MJF COLLEGE OF VETERINARY AND ANIMAL SCIENCE, CHOMU, JAIPUR

DEPARTMENT OF VETERINARY PATHOLOGY

INTRACELLULAR AND EXTRACELLULAR ACCUMULATION

ACCUMULATION

Deposition of abnormal amount of various substances (like-protein ,fat ,carbohydrate ,pigment etc.).
It may be intracellular or extracellular space.

INTRACELLULAR ACCUMULATION

Protein
Fatty changes
Glycogen Infiltration
Pigmentation

EXTRACELLULAR ACCUMULATION

Protein
Fibrinoid Degeneration
Amyloid Degeneration
Gout
Calcification

Intracellular Accumulation

1) Protein
   - Cloudy swelling
   - Hydropic Degeneration
   - Hyaline Degeneration
   - Mucinous Degeneration
   - Mucoid or Myxomatous Degeneration

2) Fatty Change
   - Fatty Degeneration
   - Fatty Infiltration
   - Obesity

3) Glycogen Infiltration

4) Pigmentation
   - Endogenous Pigmentation
   - Exogenous Pigmentation

Extracellular Accumulation

1) Protrein
   - Hyaline Degeneration
   - Fibrosis(collagen)

2) Fibrinoid Degeneration

3) Amyloid Degeneration

4) Gout
   - Articular gout
   - Visceral gout

5) Calcification
   - Dystrophic calcification
   - Metastatic calcification

- **Intracellular Accumulation:-** The location of accumulated substances may either in the cytoplasm,within organelles (lysosomes) or in the nucleus.

There are three pathways by which cells can accumulate abnormal substances-

:-A normal substances may be produced at a normal or an increased rate,but the metabolic rate is inadequate to remove it. Ex:- fatty change in liver.

:-Endogenous substances accumulates because of genetic or acquired defect in its metabolism ,transport or secretion. Ex:- 'lysosomal storage disease'

:-A abnormal outside substance may accumulate because the cell has neither the enzyme to degrate it nor the ability to transport it to other site. Ex:- Carbon(anthracosis),silica particles (silicosis) in the lungs.

1)Protein Accumulation:- incudes the following

Cloudy swelling
Hydropic Degeneration
Hyaline Degeneration
Mucinous Degeneration
Mucoid Degeneration

- Cloudy swelling (albuminous degeneration) :-This is mild and easily reversible and earlist degeneration.

-There is an alteration in the physical state of the protein.

-It is seen in highly specialised cells such as hepatocyte of liver,tubular epithelial cells of the kidneys and cardiac muscles.

Cause-Hypoxia
Toxin(bacterial,viral,plant alkaloid ,chemicals etc.)

Macroscopic-The affected organ is swollen ,has a pale or par-boiled appearance.
-On cut section, the sufaces bulge.

Microscopic-The cells are swollen and the cytoplasm has a "ground-glass" appearance.

Pathogenesis-

the mitochondria (store house of cellular enzyme) become swollen and decreased in density

↓

enzymatic activity responsible for energy production is decreased

↓

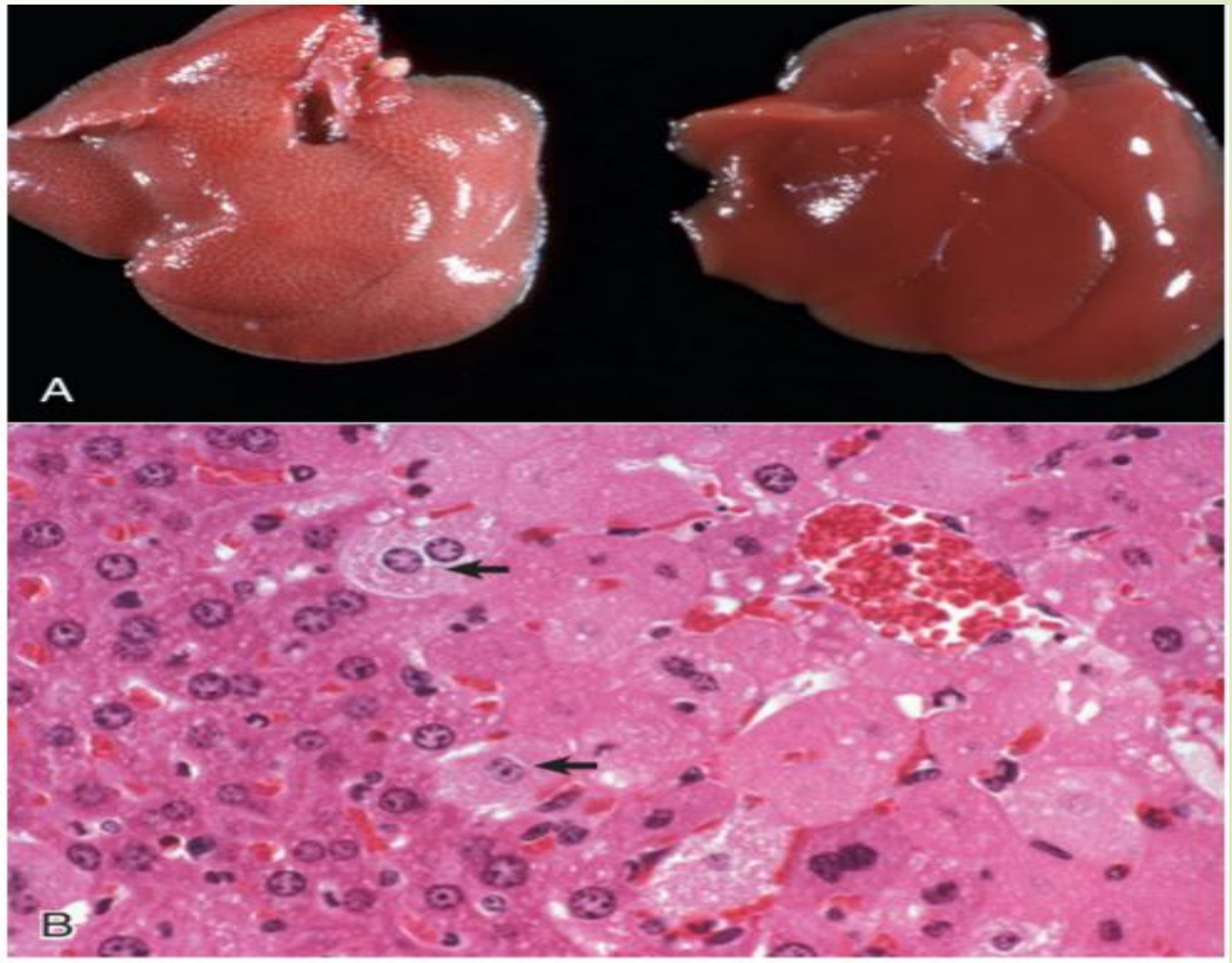
there is accumulation of intracellular sodium due to a failure of sodium pump(as energy is decreased)

↓

there is raises the osmotic pressure in the cell so water passes into the cell from intercellular fluid resulting in swelling of cell

Stain- Hematoxylin &Eosin stain (H&E stain). Intracellular fluid take pink colour with eosin and nucleus takes blue colour with hematoxylin .

