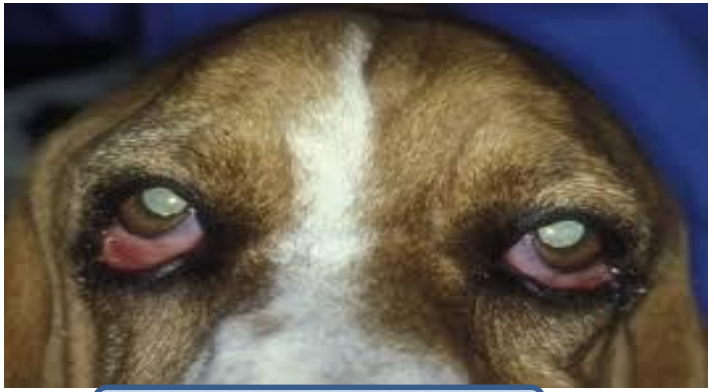
Dermoids of cornea	**Due to the sublethal factor. The cornea of one or both eyes is partly covered by skin.**
Congenital anterior synechia	There is adhesion between iris and the posterior surface of the cornea.
Microphakia	The lens is small and is spherical.
Luxation of the lens	The dislocated lens is opaque.
Cataract	A condition in which the lens becomes opaque.
Congenital aplasia of retina and hypoplasia of the optic nerve	May be met with in calves and they are born blind.

Cyclops



Dermoids of cornea

Entropion



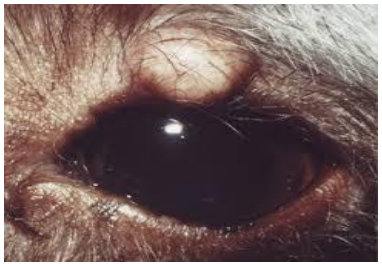
Ectropion

- Trichiasis: Turning in of the eyelashes.

- Blepharitis: Inflammation of eyelids.

- Hordeolum or stye: Inflammation or even abscess formation of the follicles of an eyelid.

- Chalazion: Abscess formation of the meibomian glands.



- Exophthalmos:Exophthalmos means protrusion of the eyeball.
- Enophthalmos: Enophthalmos means sinking of the eyeball into the orbit.
- Orbital cellulitis: Inflammation of the orbit is called orbital cellulitis.

PATHOLOGY OF LACHRYMAL GLAND

- Dacryoadenitis: Dacryoadenitis is the inflammation of the lachrymal glands.
- Conjunctivitis: Inflammation of the conjunctiva is called conjunctivitis.
- Pannus: Pannus is a condition in which vascular granulation tissue is found between the corneal epithelium and the Bowman's membrane.
- Keratitis: Inflammation of the cornea is called keratitis.
- Corneal ulceration occurs during acute or chronic conjunctivitis. There may be prolapse of the iris through the rupture (Staphyloma), followed by dislocation of the lens.

Infectious keratoconjunctivitis in cattle (Pink eye)

The causative organism is *Moraxella bovis* which is gram negative and is found in the tears. An endotoxin that causes necrosis of the skin is produced by this organism.

Luxation of the lens

The lens is anchored by the suspensory ligaments to the ciliary body. If these ligaments are ruptured, the lens may be displaced into the anterior chamber or into the hyaloid fossa or into the vitreous.

Cataract : Opacity of the lens is known as cataract.

Congenital: Failure of the hyaloid artery to regress and disappear completely or Impairment of translucence of the lens due to abnormal arrangements of the lens fibres .

Acquired: Degeneration of the lens due to Trauma, Luxation, Senility, Diabetes mellitus, deficiency of vitamin D; deficiency of vitamin C in the lens; deficiency of cystein

- Anterior synechia: Anterior synechia is the condition in which there is adhesion of the iris to the posterior surface of the cornea.
- Posterior synechia: Posterior synechia is the adhesion of the posterior surface of the iris to the anterior surface of the lens capsule.
- Iridocyclitis: This is the inflammation of iris and ciliary body and is also known as anterior uveitis. This condition in horses is known as periodic opthalmia.
- Mydriasis: Dilatation of the pupil is known as mydriasis. This can be brought about by various drugs like atropine, hyocyamine and stramonium, cocaine, adrenaline and amphetamine.
- Myasis: Constriction of the pupil is known as myasis. This can be brought about by pilocarpine, physocarpine and ergotamine.

- Glaucoma is a condition in which there is increased intraocular pressure leading to secondary changes in the eyeball like enlargement of eye ball, opaque cornea and increase aqueous humor.
- It may be unilateral or bilateral
- Increased intraocular pressure may result from a) too excessive a secretion of the aqueous humor or b) hindrance in its drainage.
- Primary glaucoma: If the causes that give rise to obstruction of the flow, leading to glaucoma cannot be determined with certainty, the condition is known as primary glaucoma.
- Secondary glaucoma: If the causes for such obstruction can be determined, the condition is known as secondary glaucoma .

PATHOLOGY OF EYE BALL

- Ophthalmitis is Inflammation of the eye ball.

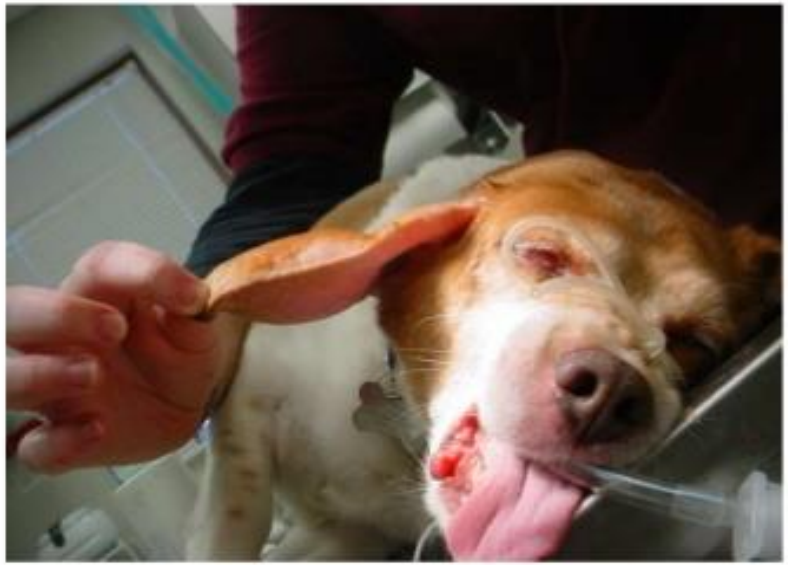
- Xerophthalmia is abnormal dryness of the eye ball, with inflammation and ridge formation, typically associated with vitamin A deficiency.

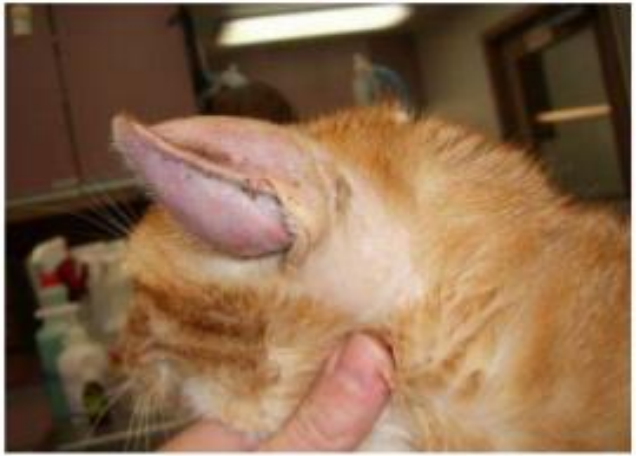
Affections of Ear

Otitis externa: Inflammation of the external ear.

Otitis media: Inflammation of the middle ear.

Otitis interna: **Inflammation of internal ear.**





Pathology of Endocrine System

Endocrine disorders may be subdivided into three groups:

- Endocrine gland hyposecretion (leading to hormone deficiency)
- Endocrine gland hypersecretion (leading to hormone excess)
- Tumours (benign or malignant) of endocrine glands

PITUITARY GLAND

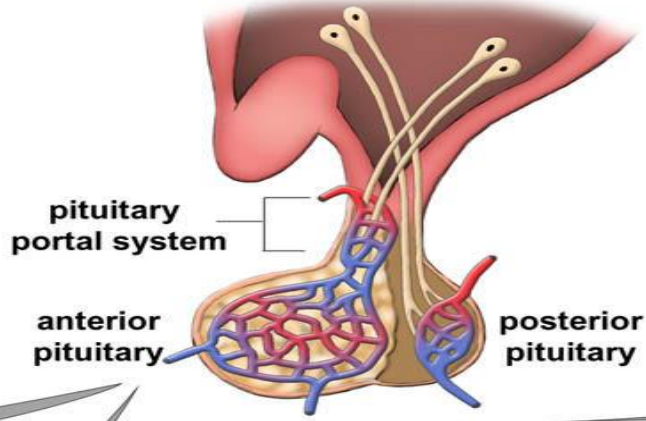
Neurosecretory cells produce releasing and release inhibiting hormones.

These hormones are secreted into a portal system.

Each type of hypothalamic eighter stimulates or inhibits production or secretion of another pituitary hormone.

The anterior pituitary secretes its hormones into a blood stream.

Hypothalamus



Neurosecretory cells produce ADH and oxytocine.

These hormones move down axons to axon endnes.

When appropriate, ADH and oxitocine are secreted from the axon endnes into the blood stream.

gonadotropins (FSH & LH)

ovaries, testes

growth hormone (GH)

bones, tissues

prolactin (PRL)

Mammary glands

adrenocorticotropic hormone (ACTH)

adrenal cortex

thyroid stimulating hormone (TSH)

thyroid gland

antidiuretic hormone (ADH)

kidney tubules

oxytocin (OT)

Mammary glands

oxytocin (OT)

smooth muscle in uterus

HYPERPITUITARISM: This condition is manifested by overgrowth and proliferation of bones.

- In man this is called "Gigantism" in young growing individuals in whom the ossification of bone has not yet stopped and "Acromegaly" in adults in whom no more growth occurs.

Gigantism

- Gigantism is due to increased secretion of somatotropin in the young. The individual grows very tall and the skin and subcutaneous tissues show fibrous hyperplasia. Since STH is diabetogenic, glycosuria is a symptom.

- If the patient lives beyond the age of epiphyseal fusion acromegaly may result.

Acromegaly (akros=extremity; megale=enlarged)

- The hands and the feet are abnormally large and the fingers are crooked and knotty. The facial bones become long and thick, especially the jaw, resulting in prognathism. Nose, lips and ears become large.
- Viscera are enlarged (splanchnomegaly or macrosplanchnia) and fibrous hyperplasia of skin and subcutaneous tissue.
- Kyphosis is also seen in some.
- Impotence in the male and amenorrhoea in the female are the other symptoms.
- Diabetes mellitus occurs due to diabetogenic action of the hormone.
- Eye lesions may be noticed due to pressure on the optic chiasma by the tumor

HYPOPITUITARISM

Causes of pituitary hypofunction

- Pressure by: a) Tumors b) Cysts
- Inflammation and sclerosis
- Infarction and necrosis
- Hydrocephalus – bulging of the floor of the ventricles
- Abnormal development
- Tuberculosis

Pituitary dwarfism or infantilism

- Hypofunction in the young children causes in pituitary Dwarfism or Infantilism. This condition is not seen in animals.

Simmond’s disease (Pituitary cachexia) or Sheehan’s Syndrome

- This condition is described in female dogs, due to postpartum necrosis of the pituitary consequent on thrombosis following hemorrhage.

Clinical signs

- Severe cachexia, loss of sexual function, weakness, low metabolic rate, loss of hair and pigmentation, mental apathy, drowsiness, microsplanchnia, extreme dehydration and emaciation.

Lesions

- Atrophy and fibrosis of the thyroid, adrenal glands, ovaries and parathyroids together with the symptoms and lesions consequent on the deficiency of the hormones secreted by these glands and structures.

Frohlich's Syndrome- Dystrophia adiposogenitalis

- This develops probably due to the pressure by a tumor or hydrocephalus and is mostly found in females.
- Decreased level of gonadotrophins.

Clinical signs

- Obesity: There is disproportionate accumulation of fat.
- Genital hypoplasia and decreased sexual function
- Idiocy or mental retardation
- Thin skin and hair
- Reduced sweat secretion

DIABETES INSIPIDUS

- In Hypo secretion of ADH, reabsorption of water from the glomerular filtrate does not occur and so large quantities of urine with low specific gravity are passed and this condition is known as diabetes insipidus.
- Lesions of the pars nervosa or any causes that injure the hypothalamus will produce diabetes insipidus.

Causes are:

- Trauma- surgical or fractures
- Pituitary tumor or metastases form.
- Meningitis- pressing on the stalk/ Encephalitis.

Pineal gland is a tiny gland located above the posterior extremity of the third ventricle of brain.

- It secrets a hormone called melatonin.
- Melatonin antagonizes the action of the melanocyte stimulating hormone.

Pineal dysfunction

- Pineal hyperfunction is associated with delayed puberty.
- Pineal hypofunction results in precocious puberty.

Neoplasms of pineal gland

- Tumors reported in pineal gland include pinealoma, glioma and teratoma.

Pancreas

- The pancreas has both endocrine and exocrine functions.
- islets of Langerhans: regions in the pancreas that contain its endocrine cells (5% of total cells)
- Both insulin and glucagon are responsible for the regulation of blood glucose levels in the body.

- Of all the diseases and disorders of the pancreas, the most well-known is diabetes.
- Type 1 diabetes: Body doesn’t produce any insulin to handle the glucose in your body.
- Type 2 diabetes: Type 2 diabetes is much more prevalent than type 1. Able to produce insulin, but their bodies don’t use it correctly. They might also be unable to produce enough insulin to handle the glucose in their body.

Adrenal gland

- The two major hormones produced by the adrenal cortex are the mineralocorticoids, which regulate the salt and water balance, and the glucocorticoids, which can regulate blood glucose and the body's inflammatory response.
- There are three main glucocorticoids: cortisol, corticosterone, and cortisone.
- The adrenal medulla produces the hormones epinephrine and norepinephrine; these hormones regulate heart rate, breathing rate, cardiac muscle contractions, blood pressure, and blood glucose levels.

- glucocorticoid: Produced by the adrenal cortex, that are involved in metabolism and have anti-inflammatory properties
- aldosterone: Secreted by the adrenal cortex, that regulates the balance of sodium and potassium in the body
- epinephrine: (adrenaline) an amino acid-derived hormone secreted by the adrenal gland in response to stress

Hyperfunction of adrenal cortex

Cushing's syndrome

- In hyperfunction of the adrenal cortex,

there is excess of circulating hydrocortisone.

The disease produces a wide variety of signs and symptoms which include obesity, excessive body hair (hirsutism), osteoporosis, and stretch marks in the skin, caused by its progressive thinning.

Adrenogenital syndrome (Adrenal virilism)

- In this condition there is an excess of androgens – masculanising hormones.

Hypofunction

Chronic hypofunction (Addison's disease): The manifestation of Addison's disease may occur only if there is bilateral destruction of the glands. This condition is exceedingly rare in animals. It is observed in tuberculosis and hypopituitarism. In this condition, there is general weakness, anemia, low blood pressure and brown pigmentation of skin.

Female Genital system

- ***Freemartinism***
  - **Genetic female born co-twin with a male**
  - Most commonly in cattle.
  - Twinning occurs in 1-2% of pregnancies in cattle
  - Anastomoses develop between the placental vascular systems of the two fetuses
  - Male fertile and female sterile

Hermaphroditism

- In hermaphrodites, there is presence of organs of both sexes in same individual animal. Both ovarian and testicular tissue occur in one animal leads to sterility in animal (true hermaphrodite) while in pseudohermaphrodite the gonadal tissue of only one sex is present but there is some degree of development of opposite sex organs.

- White heifer disease White heifer disease occurs due to a single sex linked gene defect responsible for white coat colour
- normal ovaries, oviduct but uterus is incomplete and may lack communication with cervix. There is hypoplasia of cervix and vagina.
- Uterus didelphys is the occurrence of two cervix with two uterine bodies and single or double vagina. It occurs due to failure of Mullerian ducts to fuse at their distal end.

- **Perioophoritis*:*** Inflammation of the serosal surface of the ovary
- **Oophoritis:** Inflammation of the ovary

- ***Follicular Cysts* :**
  - **G**rafian follicle does not rupture and enlarge
  - Nymphomania (persistent sexual desire) is observed in cows and bitches
- ***Luteinized cyst*:**
  - This type of cyst develops when ovulation fails to occur and the theca undergoes luteinization.

Follicular cyst	Luteal Cyst
Thin, soft and fluctuating	Always hard
May be single or multiple	Always single
Animal is nymphomanic (Buller)	Animal is anestrous
Incidence is higher	Incidence is lower.
Thickness of follicular wall is less than 3 mm	Thickness of luteal wall is more than 3 mm
Sterility hump	Adrenal virilism
P4<1ng/ml in serum is indicative of follicular cyst.	P4 concentration >2ng/ml in milk and >1ng/ml in serum
High estrogen in blood	Low estrogen in blood

- **Salpingitis** means inflammation of the oviduct
- **Hydrosalpinx** denotes a cystic dilatation of a part of the oviduct, containing clear fluid.
- **Pyosalpinx** means pus in the salpinx

- **Abnormalities of position or location**
- ❶Torsion of the uterus: uncommon except in the cow and mare.
- ❷Prolapse of the uterus: commonly in ruminants

- **Endometritis:** Inflammation is restricted to the endometrium of the uterus

- **Metritis:** Inflammation of the uterus and is found in all animals.

- **Perimetritis** : Inflammation of the serosa is known as perimetritis .

- **Pyometra:** literally means pus in the uterus. But usually this term is applied to chronic suppurative metritis
- ***Hydrometra and mucometra***
- The accumulation of thin (hydro) or viscid fluid (muco) in the uterus is concurrent with the development of endometrial hyperplasia or is proximal to an obstruction of the lumen of the uterus, cervix, or vagina.