Cell Swelling, Liver, Mouse. A, Hepatic swelling in a mouse exposed to chloroform . slight pallor in the liver on the left are the result of acute cell swelling and necrosis of hepatocytes. The right liver is normal. B, Liver from a mouse with chloroform toxicosis. Although many hepatocytes in the centrilobular areas (at right) are necrotic, several cells at the interface of normal and necrotic (arrows) are still undergoing acute cell swelling. H&E stain.



- Hydropic Degeneration:- Closely related to cloudy swelling and reversible.

-the cytoplasm contains one or two large vacuoles or few small ones extent that they swell and may burst.

Causes- Mechanical injury (rubbing of skin to the hard surface lead to blister).

Thermal injury- heat ,cold,burn(blister on skin)

Chemical injury

Infectious agent (viruses such as Pox Disease , Foot and Mouth Disease).

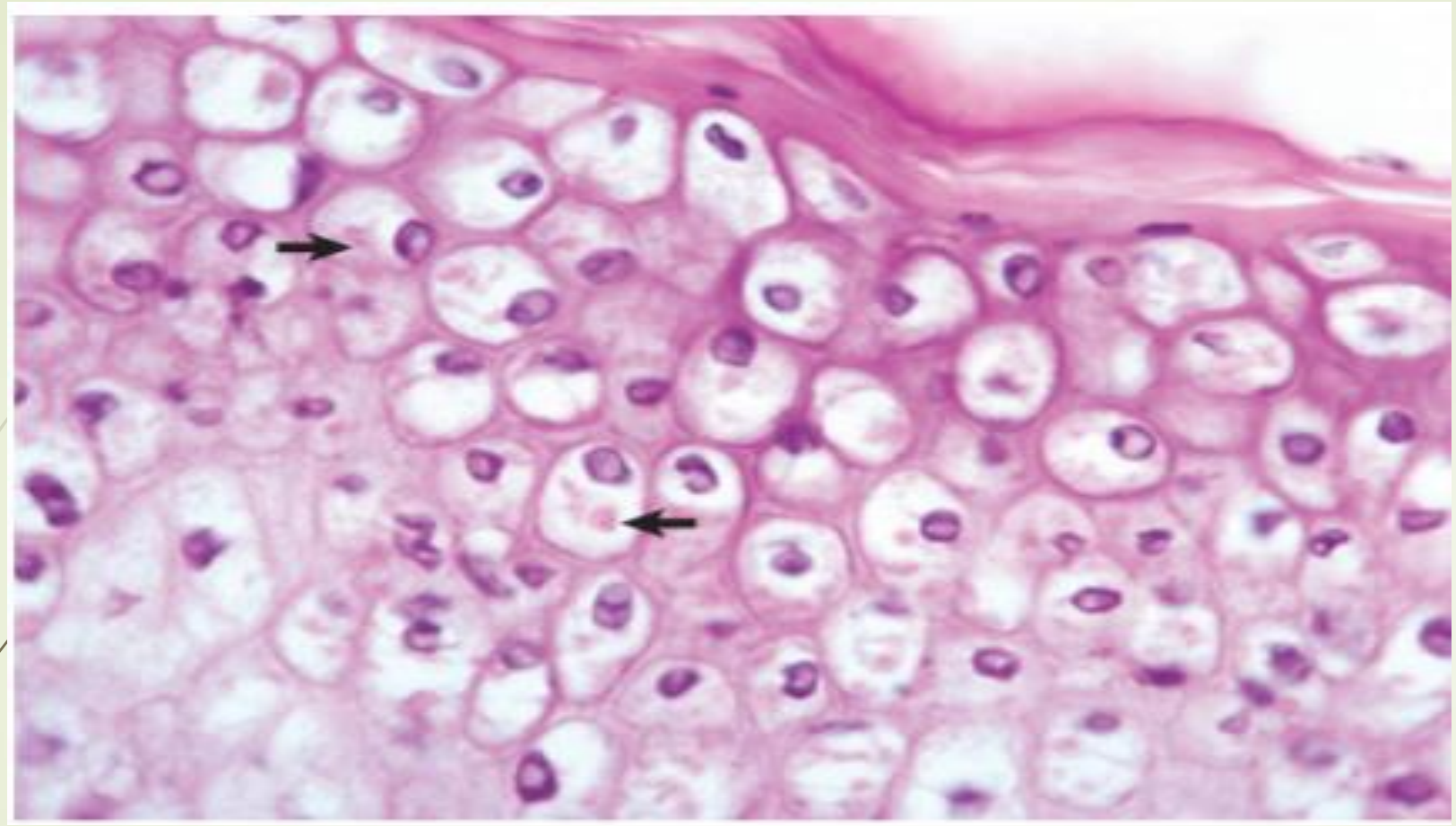
Neoplasms.

Macroscopic- It may seen as a blister on the skin.Upon incision,fluid escapes and the blister collapses.

Microscopic-There is increase in the size of the cell due to accumulation of fluid. Small clear vacuoles seen with in cytoplasm(called Vacuolar Degeneration .

Pathogeneis- Due to more severe irritant , the permeability of the cell membrane increased accompanied by loss of potassium ions and passage of sodium ions into the cell.

Stain- H&E Stain (the hydropic fluid stains pink with eosin due to protein content).



Ballooning Degeneration, Papular Stomatitis, Oral Mucosa, Ox. Cells infected by certain poxviruses (e.g., papular stomatitis virus) cannot regulate their volume and undergo hydropic degeneration . These cells may become so distended (ballooning degeneration) that they eventually rupture. Note cytoplasmic viral inclusion bodies (arrows). H&E stain.

- Hyaline Degeneration:- It is both type of accumulation intracellular and extracellular.

-It is physical appearance of tissue rather than its chemical composition.

-Any alteration within cell or in the extracellular space ,gives Homogenous ,glassy (Hyolos =Glass) translucent, pink appearance in histological section with H&E stain.

-The affected cells and tissue lose their structural characteristics and fuse together into homogenous mass.