- **Abortion:** an abortion is defined as the expulsion of a fetus before term
- ***Stillborn***: A dead fetus delivered within the period of expected parturition
- **Premature birth**: The birth of a viable fetus before term

- **Mummification:**
  - In absence of any bacterial infection, the fluids are resorbed and the membranes become closely applied to the desiccated fetus.
  - The whole mass becomes brown or black and rather leathery

- **Maceration:** fetal death, regression of corpus luteum but abortion fails to occur. It stays in uterus and starts getting putrefied. This is due to infection present in uterus or may be introduced from outside.
- **Adenomyosis:** the presence of endometrial glands and stroma between the muscle bundles of the myometrium

- **EPIVAG**: Infectious bovine cervicovaginitis and epididymitis – Bovine herpesvirus 1
- **Infectious pustular vulvovaginitis** of cattle
- **Pneumovagina:**
  - Common in mare
  - Sucking of air through vagina

ABORTION

- Expulsion of a dead fetus prior to the normal full gestation period is called abortion
- Abortion is mostly due to infection of the
  - Fetus
  - Placenta
  - Uterus
  - since these conditions cause death of the fetus.

Etiology - First Trimester

- **TRICHOMONIASIS:** *Trichomonas fetus*
- Bull harbors the flagellate in the mucous membrane of the penis, terminal portion of urethra and prepuce
- Abortion will occur within about 16 weeks of pregnancy

Etiology - Second Trimester

- **VIBRIOSIS** : (*Campylobacter fetus*)
- In the cow abortion occurs between the 5th and 7th months of
- pregnancy
- In the sheep, abortion occurs at 2nd month of pregnancy.

Etiology - Third Trimester

- **BRUCELLOSIS: *(Brucella abortus)***
  - 7th month of gestation in the cow
  - Produced Placentitis – Fetal death & Abortion
  - Retention of placenta is most common complication
- **LISTERIOSIS: *(Listeria monocytogenes)***
  - Fetus die to septicemia
- **LEPTOSPIROSIS: *(Leptospira interrogans, serovars pomona and hardjo.)***
- abortion after 6th month of pregnancy

- Enzootic abortion of ewes
  - *Chlamydophila abortus (C. psittaci)*
- Toxoplasmosis
  - *Toxoplasma gondii*
- *Bovine herpesvirus 1*
- Bovine Virus Diarrhea – 1st or 2nd trimester
- Infectious Bovine Rhinotracheitis - 2nd or 3rd trimester
- Equine viral arteritis:- 9th or 10th month.

MALE GENITAL SYSTEM

- Testicular hypoplasia occurs in animals with chromosomal abnormality such as XXY chromosomes or Klinefelter's syndrome. Hypoplasia is also seen in hermaphrodites and in animals with cryptorchidism.
- Cryptorchidism: The testicle fails to descend in scrotum through inguinal canal after birth and remains in abdominal cavity.
- Phimosis is the failure of extension of penis from its sheath.
- Paraphimosis is the failure of withdrawal of extended penis.
- Priapism: Prolonged erection of penis

- Hypospadias: In hypospadias, there is urethral opening in ventral side of the penis.
- Epispadias: There is urethral opening on the dorsal side of the penis
- Phallocampsis: is the deviation of penis, which may be spiral (Cork screw penis) or ventral deviation (rainbow penis).
- ORCHITIS: inflammation of testes characterized by edema, necrosis and infiltration of neutrophils, macrophages, lymphocytes and proliferation of fibrous tissue leading to atrophy in chronic cases.
- Accumulation of serous fluid in scrotal sacl tunica vaginalis is called as hydrocele.
- Epididymitis is the inflammation of epididymis characterized by catarrhal or suppurative exudate with necrosis of lining epithelium.

- Funiculitis is inflammation of scirrhous cord characterized by enlargement of scrotum due to chronic abscess.
- Balanoposthitis is the inflammation of prepuce and glans penis characterized by phimosis or paraphimosis and pain during copulation. Balanitis is inflammation of glans penis and posthitis is inflammation of prepuce.

PATHOLOGY OF URINARY SYSTEM

- Aplasia: Absence of one or both kidneys
  - Absence of one kidney is observed in animals with compensatory hypertrophy of another kidney and such animals may survive
  - **Hypoplasia**: Size of kidneys remain small which don't grow properly

Cyst in Kidney

- Single or multiple cysts in pig and dog kidney
- Arise from nephron due to its distension
- Presence of multiple cysts is also termed as congenital polycystic kidney
- Type-I polycystic kidney: Due to dilation and hyperplasia of collecting tubules
- Type-II polycystic kidney: Due to absence of collecting tubules and failure of nephron
- Type-III cysts in kidneys: occur due to multiple abnormalities during development. Cysts develop from tubules or Bowmen's capsule with part of glomeruli in cyst.

Proteinuria

- Presence of protein particularly albumin in urine
- As smooth, homogenous, pink staining precipitate also called as „cast“
- Presence of albumin in urine is indicative of damage in glomeruli
- Characterized by oedema due to protein deficiency

Haematuria

- blood in urine
- Due to damage or haemorrhage from glomeruli to urethra
- Most important cause of haematuria In fern toxicity
- Intact erythrocytes are present and settle down after some time leaving clear urine as supernatant

Haemoglobinuria

- Presence of haemoglobin in urine
- Urine becomes brownish red in colour
- Caused by Leptospira sp., Babesia sp. or phosphorus deficiency in animals
- Urine remains turbid and coloured on centrifugation

Glycosuria

- Presence of glucose in urine
- Also known as diabetes mellitus
- May occur due to insulin deficiency
- In sheep due to enterotoxaemia caused by *Clostridium welchii* type D.

- **Ketonuria**
  - Presence of ketone bodies in urine
  - Common in diabetes mellitus, pregnancy toxaemia, starvation
- **Oligouria**: Decreased amount of urine

- Anuria: Absence of urine is known as anuria
- Polyuria: Increased amount of urine leading to frequent urination caused due to diabetes insipedus, hormonal imbalance and polydypsia.
- Uremia: The presence of harmful waste products like uric acid, creatinine and urea in blood.

NEPHROSIS

- Nephrosis is the degeneration and necrosis of tubular epithelium without producing inflammatory reaction. It mostly includes acute tubular necrosis as a result of ischemia or toxic injury to kidney. Nephrosis is characterized by necrosis and sloughing of tubular epithelial cells exhibited by uremia, oligouria, anuria.

- Etiology: Hypotension, Heavy metals, Mycotoxins e.g. Ochratoxin, Antibiotics e.g. Gentamicin

GLOMERULONEPHRITIS

- Inflammation of glomeruli primarily characterized by pale and enlarged kidneys with potential haemorrhage, oedema of glomeruli, congestion and infiltration of inflammatory cells
- Due to presence of mesangial proliferation, it is also called as mesangio proliferative glomerulonephritis (MPGN)

- **Etiology**

  - Streptococci infection
  - Immune complexes
  - Environmental pollutants - Organochlorine pesticides

- ***Macroscopic features***

  - Enlarged kidneys
  - Oedema, pale kidneys
  - Petechiae on kidneys
  - Proteinuria, uremia, hypercholesterolemia and increased creatinine level in blood

Interstitial nephritis

- Interstitial nephritis is the inflammation of kidney characterized by degeneration and necrosis of tubular epithelium, edema and infiltration of inflammatory cells in interstitium.
- **Etiology**
  - Ochratoxins and atrinin
  - Leptospira
  - Toxins/ poisons e.g. Pesticides
  - Herpes virus
  - Endogenous toxaemia e.g. Ketosis
  - Immune complexes

PYELONEPHRITIS

- Pyelonephritis is the inflammation of renal pelvis and parenchyma i.e. tubules characterized by congestion, suppurative inflammation and fibrosis.

- **Etiology**: Corynebacterium renale, Staphylococcus aureus, E. coli, Actinomyces pyogenes, Pseudomonas aeruginosa

- Congestion, hemorrhage and abscess formation - cortex, pelvis and ureters.

- Pyuria- Pus mixed urine in bladder.

- Enlargement of kidneys • Congestion, hemorrhage

- Nephrosclerosis is chronic fibrosis of kidney characterized by loss of glomeruli and tubules and extensive fibrosis.
- Urolithiasis is the formation of stony precipitates any where in the urinary passage including kidneys, ureter, urinary bladder or urethra.
- Ureteritis is the inflammation of ureter characterized by enlargement, thickening of wall due to accumulation of urates, or calculi, pyonephrosis and pyelonephritis.

CYSTITIS

- Cystitis is the inflammation of urinary bladder characterized by congestion and fibrinous, purulent or hemorrhagic exudates.
- Etiology • Urinary calculi • Tuberculosis • Blockage in urethra • Bracken fern poisoning

Pathology of Nervous System

- Necrosis of neurons in brain - encephalomalacia
- necrosis of neurons in spinal cord - myelomalacia.
- Necrosis in gray matter - polioencephalomalacia
- necrosis in white matter - leukoencephalomalacia.
- The necrosis of nerve fibers starts from myelin sheath and this change is called as demyelination or Wallerian degeneration.