-Three major types of hyaline change:-

a)The connective tissue hyaline

b)Epethelial hyaline

c)Muscle hyaline

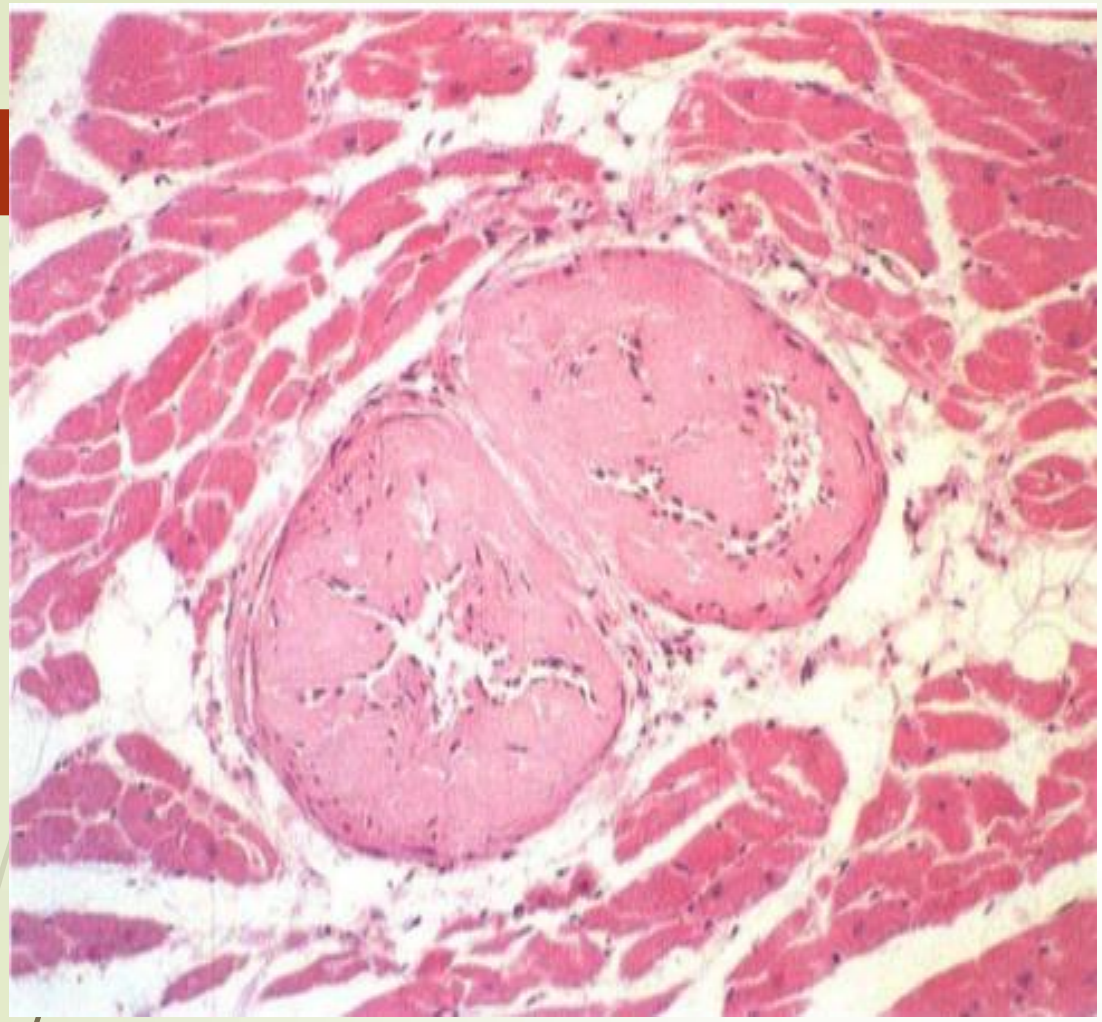
a)Connective tissue hyaline :-

-Glomeruli in chronic nephritis
-arteries in arteriosclerosis
-chronic lymphadenitis

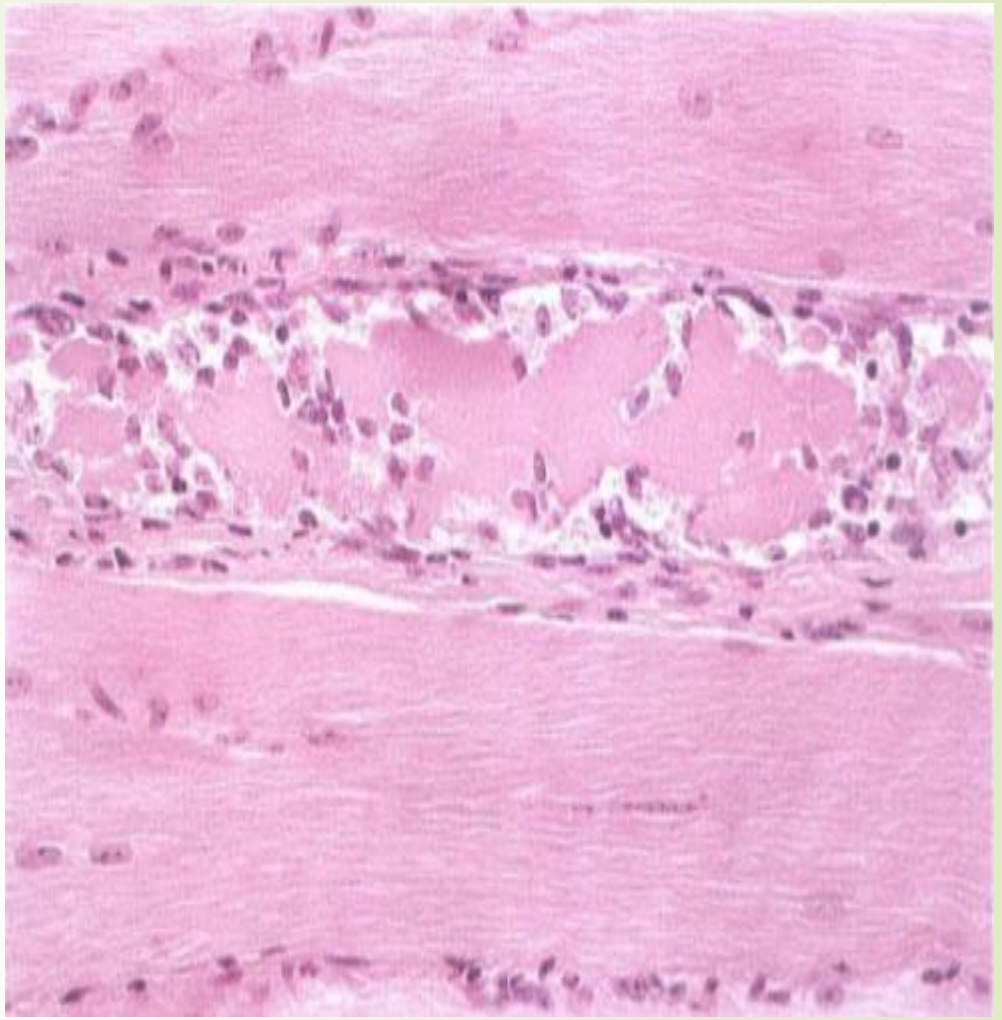
b)Epithelial hyaline:- Stratum corneum of skin best example. It become pathological when hyperkeratosis occur these structures called Carpora amylaceae which stain deeply with iodine like starch. Observed in prostate gland.

c)Muscle hyaline:- Muscle resemble "fish-flesh" and lose their fibrillar staning .

-Equine azoturia in equines
-White muscle disease in calves
-Stiff lamb disease in lambs



Amyloid deposition Intramural arteryof the heart Homogeneous. Pink thickening of the vessel wall with narrowing of the lumen. Deposition of amyloid in Intima and media, except for a thin interrupted rim at the periphery. HE



Hyaline degeneration Homogeneous, eosinophilic, fragmented muscle fiber . HE.

- Mucinous Degeneration:- It is the excessive accumulation of mucin or mucus in degenerating epithelial cells.

-Mucin is a glassy,viscid, stringy, slimy glycoprotein is normally produced by columnar and cuboidal epithelial cells.

-In mucus membrane of the large intestine the large mucin producing cells called Goblet cell.

Cause-Any mild irritant,mechanical,thermal and viral (Canine distemper)

-Neoplasm of columnar epithelium(cancer of stomach, large intestine ,mammary gland).

-Catarrhal inflammation of mucus membrane of respiratory, digestive and reproductive system.

Macroscopic:- Mucus is a slimy ,glassy fluid ,precipitated by acetic acid.

-In acute rhinitis there is profuse watery mucus secretion.

Microscopic:- Mucus in cytoplasm of cells as small droplets or when these coalesce as a large droplet ,compressing and displacing the nucleus to a side.

Stain:- Mucin stains blue with Hematoxylin(basic dye)

-Purplish red colour with Periodic Acid Schiff reagent(PAS)

-Blue colour with Alcian Blue.

Pseudomucin- Cystadenoma of ovary contain a viscid material

-its staining pink with Eosin(acid dye).

- Mucoid or Myxomatous Degeneration:-Connective tissue cells of fetus ,produce mucin like glycoprotein which not present in adult tissue if this substance found in adult tissue called mucoid degeneration.

  Cause- Neoplasm (myxosarcoma –connective tisse tumor)
  -Malnutrition(seen in bone marrow,cartilage,adipose tissue)

  Macroscopic-Tissue is shrunken, flaccid and flabby in consistency and jelly like appearance .

  Microscopic-Mucoid stains blue with Haematoxylin,the nuclei are hyperchromatic,fluid has a slightly bluish tinge.

2)Fatty Change:- Fatty Degeneration
Fatty Infiltration
Obesity

Refers to any abnormal accumulation of natural fat within parenchymal cells.

- Fatty Degeneration:- Found in parenchymatous cell of liver, kidney,heart.

Cause- hypoxia
Poison-hepatotoxics (chloroform)

Pathogenesis-When mitochondria are damaged due to irritant

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Enzymes concernd in metabolism of fat are disrupted

↓

So fat should be colloidal in protoplasm, accumulate and become visible

Macroscopic- Liver and kidney are enlarge, soft ,paler,frible.
-Heart is flabby.Persence of fat on ventricular endocardium gives speckled appearance (Thrush-breast heart)

Microscopic- Hepatic cells contain numerous vacuoles.
-The nucleus is usually not displaced and show Pyknosis or karyrrhexis
-Cells of kidney and heart contain small numerous fat droplets

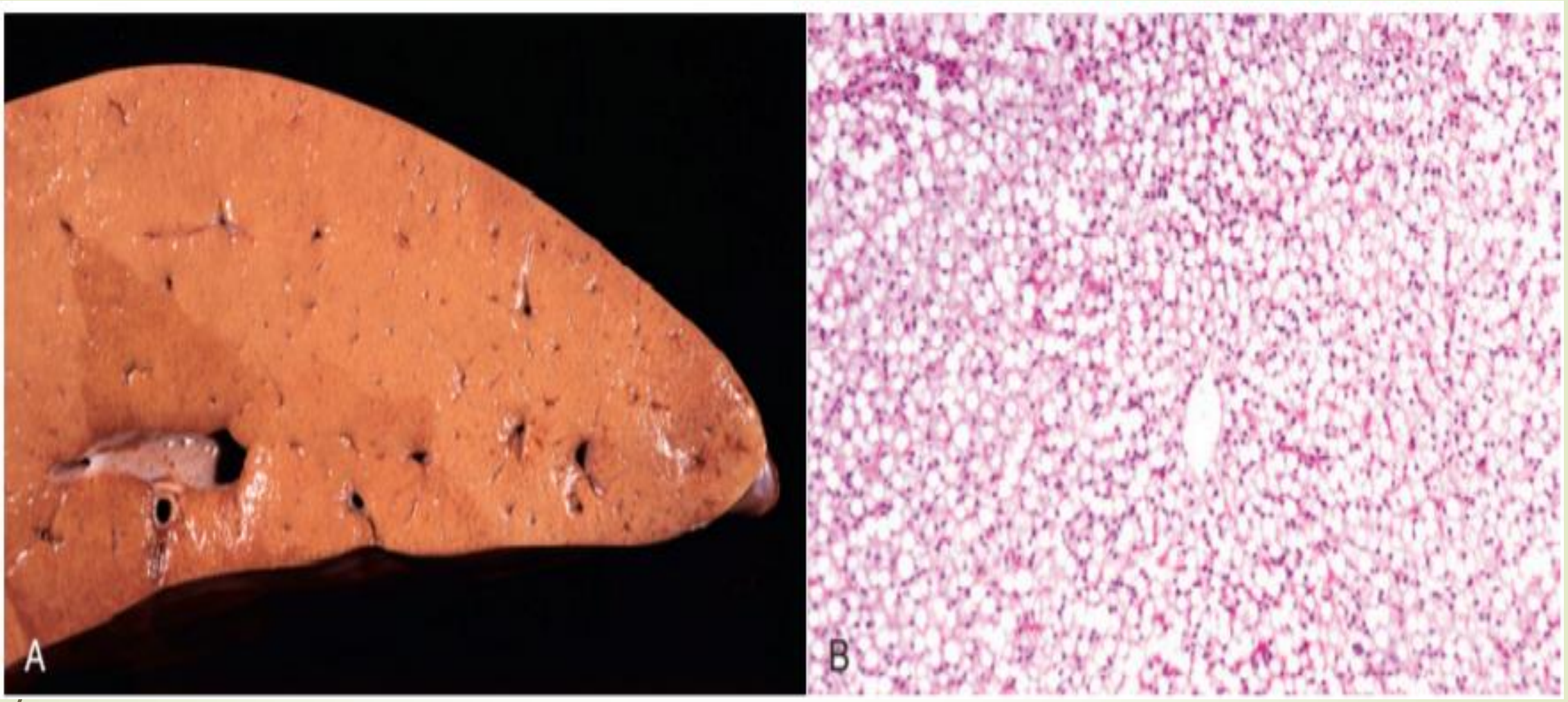
- Fatty Infiltration:-The liver is the only organ that suffers.May occur when too much fat is loaded into the hepatocytes due to deficiency of choline.

Cause-deficiency of choline

Macroscopic- Enlargement of liver, soft ,yellow.
Microscopic- One or two large fat vacuoles in hepatocytes which displace the nucleus to a side.

- Obesity:-Fat accumulate in connective tissue cells and convert into fat cells.
  - Seen in the heart, pancreas,and voluntary muscles in muscular dystrophy.

Fat Stain:-Osmic acid- This stains fat Black.
SudanIII and 4- This stains fat Red
Scarlach R
Oil Red O



Steatosis (Fatty Liver, Fatty Change, Hepatic Lipidosis), Liver, Ox. A, Note the uniformly pale yellow-tan color. The liver is enlarged with rounded edges, bulges on incision, and may feel greasy. B In this severely affected liver, all hepatocytes contain unstained, sharply defined cytoplasmic lipid vacuoles that displace the nucleus to the periphery of the cell. H&E stain.

3)Glycogen Infiltration:- Excessive intracellular accumulation of glycogen.

-Site- liver,loop of henle in kidney,neutrophil in inflammed tissue, cardiac muscle, skeletal muscle.

- Glycogen storage disease-is a hereditary condition resulting in deficiency of enzyme for glycogen metabolism.