Inflammation

- Encephalitis- brain
- Myelitis- spinal cord
- Encephalomyelitis- brain and spinal cord
- Meningitis- meninges
- Pachymeningitis- duramater
- Leptomeningitis- pia- arachnoid mater
- Meningoencephalomyelitis- meninges, brain and spinal cord
- Polioencephalitis- grey matter in brain
- Poliomyelitis- grey matter in the spinal cord

- Paralysis- complete immobility of a muscle due to defective innervation
- Paresis- incomplete loss of motion due to defective innervation
- Hemiplegia- paralysis arising in the brain cortex and in the peripheral nerves and is unilateral (paralysis of one side of the body)
- Paraplegia-bilateral paralysis of the posterior parts of the body and hind limbs resulting from injury to the spinal cord

- Anencephaly means absence of brain.
- Microencephaly means small size of brain.
- Cranioschisis is failure of cranium to fuse which results in hernia of meninges and known as meningocele.
- Hernia of meninges and brain is known as meningoencephalocele.
- Rachicele- hernia of the spinal cord
- Hydrocephalus: excessive accumulation of fluid in the brain.

- Blood vessels acquire a meningothelial sheath and a second outer sheath derived from the pia.
- A perivascular space is formed between these sheathsthe space of Virchow- Robin. In this space the cells accumulate and give rise to “perivascular cuffing

- Spongiform encephalopathy is characterized by the presence of vacuoles in grey and/or white matter.
- Etiology:
  - Prion proteins
  - Scrapie in sheep
  - BSE in cattle

Lymphocytic meningoencephalomyelitis

- Rabies- intracytoplasmic inclusions- hippocampus in dogs and cerebellum in cattle
- Pseudorabies- Herpes virus- pigs
- Swine fever
- Canine distemper
- Equine encephalomyelitis
- Louping ill
- Epidemic tremor
- Ranikhet disease –pneumoencephalitis of poultry
- Parasitic- Hypoderma bovis larvae, Oestrus ovis larvae- Myiasis • Coenurus cerebralis- larvae of Multiceps multiceps – Gid or sturdy • Cerebral nematodiasis (Neurofilariasis, kumri)- Setaria digitata

- Osmotic encephalopathies
- Sodium chloride (salt) poisoning: “sodium ion toxicosis”, “water deprivation syndrome”
- Host- pigs, poultry & occasionally in ruminants.
- The disease is due to hypernatremia caused by excessive intake of sodium salts or severe dehydration followed by rehydration

Thiamine deficiency

- Function of thiamine: Vitamin B1 is a necessary cofactor for the enzyme transketolase
- Transketolase is the rate limiting enzyme in the hexose monophosphate shunt (pentose phosphate pathway)
- This is the major metabolic pathway for glucose utilization in the brain
- Also a co-factor for other enzymes (i.e. pyruvate decarboxylase) in the Kreb‟s cycle
- Neurologic disease is thought to represent an energy deficit due to the inhibition of these metabolic pathways.

- Carnivores (dogs, cats) – Chastek’s paralysis
- Herbivores (including ruminants) have no or little dietary requirement for thiamine.
- disease in ruminants has been given the name polioencephalomalacia or laminar cerebrocortical necrosis.

- In horses, thiamine deficiency encephalopathy has been associated with horses eating plants containing a thiaminase enzyme such as bracken fern (Pteridium spp.), horsetails (Equisetum spp.) or given the coccidiostat amprolium (a structural analog of thiamine – may inhibit uptake from the gut)
- Polyneuritis in Poultry

Pathology of Hemopoitic and Immune System

- Autoimmune hemolytic anemia in foals: incompatible blood group antigens of male and female parents. The mare does not have that blood group antigen but foetus acquires it from father.
- The foetal blood exposed to dam through placental exchanges that leads to induction of antibody production in mares against foetal blood group antigen.
- These antibodies accumulate in colostrum and when foal suck the milk from mares, they are readily absorbed through G.I. tract of foals in blood and causes destruction of erythrocytes leading to anemia.

- Chediak Higashi Syndrome: This syndrome is related with defects in phagocytic cells such as defective neutrophils and monocytes.
- The defects are in chemotaxis, engulfment and killing of bacteria and associated with defective assembly of cytoplasmic microtubules

Anemia

- decrease in number of erythrocytes or hemoglobin concentration in erythrocytes per unit of blood and is characterized by pale mucus membrane, dyspnoea, cardiac hypertrophy and weakness.

Macrocytic anemia

- characterized by increased size of RBC and occurs due to acute blood loss or hemolysis resulting in excessive production and availability of immature erythrocytes in blood.
- Such cells also have reduced amount of hemoglobin and termed as hypochromic.
- Macrocytic normochromic anemia is increase size of RBC with normal hemoglobin and has been observed in deficiency of folic acid, niacin and vitamin B12

- Normocytic anemia are most common in animals occurs due to neoplasia, irradiation and are also known as aplastic anemia as a result of aplasia or agenesis of RBC.
- Normocytic normochromic, normal size of RBC with normal hemoglobin anemia occurs as a result of depression of erythrogenesis.
- Microcytic anemia is reduction in size of erythrocytes with decreased hemoglobin (Microcytic hypochromic) and occurs in deficiency of iron and pyridoxine or chronic blood loss.

- In anemia, the size of RBC varies markedly with some large and some small size and is known as anisocytosis.
- The presence of abnormal shape (elongated, angular, ovoid, distorted) of RBC is termed as poikilocytosis.

- **Basophilic stippling (Punctate basophilia)**

➢ Here the erythrocyte has blue staining granules scattered through out.

➢ These are remnants of RNA. This condition is seen in anaplasmosis in bovines, haemonchosis in sheep and in lead poisoning.

- Some erythrocytes stain unevenly with some dark and light colour spots and are known as *polychromatophilia* which is an indication of active erythrogenesis.
- The denaturation and precipitation of hemoglobin leads to appearance of purplish granules in RBC near the cytoplasmic membrane which are known as *"Heinz bodies“*
- Heinz body anemia is a type of anemia that occurs when red blood cells break down faster than the body can replace them. It's caused by Heinz bodies, which are clumps of damaged hemoglobin in red blood cells.

- Hemolytic anemia occurs due to excessive lysis of erythrocytes and characterized by icterus, hemoglobinuria, and presence of nucleated erythrocytes in blood and hemosiderosis in spleen.
- Hemorrhagic anemia occurs due to severe haemorrhage, extravasation of blood and characterized by pale mucus membrane and hemorrhage in body.
- Deficiency anemia occurs as a result of deficiency of iron, copper, cobalt and vitamins (vitamin B12, Pyridoxine, riboflavin and folic acid) and characterized by pale mucus membrane, weak and debilitated body and decreased number of erythrocytes with hypochromasia in blood.

- Toxic aplastic anemia is agenesis or aplasia of hemopoietic tissues in bone marrow and there is lack of erythrocyte production.
- Autoimmune hemolytic anemia occurs as a result of destruction of erythrocytes by immune mechanisms developed against erythrocytes.

- Polycythemia is increase in number of erythrocytes in circulating blood. It may be relative increase as a result of dehydration or decrease in plasma volume or absolute due to anoxia.
- Oligocythemia: decrease in number of RBCs

- Leucocytosis is increase in number of leucocytes in circulating blood caused by various infections.
- There is also increase in white blood cells in blood due to neoplastic condition and is known as Leukemia.
- increase in number of neutrophils is termed as neutrophilia, eosinophils as eosinophilia
- lymphocytes as lymphocytosis, basophils as basophilia and of monocytes as monocytosis.

- Leucopenia is decrease in number of white blood cells.
- If there is decrease in number of all 5 cells of leucocytes, it is known as panleucopenia.
- Decrease number of neutrophils is termed as neutropenia and lymphocytes as lymphopenia.

Oncology

- Oncology: (Oncos= tumor, logos= study)
- Key points
  - Continuous growth
  - Resemblance to embryonic cells
  - No structural arrangement
  - No useful function
  - No clear etiology
- Greek language means “New formations or new growth” (Neo= new, plasm= growth)
- A mass of tissue formed as a result of abnormal, excessive, uncoordinated, autonomous and purpose less proliferation of cells

Important growth disturbances

- Agenesis - Complete absence of growth of an organ/ tissue.
- Aplasia - Congenital disturbance with complete failure of development of an organ or tissue. Only primitive structure or rudimentary structure is present.
- Hypoplasia - Failure of an organ to develop to its normal size.
- Atrophy - Reduction in size of an organ/ tissue less than its former normal size. The reduction of size is either due to decrease in number or size of cells of an organ.
- Hypertrophy - Increase in size of an organ or tissue due to increase in the size of cells of that organ.

- Hyperplasia - Increase in size of an organ or tissue due to increase in the number of cells of that organ.
- Metaplasia - Substitution of one cell type by another type of cells. e.g. Squamous metaplasia of oesophageal glands of poultry in Vitamin A deficiency (nutritional roup).
- Dysplasia - Abnormal development of cells in a tissue/ organ.
- Anaplasia - Reversion of cells to a more primitive or embryonic and less differentiated type.