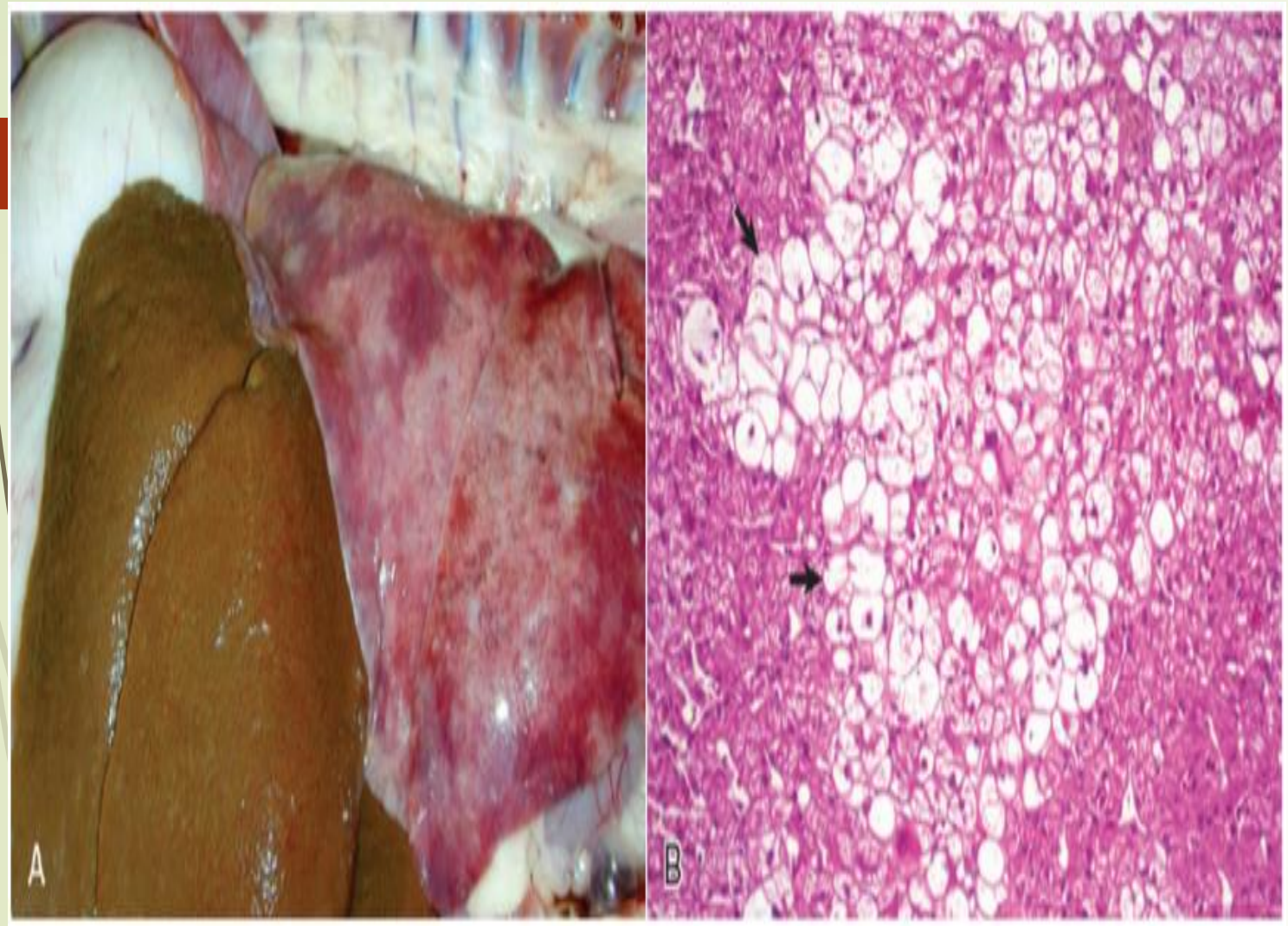
Microscope-glycogen appear as clear vacuoles with in cells .

- Glycogen only carbohydrate that can be seen under the microscope .

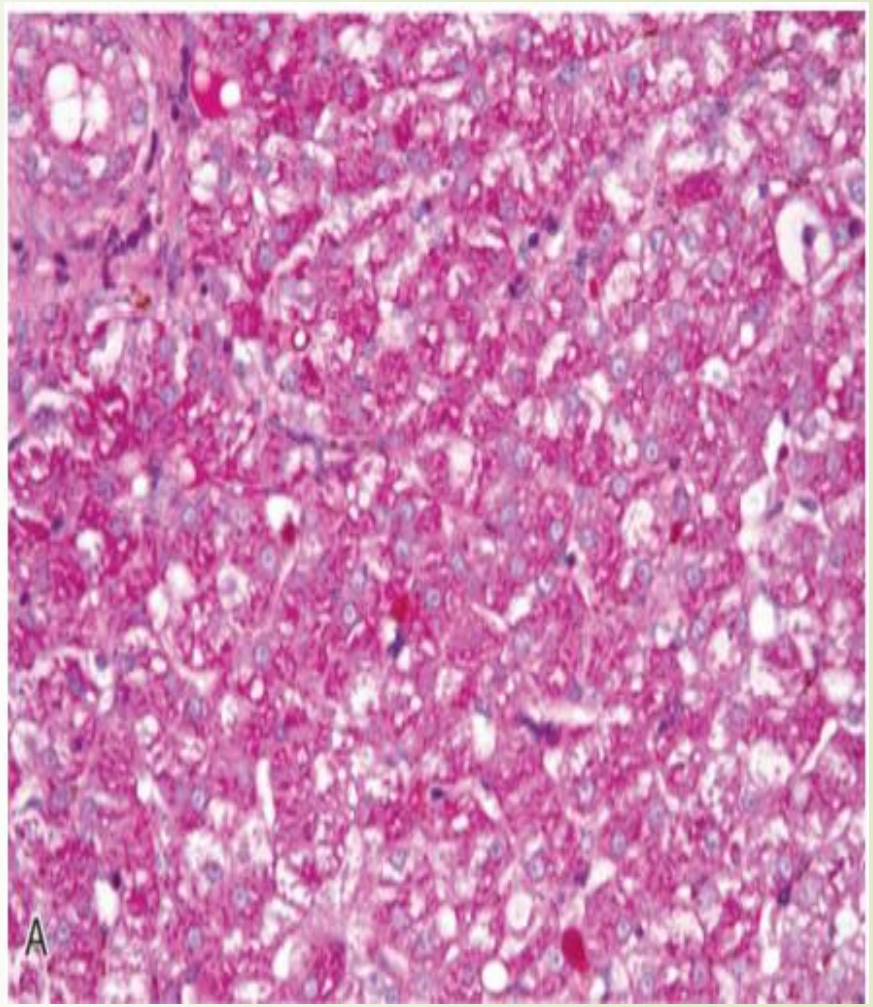
- tissue must be fixed immedietly after death otherwise glycogen convert into glucose which is not stainable so fixative use nonaqueous fixative (absolute alcohol).

Stain- IODINE- gives reddish brown colour

- Best Carmine AND Periodic Acid Shiff (PAS)-gives bright red



Liver, Dog. A, Extensive hepatocellular accumulation of glycogen leads to an enlarged and pale brown liver in dogs with glucocorticoid excess from endogenous or exogenous sources. B swollen hepatocytes (arrows) with extensive cytoplasmic vacuolation. H&E stain



- Glycogen Accumulation, Liver, Dog. A Glycogen, accumulated in the cytoplasm of hepatocytes, appears as magenta granules with the periodic acid–Schiff technique.

4)Pigmentation:-

Endogenous

-Melanin
- lipofusin
-Hb derivatives (Hemosiderin, Porphyrin, Bilirubin)

Exogenous

-Pneumoconiosis
-Anthracosis
-Siderosis
-Silicosis
-Plumbism
-Argyria
-Tatooing

Melanin- Increase melanin production(melanomas,addision disease,Acanthosis nigricans in dogs)

-Little production of melanin(Albinism,Leucoderma)

-Microscopically appears as very minute , uniformaly regular dirty brown ,spherical granules .

Lipofusin- 'wear-and-tear' or Aging pigment.

-prominent in liver and heart(Brown Atrophy)of aging patient.

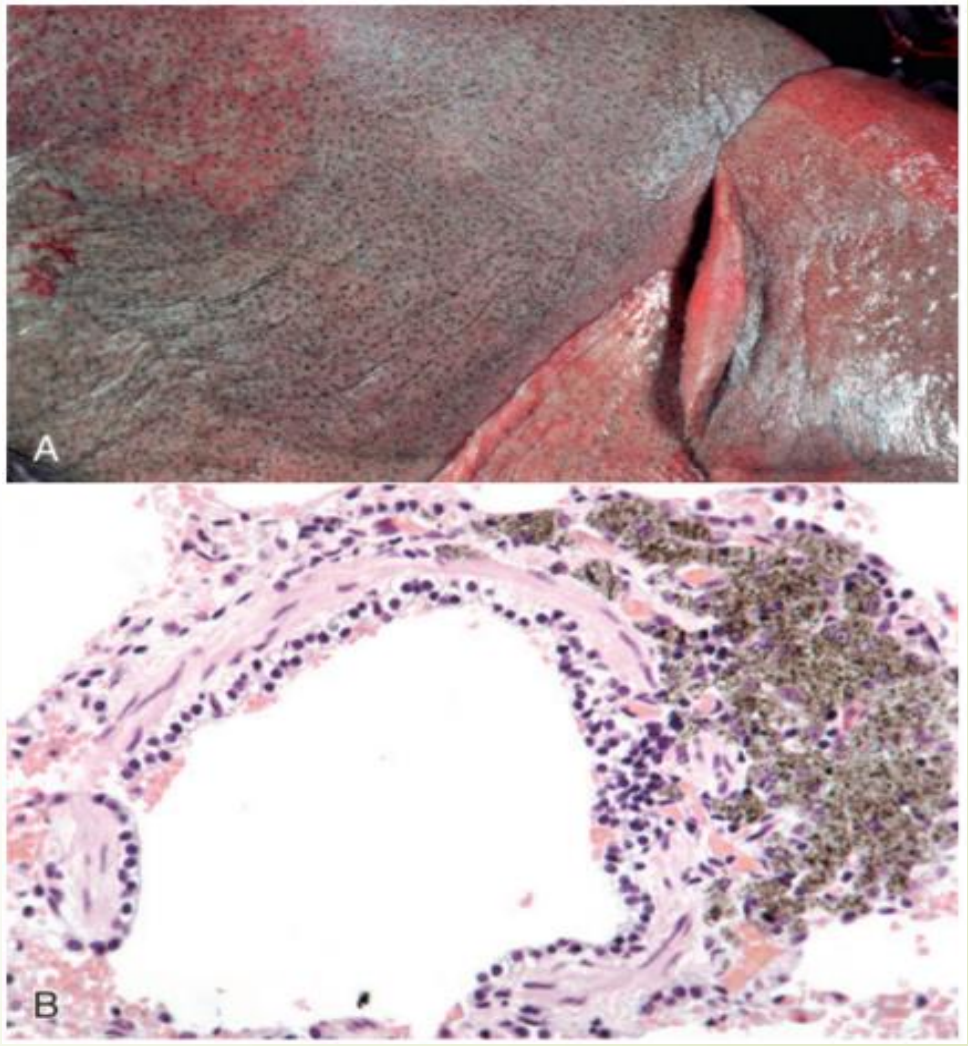
Heamoglobin derivative-

a)Heamosiderin- Golden yellow crystal within macrophages in spleen (increase- Heamosiderosis)

b)porphyrin- iron containing blood pigment.

c)Bilirubin- excessive bilirubin in blood (Jaundic).

Pnemoconiosis- Accumultion of dust particles in the lungs.
Anthracosis-Accumulation of carbon particles (coal dust) in the lungs.



Anthracosis, Lung, Aged Dog. A, The fine black subpleural stippling represents peribronchiolar deposits of carbon. B Inhaled carbon (black) has been phagocytized by macrophages and transported to the peribronchial/peribronchiolar tissue. H&E stain.

Siderosis- Accumulation of iron particles in lungs.
Silicosis- Accumulation of silicon(stone dust) in lungs.
Plumbism- Chronic poising of lead called plumbism.
Argyria-Noticed in long continued therapy with silver salt.
-skin and counjuctiva become gray and internal organ also.
Tatooing- In tattooing ,pigment particles are transported by the macrophages to the connective tissue in the corium.

❖ **Extracellular Acccumulation:-** Accumulation of substances between the cells or intercellular space.

1)Protein degeneration:- Hyaline Degeneration (Connective tissue hyaline).

Collagen(Fibrosis):-

-Fibrosis is an excess in fibrous collagen, predominantly type I collagen fibers, in the interstitium of organs or tissues.

-In the liver stellate cells are the source of the collagen in fibrosis. Macrophage(Kupffer cells in the liver) direct fibrosis by release of cytokines and growth factors.

2)Fibrinoid Degenaration:-

Fibrinoid is a modified form of plasma fibrin.

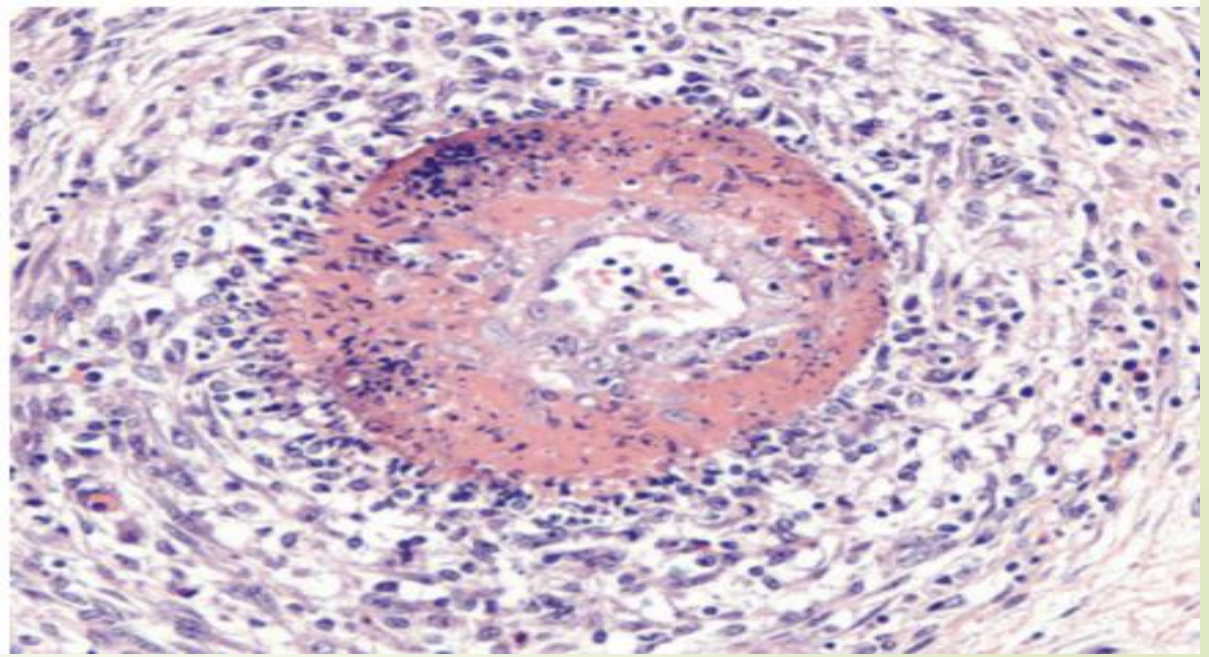
-In this degeneration accumulation of acidophilic homogenous material(fibrinoid) in blood vessels's wall of connective tissue.