NEOPLASM

- A neoplastic growth does not obey the laws of the healing
- Cells of a neoplasm continue to multiply indefinitely
- Irrespective of any structural or functional requirements and form an ever increasing mass of tissue
- Size: One mm diameter to several centimeter
- Weight: Few milligram to several kg

Colour

- Grayish white, yellow, red, brown or black
  - Fatty tissue
    - Yellow
  - Haemorrhage or congestion
    - Pink or red in colour
  - Melanoma or melanosarcoma
    - Black colour
  - Haemoglobin
    - Brown colour

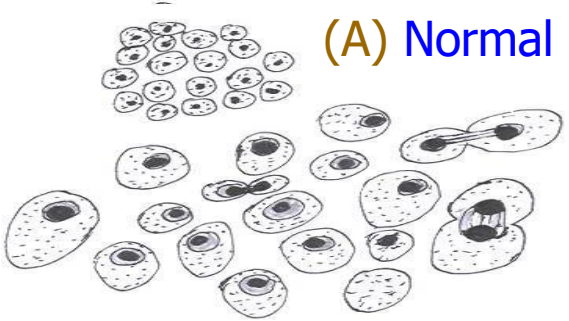
Consistency

- Tumour of bone
  - Hard
- Connective tissue tumours
  - Firm
  - Dense
  - Sclerotic
- Brain tumours
  - Soft

- **TYPES**
  - Benign tumours: Adult type
  - Malignant tumours: Embryonic stages

- Microscopically, the tumour is composed of cells which resembles the type of tissue/ organ involved.
- The appearance of cells vary on degree of malignancy.
- In benign tumours, the cells are of adult type while in malignant tumours these cells are having characteristics of embryonic stages.
- This reversion towards embryonic type is also known as anaplasia.

- **Anaplasia**
  - More anaplastic - more malignancy



(A) Normal

(B) Anaplastic cells

Degree of anaplasia

- Enlargement of nucleus
- Multiple nuclei in a cell
- Enlargement of nucleolus
- Increase number of mitotic figures
- Hyperchromasia of the cell
- Embryonic type cells

1. Enlargement of nucleus: The nucleus of tumour cell is enlarged which is indicative of a rapid cell growth and towards embryonic stage of the cell.
2. Multiple nuclei in a cell: The tumour cells having multiple nucleus are indicative of rapid cell division and such cells are known as tumour giant cells.
3. Enlargement of nucleolus: The increased size of nucleolus is also an indication of rapid cell growth; sometimes it becomes 2-3 times larger in size than normal.
4. Increase number of mitotic figures: More number of mitotic figures, the more severe malignancy will be there.
5. Hyperchromasia of the cell: The neoplastic cell takes intense colour and if it is more embryonic, it takes more intense colour and nucleus stains dark with hematoxylin.
6. Embryonic type cells: The neoplastic cell loses its resemblance to adult cells. The cell growth is not under control.

ETIOLOGY

- **Intrinsic or predisposing factors**
  - Heredity: Chicken leucosis
  - Age: More common in old age
  - Pigmentation: White horses melenosarcoma and Hereford cattle squamous cell carcinoma
  - Sex: mammary tumor in females
  - Extrinsic factors
    - Physical: Radium, UV-rays, X-rays, ionizing radiation

Initiators

- **Chemicals**
  - Coal-tar
  - Naturally occurring products: Aflatoxins, Actinomycin D, Mitomycine, Safrole
- Polycyclic aromatic hydrocarbons: Tobacco, smoke, pollutants, methylcholanthrene, benzapyrene, benzanthracene
- Aromatic amines: naphthylamine bezidine
- Metals: Nickel, lead, cobalt, chromium
- Insecticides: Aldrin, Dieldrin, Chlordane

- **Promoters**
  - Phenols
  - Hormones: Estrogen
  - Drugs: Phenobarbital
- Artificial sweetness: Saccharine
- Coloring / flavoring agents, preservatives

- **Virus**
  - Papilloma virus
  - Polyoma virus
  - Adeno virus - Hamsters- Sarcoma
  - Poxvirus- Rabbit- Myxomatosis
  - Hepdna virus- Hepatitis B virus
  - Retrovirus
  - Herpes virus

- Neoplasms are divided into two major groups:
- (1) benign and (2) malignant.
- Benign tumour usually does not kill the patient, grows slowly, and does not spread to distant organs.
- Malignant tumour, on the other hand, kills the patient by progressive local invasion and also by spread to distant organs (metastasis).

All tumours, both benign and malignant, have two basic components:

(1) the parenchyma. This is made up of transformed or neoplastic cells

(2) the supporting, host-derived non-neoplastic stroma, made up of connective tissue and blood vessels.

The parenchyma determines the biological behaviour of the neoplasm.

The stroma carries the blood supply and provides support for the growth of parenchymal cells.

In general, benign tumours are designated by attaching the suffix , ‘oma’ to the cell type from which the tumour arises.

TYPES OF NEOPLASM

- Benign neoplasms
  - Fibroma, Chondroma, Adenoma, Papilloma
- Malignant neoplasms
  - Lymphosarcoma, Adenocarcinoma, Squamous cell carcinoma

- Malignant tumours are commonly called cancers.

Tumour Classification

(A) Epithelial: Tumours derived from epithelial surfaces, either squamous or glandular.

(1) Benign

(a) Papilloma: involves an epithelial surface

(b) Adenoma: involves glandular epithelium.

(2) Malignant

(a) Carcinoma: involves either squamous or glandular epithelium.

(B) Non-epithelial: Tumours derived from connective tissue in general (fibrous tissue, cartilage, bone, muscle).

(i) Benign: The name of the tissue plus' oma' (fibroma, chondroma, osteoma).

(ii) Malignant: Indicated by the term sarcoma (fibrosarcoma, chondrosarcoma, osteosarcoma).

(C) Dermal cyst tumour: This tumour arises from an embryonic defect in growth and is composed of one germ layer only, the ectoderm, and contains teeth, hair, and other dermal structures.

(D)Teratoma: This tumour also arises from an embryonic defect in growth and is composed of two or more germ layers.

	Tissue of origin	Benign	Malignant
I	Neoplasms of one parencymal cell type		
(i)	Epithelial neoplasms		
1.	Squamous epithelium	Papilloma	Squamous cell carcinoma
2.	Transitional epithelium	Papilloma	Transitional cell carcinoma
3.	Glandular epithelium	Adenoma	Adenocarcinoma
4.	Basal cell layer	-	Basal cell carcinoma
5.	Melanoblasts	Melanoma	Melenocarcinoma
6.	Hepatocytes	Liver cell adenoma	Hepatocellularcarcinoma
7.	Placenta	-	Choriocarcinoma

	Tissue of origin	Benign	Malignant
(ii)	Non-epithelial neoplasms (mesenchymal)		
1.	Adipose tissue	Lipoma	Liposarcoma
2.	Fibrous tissue (adult)	Fibroma	Fibrosarcoma
3.	Fibrous tissue (embryonic)	Myxoma	Myxosarcoma
4.	Bone	Osteoma	Osteosarcoma
5.	Cartilage	Chondroma	Chondrosarcoma
6.	Smooth muscle	Leiomyoma	Leiomyosarcoma
7.	Skeletal muscle	Rhabdomyoma	Rhabdomyosarcoma
8.	Blood vessels	Hemangioma	Hemangiosarcoma

	Tissue of origin	Benign	Malignant
9.	Lymph vessels	Lymphangioma	Lymphangiosarcoma
10.	Meninges	Meningioma	Invasive meningioma
11.	Lymphoid tissue	Lymphoma	Malignant lymphoma
12.	Brain nerve sheath	Neurofibroma	Neurogenic sarcoma
13.	Brain nerve cell	Ganglioneuroma	Neuroblastoma
14.	Blood cells (lymphocytes)	-	Leukemia
15.	Mesothelium	-	Mesothelioma

Tissue of origin	Benign	Malignant
(A) Tumours of mesenchymal origin		
1. Connective tissue and derivatives		
Fibrous connective tissue cell	Fibroma	Fibrosarcoma
Embryonal connective tissue that produces mucin	Myxoma	Myxosarcoma
Adipose tissue cell	Lipoma	Liposarcoma
Chondrocyte	Chondroma	Chondrosarcoma
2. Endothelial and related tissues		
Blood vessels	Haemangioma	Haemangiosarcoma
Lymph vessels	Lymphangioma	Lymphangiosarcoma
Mesothelium	–	Mesothelioma
Meninges	Meningioma	Invasive meningioma
3. Tumours of haematopoietic cells		
Lymphoid cells	–	Lymphoid leukaemia
	Lymphoma	Lymphosarcoma
Myeloid cell	–	Myeloid leukaemia
Plasma cells	–	Multiple myeloma
4. Tumours of muscle		
Smooth	Leiomyoma	Leiomyosarcoma
Striated	Rhabdomyoma	Rhabdomyosarcoma
(B) Tumours of nervous tissue		
Glia		Glioma Gliosarcoma
Neuron	Neuroma	Neuroblastoma
(C) Tumours of epithelial origin		
1. Stratified squamous	Papilloma	Squamous-cell (or epidermoid) carcinoma
2. Basal cells of the skin or adnexa	–	Basal cell carcinoma
3. Glandular epithelium	Adenoma	Adenocarcinoma
4. Neuroectoderm (melanocytes)	Melanoma	Melanocarcinoma
5. Urinary tract epithelium (transitional)	Transitional cell papilloma	Transitional cell carcinoma
6. Testicular epithelium (germ cells)	–	Seminoma