-Found in following conditions:-

a)Necrotic areas in the muscles in FMD.

b)Mesentric arteries in Polyarteritis nodusa.

c)'Diamond ' lesion of Swine erysipelas.



POLYARTERITIS NODUSA Fibrinoid Change, Artery. the deeply eosinophilic circumferential deposits in the arterial tunica media. The fibrinoid change is accompanied by leukocytic infiltration and medial necrosis. H&E stain.

3)Amyloid Degeneration:-

Amyloid is a homogenous, transulant pink-staining material found in ground substance,between the cells.

-The affected organ appear waxy (on cut section) so called Waxy Degeneration.

-Affected organs:- Liver,kidney,spleen,pancreas.

Other organs- Adrenals, lymph node and intestine.

The changes that occur in the tissue in amyloidosis:-

a) The amyloid deposited around the blood vessels, compresses them,cause stenosis, resulting in ischemia of the affected organ.

b) Increasing deposition of the amyloid produces pressure atrophy of the surrounding tissue cells (in liver).

c) Deposition of the amyloid on the walls of capillaries makes them thicker so impossible for transfer of nutrients, gasses and metabolic waste products between the the capillary blood and tissue cells .

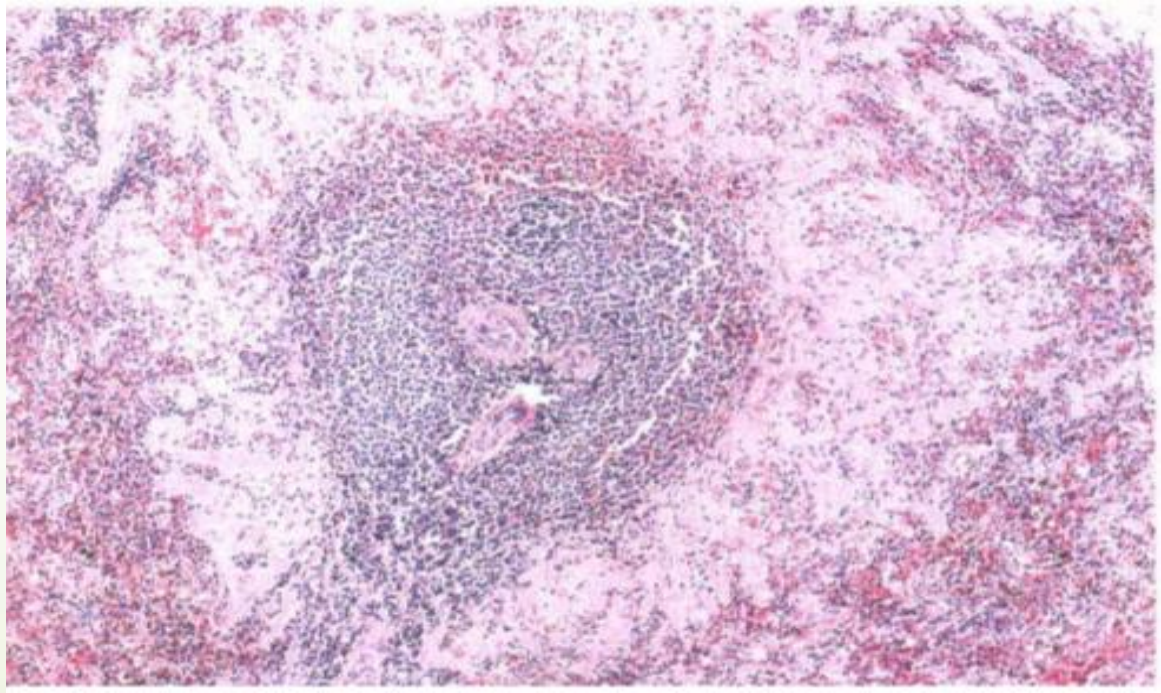
SPLEEN:- Macroscopic- spleen enlarged,paler and firm,edges are sharp.

Microscopic- 1) In the common variety .it is deposited around the central arteries of the malpighian corpuscles.

-Lymphoid tissue is replaced by amyloid and gives an appearance of grains of boiled sago scattered over the ogan known as "Sago-Spleen".

2)In the rare variety, amyloid is laid in the connective tissue of the sinuses and reticulum of the pulp. Here the infiltration is more diffuse and organ is enlarged called "BaconSpleen".

Amyloid deposition- Amorphous proteinaceous substance in the red pulpcords around lymphoid follicles, resulting in a 'lardaceous'spleen. In other cases, amyloid deposition is limited to the follicles, producing a 'sago' spleen with tapioca-like granules. Amyloidosis. Pig. HE.



KIDNEY:-

Macroscopic- Give the kidney a spotty appearance indtead of a waxy look.

Microscopic- Deposited in the connective tissue of the glomerular capillaries.

PANCREAS:-

Deposited between the capillaries and cells of islets of Langerhans.

LIVER:-

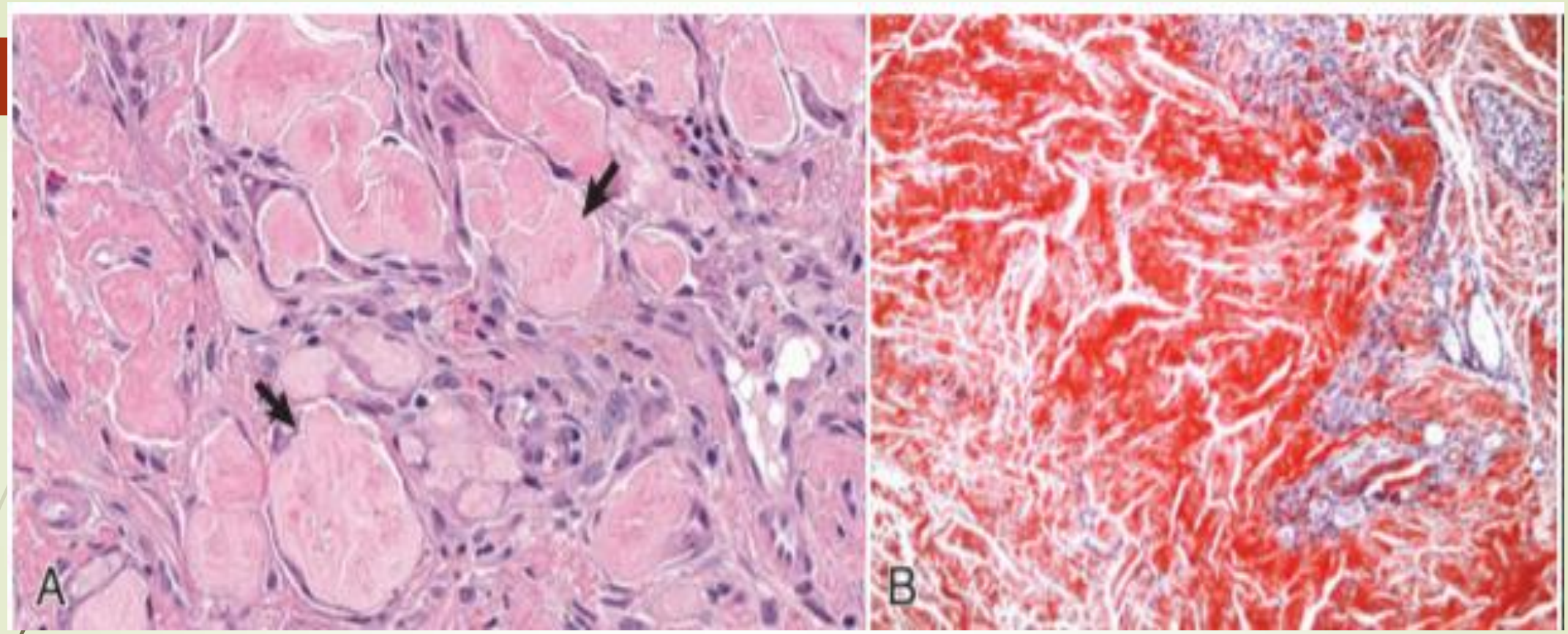
Macroscopic- Greatly enlarged and edges rounded.