Table 1.3. Difference between benign and malignant tumours

Sl.No.	Characteristics	Benign	Malignant
1.	Growth rate	Slow	Rapid
2.	Growth limits	Circumscribed/ covered	Unrestricted
3.	Mode of growth	Expansion	Invasion
4.	Differentiation	Good	Anaplasia
5.	Metastasis	Absent	Frequent
6.	Recurrence on surgery	Rare	Frequent
7.	Microscopic features	Resembles with tissue of origin	Poor resemblance with tissue of origin
8.	Basal polarity	Retained	Often lost
9.	Pleomorphism	Absent	Present
10.	Tumour giant cells	Absent	Present
11.	Anaplastic	Often absent	Present

- Preneoplastic conditions There are some preneoplastic lesions which predisposes the subsequent development of cancer. These are as follows:

a. Chronic inflammatory conditions of liver of old dogs have multiple nodules which are considered preneoplastic nodules and neoplastic cells do arise from such nodules. Such dogs have higher incidence of hepatocellular carcinoma.

b. Intraepithelial neoplasia are restricted to the epithelium only without infiltration in adjacent tissue. On cytology there are malignant features of the cells but with no invasion and they remain confined to epithelium. e.g. Uterine cervix, Solar keratosis, Bowen's disease of skin, Oral leucoplakia

c. Role of pre neoplastic lesions in squamous cell carcinoma, transitional cell carcinoma of bladder and malignant melanomas of skin and oral cavity is well established.

d. Some benign tumours like multiple adenoma of large intestine becomes malignant (adenocarcinoma) after sometime

- Neoplasia like malformations
- A hamartia is a tissue defect of cells normally found in a particular area. Hamartoma is a tumour characterized by excessive focal overgrowth of mature cells in an organ.
- Chorista is a tissue defect of structures not found normally in that area. Choriostoma is tumour of such structures.
- Teratoma are made up of a number of parenchymal cell types arising from more than one germ layer.

NEOPLASTIC CELL GENESIS (CARCINOGENESIS)

- **Cell differentiation**
  - Specialized cells derived from less specialized cells (embryonic cells) is controlled by specific gene.
  - Genes for embryonic characters are switched off
  - Genes for differentiated characters activated
  - In neoplastic cells, the presence of abnormal genes (genetic mechanisms) or normal genes expressed at abnormal level (epigenetic mechanism) favour proliferation over differentiation.

- **In neoplastic cells**
  - Abnormal genes (genetic mechanisms)
  - Epigenetic mechanism: Genome is normal in cancer cell but transcription and translation is abnormal which is responsible for abnormal growth of cells.

VIRAL ONCOGENESIS

- **Oncogenes:** Oncogenes are the transforming genes present in host tumour cells of animal and man. It is also present in certain viruses.
  - Cellular oncogenes (c-oncs) or
  - Proto-oncogenes

- Proto-oncogenes are converted into active oncogenes through following mechanisms:
  - Point mutation
  - Translocation
  - Gene amplification
  - Inappropriate expression of proto-oncogenes
  - Integration of viral DNA into host cell DNA

- Cellular oncogenes of host cell can transcribe its copies in viral genome (retroviruses) and then it is known as v- oncogenes (voncs). So c-oncs or v-oncs are closely related genes and have high degree of homology.
- neoplastic growth occurs either as a result of activation of oncogene or due to inactivation of antioncogene.

- How the viruses cause cancers
  - A direct effect of gene (v-oncs)
  - A viral factor that affects a host gene (c-oncs)
  - A factor that inactivates the antioncogene
  - Genes that do not affect the cell growth but influence the expansion / metastasis

Oncogenes

- Rous Sarcoma Virus – src
- Avian Leucosis Virus – myc, erb-B
- Feline Leukemia Virus – pim-1, myc
- Papilloma virus- src, raf, myc
- Hepadna virus- hap

- Possible viral induced tumours
  - Pulmonary adenomatosis of sheep
  - Nasal adenocarcinoma of sheep
  - Equine cutaneous histiocytoma

NEOPLASTIC CELL METABOLISM

- Normal regulation of programmed protein synthesis is lost
- Gene expression and mRNA translation is being directed towards
  - Purine synthesis to meet the requirement of mitosis
  - Defective sodium pump (ATPase)
  - Increased glycolysis

NEOPLASTIC CELL STRUCTURE

- Anaplasia
- Loss of contact
  - Decreased adhesiveness
  - More negative charge
  - Decreased calcium content
  - Abnormal glycoprotein and glycolipids
  - Absence of fibrinolactin

- Neoplastic cell lack contact inhibition: Absence of gap junctions (Vitamin A promotes gap junctions)
- Abnormal cytoskeleton of cells
  - Abnormal microfilament
  - Defective actin polymerization
  - Abnormal microtubules
  - Abnormal polymerization of tubulins and Abnormal shape

Metastasis

- **Infiltration**
  - Growth of new cells so as to increase the size
  - Lack of contact inhibition in malignant tumour cells
  - Motility of malignant cells
  - Secretion of lytic enzymes by some malignant cells
  - Role of chemotactic factors and activation of complement

Mode of spread

- Expansion: Benign tumours are encapsulated and surrounded by fibrous tissue and hence they do not infiltrate in neighbouring tissue. However, they expand as their growth increases.
- Distant spread / metastasis

Lymphatic spread

- In general, epithelial tumours like carcinomas spread through lymphatic route.
- Sometimes lymphatic metastasis do not develop due to obliteration of lymphatics by inflammation; this is known as skip metastasis.
- Obstruction of lymphatics by tumour cells also disturbs the lymphatic flow and is responsible for metastasis at unusual sites. This is termed' as retrograde metastasis.
- e.g. 1. Carcinoma of prostate to supra clavicular lymph node, 2. Metastasis in adrenals from lung cancer.

Hematogenous spread

- Metastasis through blood is common route for most of the sarcomas (connective tissue tumours).
- Common sites of lodgment of tumour cells are liver, lungs, kidneys, brain and bones.

- **Mode of spread**
  - Transcoelomic spread
  - Spread along epithelial lined surfaces
  - Spread via Cerebrospinal Fluid (CSF)
  - Implantation: tumour cells are implanted at another site inadvertently

Process of metastasis

- Penetration (Invasion)
- Separation
- Dissemination
- Establishment
- Subsequent Proliferation

- Escape of neoplastic cells from immunological destruction
  - Delayed immunostimulation
  - Antigenic modulation
  - Antigenic overload
  - General immunodeficiency
  - Specific immunodeficiency
  - Humoral antibodies

BENEFICIAL EFFECTS OF TUMORS

- Monoclonal antibody production
  - Advantages
    - High titre
    - Mono specificity
    - Immortal clones
    - On mass scale in culture media one can produce even up to 1000 liters of antibody
    - Confirmatory diagnosis of diseases
- Cell culture

- **Clinicopathological effects**

  - Local effects: Pressure atrophy, Obstruction, Pain

  - Systemic effects: Cachexia, Hypoglycemia, Anemia

- **Clinicopathological effects**
  - Anemia
    - Haemorrhage
    - Decreased erythropoiesis
    - Increased erythrocyte fragmentation
    - Spleenomegaly
    - Iron deficiency
    - Anticancer therapy
    - Autoimmune anemia
    - Suppression of erythropoitin

- **Clinicopathological effects**
  - Thrombocytopenia
  - Thrombosis
  - Hypercalcemia
    - Osteolytic metastasis
    - Excessive bone resorption
  - Diarrhoea
  - Fever

PROGNOSIS OF NEOPLASMS

- Grading of neoplasms
- Staging of neoplasms

GRADING OF NEOPLASMS

- (Broder’s grading)

- Grade I: Well differentiated tumour (<25% anaplastic cells)
- Grade II: Moderately differentiated tumour (25-50% anaplastic cells)
- Grade III: Low differentiated tumour (50-75% anaplastic cells)
- Grade IV: Poorly differentiated tumour (>75% anaplastic cells**)**

STAGING OF NEOPLASMS

- TNM System
- T (primary tumour)

T0	=	No evidence of tumour
T1	=	Tumour confined to primary site
T2	=	Tumour invades adjacent tissue

- Lymphnode (penetration / metastasis)
- (N = local lymph node)

N0	=	No evidence of tumour
N1	=	Regional node involvement
N2	=	Distant node involvement

- Metastasis
- (M = distal lymph node)
  - M0 = No evidence of metastasis
  - M1 = In same cavity/place as primary tumour
  - M2 = Distant metastasis
- Stage I = T1, N0, M0
- Stage II = T1, N0, /N1, M1
- Stage III = T2, N1/N2, M2

- American Joint Committee (AJC) Staging
  - Stage 0 – IV
- ABC Staging System
  - Stage A: When tumour is confined to sub mucosa and muscle and has a cure rate 100%
  - Stage B: When tumour has penetrated the entire thickness of the wall into peri colic tissue and cure rate is 70%
  - Stage C: It is characterized by lymph node metastasis and reduces the cure rate to 30%

TUMOURS OF DIFFERENT TISSUE

TUMORS OF CONNECTIVE TISSUE

1. Fibroma & Fibrosarcoma
2. Myxoma & Myxosarcoma
3. Lopoma & Liposarcoma
4. Chondroma & Chondrosarcoma
5. Osteoma & Osteosarcoma
6. Histiosarcoma
7. Mast-Cell Tumour

TUMOURS OF EPITHELIAL TISSUE

1. Papilloma/Wart
2. Squamous Cell Carcinoma
3. Basal Cell Carcinoma
4. Adenoma
5. Seminoma

TUMOURS OF DIFFERENT TISSUE

TUMORS OF HAEMATPOITIC CELLS

1. Leukaemia
2. Multiple Myloma
3. Leukosis/Sarcoma

TUMOURS OF ENDOTHELIAL& RELATED TISSUE

1. Haemangioma and
2. Haemangisarcoma

TUMOURS OF DIFFERENT TISSUE

TUMORS OF NERVOUS TISSUE

1. Neuroblastoma
2. Pinealoma
3. Meningioma

TUMOURS OF MUSCLE

1. Leiomyoma &leiomyosarcoma
2. Rhabdomyoma & Rhabdomyosarcoma

TUMOURS OF CONNECTIVE TISSUE

1. FIBROMA & FIBROSARCOMA

Nasal polyps

It is an examples of soft fibroma (amount of collagen fibre are very less) It occurs commonly in the nasal passage of horses.

Gingival fibroma

found along gum line and called as Epulus/Epuli

Equine Sarcoid

It arises from fibrous connective tissue and occurs in the head , neck and fore-legs of horses & mules. It is indistinguishable from fibroma & Fibrosarcoma, as it recur after excision and doesn't metastasize Neoplastic cells are usually arranged in a whorled pattern of spindle-shaped cells.

Rous sarcoma of poultry:

It is a tumor of connective tissue induced by RNA viruses

Shope fibroma of rabbit:

Described by Shope in 1933.

It is a tumour of spindle shaped cells of connective tissue caused by DNA oncogenic viruses.

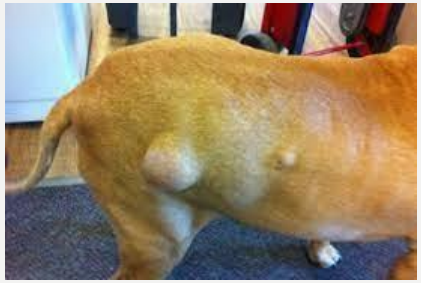
Occures as firm subcutaneous mass in rabbit

TUMOURS OF CONNECTIVE TISSUE

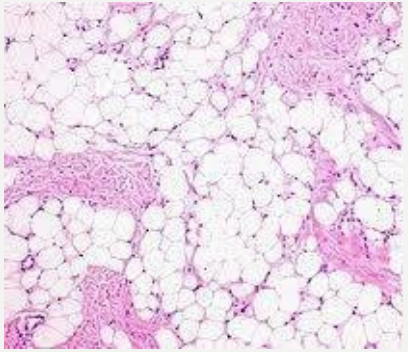
2. MYXOMA & MYXOSARCOMA

- These are tumours of connective tissue that are capable of producing mucin like material .
- Infectious Myxomatosis of rabbits is myxosarcoma caused by viruses and occurs as elevated nodular lesion on the head, neck and abdomen regions. These are tumours of connective tissue that are capable of producing mucin like material .

TUMOURS OF CONNECTIVE TISSUE



3. LIPOMA & LIPOSARCOMA



- It is chiefly a tumour of adipose tissue
- It occurs in older dogs.
- Lipoma is more common than Liposarcoma

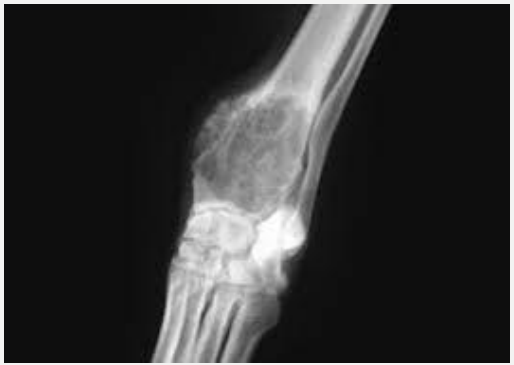
4. CHONDROMA & CHONDROSARCOMA

- These are tumours of primarily cartilaginous cells.
- Generally, it occurs at the epiphyses of long bones of extremities, costochondral and chondro-sternal junctions.
- Chondrosarcoma frequently metastasize to lungs, if left untreated.

TUMOURS OF CONNECTIVE TISSUE

6. OSTEOMA & OSTEOSARCOMA

- ✓ These are tumours of bone.
- ✓ In animals, osteomas are rare except in the dog.
- ✓ Osteosarcoma are also relatively more common in dogs and cats and occurred rarely in Horses and cattle .
- ✓ Osteoma must be differentiated from exostosis (inflammatory formation of



TUMOURS OF CONNECTIVE TISSUE

7. HISTIOSARCOMA/ CANINE TRANSMISSIBLE VENEREAL TUMOUR (CTVT)

Synonyms:
Canine Venereal Granuloma/ Transmissible Infectious Sarcoma / Sticker Tumour / Canine Condyloma / Transmissible Lymphosarcoma

Historical Importance:

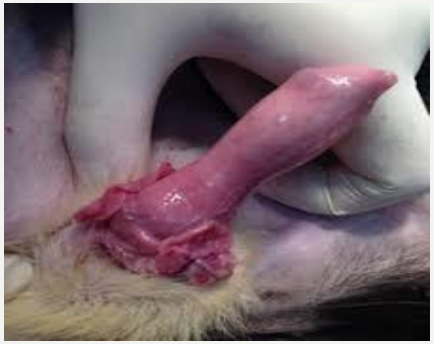
- It is the first neoplasm to be successfully transplanted from one animal to another.
- M A Novinsky -a Russian veterinarian was the first to demonstrate that it could be transplanted to other dog since the tumour in nature is spread by coitus is called when venereal (resulting from sexual intercourse) granuloma

- ❑ It is composed of histiocytes- Cells of connective tissue
- ❑ It spreads during coitus i.e., venereal
- ❑ Occurs in genital organ of dogs especially at glance penis/vagina
- ❑ It's a tumour of younger dogs (1-6 Years of Age)
- ❑ Common among Bitches
- ❑ **Grossly**: veginal mucosa is often red/ ulcerated/ protruded from vulva/ seems to be cauliflower like growth.
- ❑ **Microscopically:** large round oval or polyhedral with in distinct count and poorly obtained cytoplasm in H &E staining

TUMOURS OF CONNECTIVE TISSUE

7. HISTIOSARCOMA/ CANINE TRANSMITTABLE VENEREAL TUMOR (CTVT)

TVTs are sexually transmitted through skin-to-skin contact.



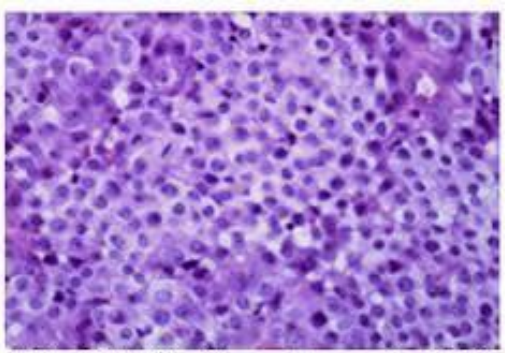
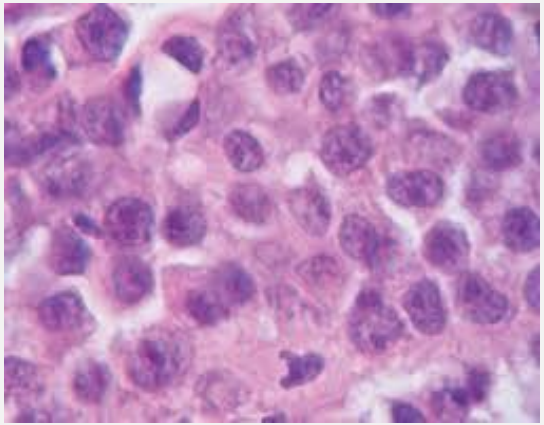


Fig.2. Genital CTVT (Dog 6). Tumor cells were round and had large, round vesicular nuclei with single prominent nucleoli and pale, amphophilic cytoplasm. Mitotic figures were frequent. HE, obj.40x.

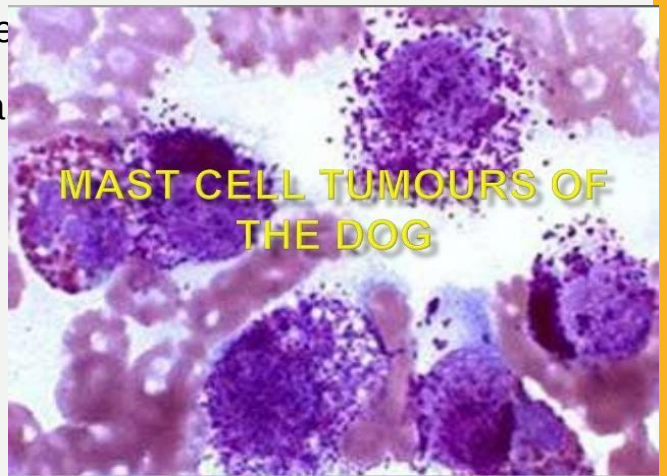


TUMOURS OF CONNECTIVE TISSUE

8. MAST-CELL TUMOURS

Synonyms: Mastosarcoma/ Mastocytoma

- It arises from the mast cell of connective tissue of skin
- Mast cells are produced from undifferentiated mesenchymal cells in connective tissue.
- It is chiefly a tumour of the dog and occasionally also of the
- It usually develops on thigh and rarely on external genitalia
- Tumour appears at latter age between 6 to 15year



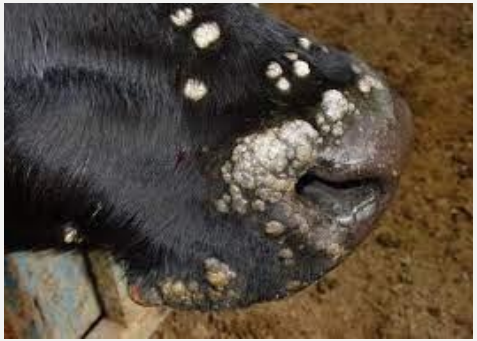
TUMOURS OF EPITHELIAL TISSUE

1. PAPILLOMA/WART

A benign tumour of the St. Sq. epi. Of the skin or a mucous membrane.

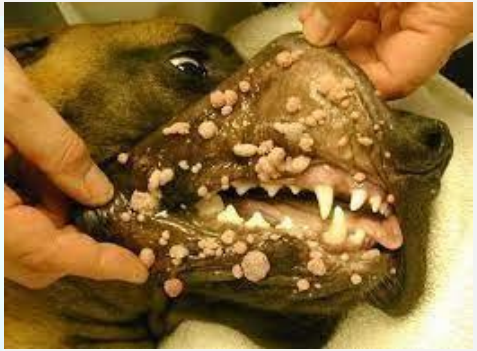
Most common in cattle than any other domestic animals

Etiology: Bovine papilloma virus virus (BPV) or papilloma



Gross Lesion:

- Finger like (or nipple like or Horn like) projections from skin.
- Tumouros Growth is pedunculated
- size varies from few mm to 10 cm in diameter



Microscopic Lesion:

- Finger like processes of stratified squamous epithelium protruding above the surrounding epithelial surface and contain a connective tissue core.
- There is NO break the basal /basement layer

TUMOURS OF EPITHELIAL TISSUE

1. SQUAMOUS CELL CARCINOMA (SCC)

A malignant tumour of stratified squamous epithelium
It is a common tumour of cattle; for example

- SCC of eye in Herford cattle
- SCC of Bovine Eye
- Horn cancer in Bullock (castrated Bull)

Etiology: possibly viruses, chronic irritation, hormonal imbalance is the prime reason behind the horn cancer in castrated animals **Lesions**

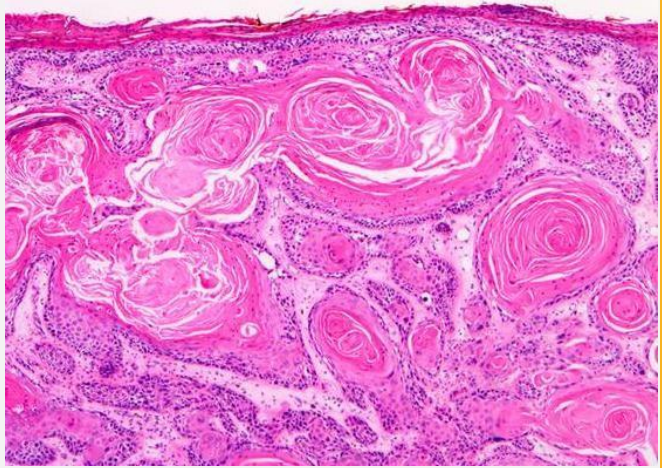
Macroscopic:

- resembles **Cauliflower head** in slow growing tumours

Microscopically:

- **Epithelial Pearl or Cell Nest**
- (round laminated structures
- arranged concentrically
- formed by keratinization
- of stratum corneum at
- centre).

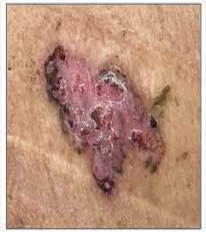
The earliest sign if Horn Cancer is
a) Bending of horn b) Tilting



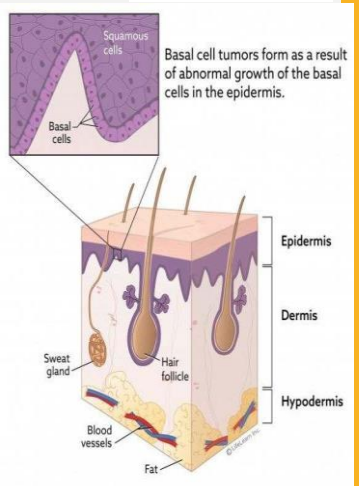
TUMOURS OF EPITHELIAL TISSUE

1. BASAL CELL CARCINOMA (BCC)

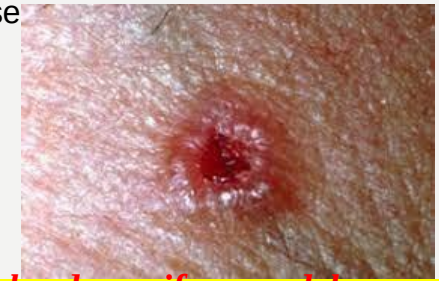
*It is a most common form of **skin cancer** and begins in the **basal cells** — a type of **cell** within the skin (st. germinativum) that produces new skin **cells** as old ones di e off. **Basal cell carcinoma** often appears as a slightly transparent bump on the skin*



- These are locally invasive but never metastasize.
- Etiology: Not Known
- it is most commonly found in dog Horses and cat on Head & Shoulder
- Tumor is also called as **rodent ulcer**



- Macroscopically:
- - slow growing tumor
  - Firm and nodular attached by broad base
  - tumour surfaces ulcerated



characterized by an area rimmed by a pearly border as if gnawed by a rodent.

TUMOURS OF EPITHELIAL TISSUE

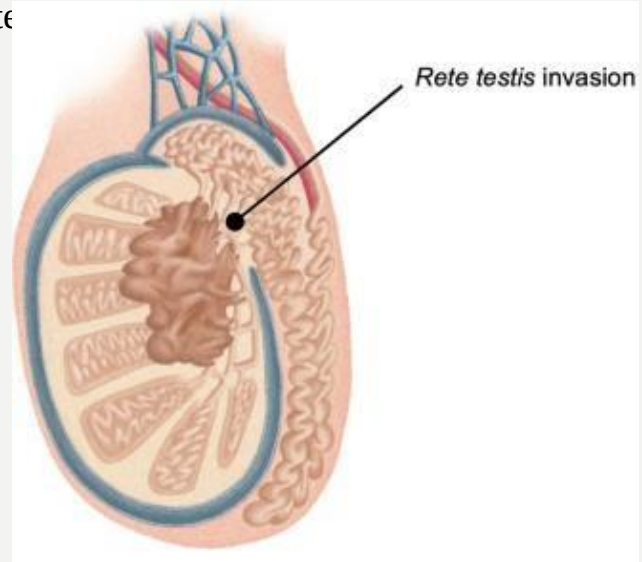
1. ADENOMA

- It is a benign tumour of glandular epithelium.
- In the Dog, like mammary, prostate, and sebaceous gland adenoma are fairly common.
- **Gross Appearance:**
- **Cystadenoma**
  - Mucinous **cystadenoma** arises from the surface epithelium of the glands wherein the secretions are retained in the acini
  - usually found in thyroid gland of older dogs and horses.
- **Papillary adenoma**
  - proliferating epithelium grows into the lumen of acini and forms branching papillae
- **Polypoid adenoma**
  - Sharply circumscribed and encapsulated polyps in the stomach and intestine are common.

TUMOURS OF EPITHELIAL TISSUE

1. SEMINOMA

- It is **adenocarcinoma** of testicular tissue arising from germinal epithelium of seminiferous tubule.
- They occur mostly in older dogs and vary from 1-3 cm in diamete
- Metastases occur in the regional lymph nodes and other organs.
- Sustentacular cell tumour (Sertoli cell tumour) and Interstitial cell tumour (Leydig cell tumour) are another examples tumours of testicular tumour.



- Cytopathology deals with interpretation of cells from animal body that either exfoliate/ desquamate spontaneously from epithelial surface or are obtained from organs/ tissues through biopsy. Histopathology is based on interpretation of distortions in tissue architecture, and the cytopathologic diagnosis rests upon alterations in morphology of a single or group of cells.

- Exfoliative cytopathology: includes the examination and interpretation of cells shed off from epithelial surfaces in body cavities or body fluids, cells obtained through scraping, brushing and/ or washing of mucosal surfaces are also included in exfoliative cytopathologic diagnosis.

- Interventional cytopathology includes the samples obtained from aspiration or surgical biopsy.
- includes fine needle aspiration cytology (FNAC) and imprint cytology.