Microscopic- Deposited between the endothelium of the sinusoids and the hepatic cells .

STAIN:- a) Iodine gives a mahogany brown colour.

b) Methly violet gives a metachromatic stain –the amyloid stain rose-red while the surrounding tissue is stained blue.

c) Congo red amyloid is stained red.



Equine Nasal Amyloidosis. A, The amyloid appears as homogeneous to faintly fibrillar, pink eosinophilic deposits (arrows) in the nasal mucosal interstitium. H&E stain. B, Congophilic substances, such as amyloid, are red-orange with Congo red stain.

4)GOUT

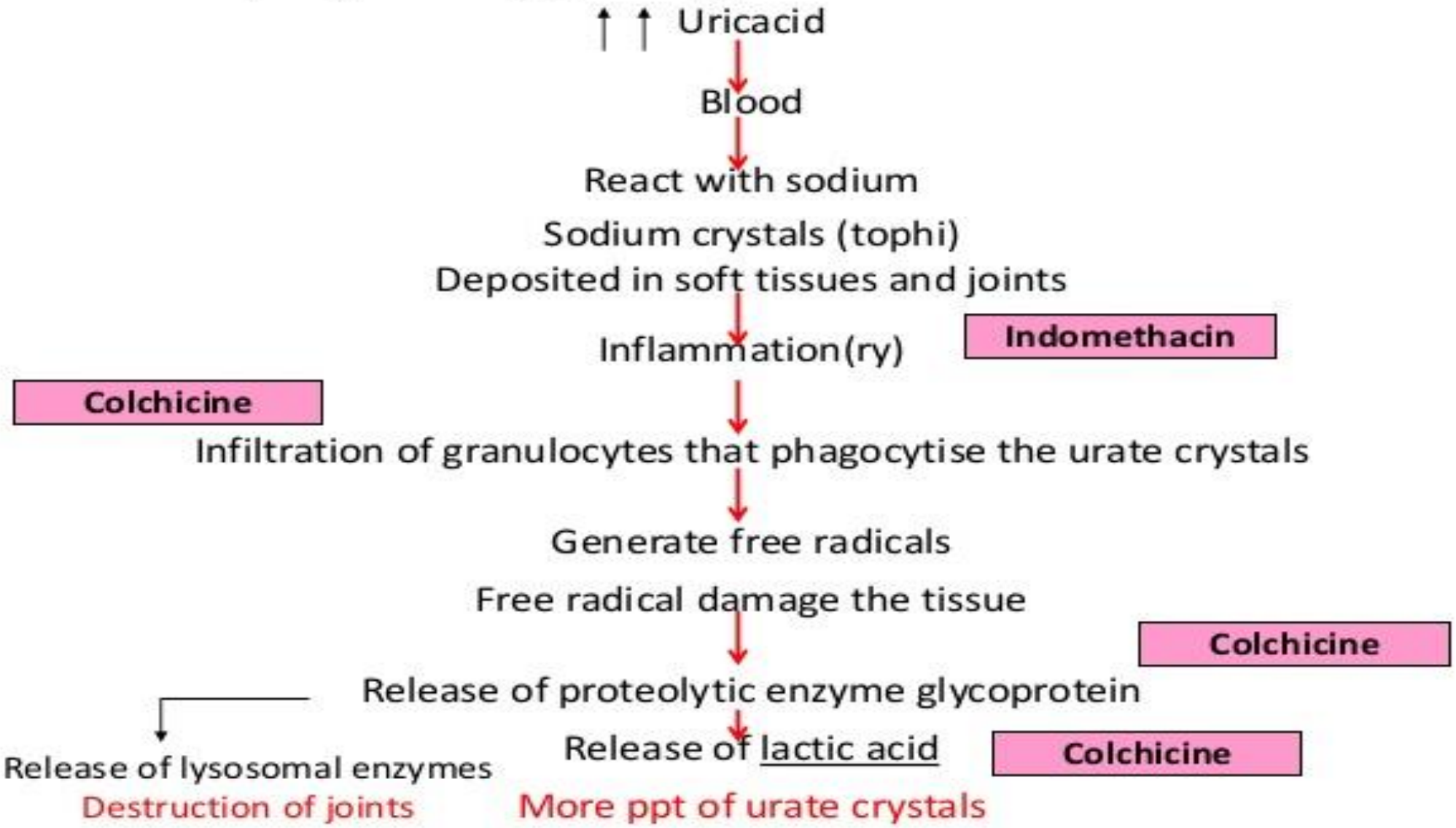
-It is a condition in which crystals of uric acid or urates of sodium and calcium are deposited in the tissue.

- This condition is met with in man, ape and birds (Due to deficiency of uricase enzyme)

Causes-In birds specially in laying hens with a high protein diet.

-Deficiency of Vitamin A.

Pathophysiology of gout



In gout there is hyperuricemia ,due to:-

-Over production of uric acid.

-Impaired destruction of uric acid (deficiency of uricase enzyme)

-Decreased excretion or impaired filtration in tubules.

In birds two form of gout appears- Articular gout (in joints)
Visceral gout (in visceral organs)

Macroscopic- In articular form the affected joints (wing and leg joints)are swollen,with deposition of chalk-like material(taphi) around the joint.
-In visceral form chalk like crystal deposited on the serous membrane and tissue around kidney.

Microscopic- In tissue of joint foreign body reaction seen , inflammatory changes occur and infiltration of cells seen.
- Degenerative changes of tubules are seen.
- needle like crystal found in kidney.

5) CALCIFICATION

It is a process in which abnormal calcium level increase in body tissue except bone and teeth ,causing the tissue to harden.

TWO TYPE:-

1)Dystrophic Calcification (local calcification)

Necrotic areas

Ex:-Caseous tuberculosis, Degenerating tumors etc.

2)Metastatic Calcification (General calcification)

Affected organs-kidney, lungs, stomach

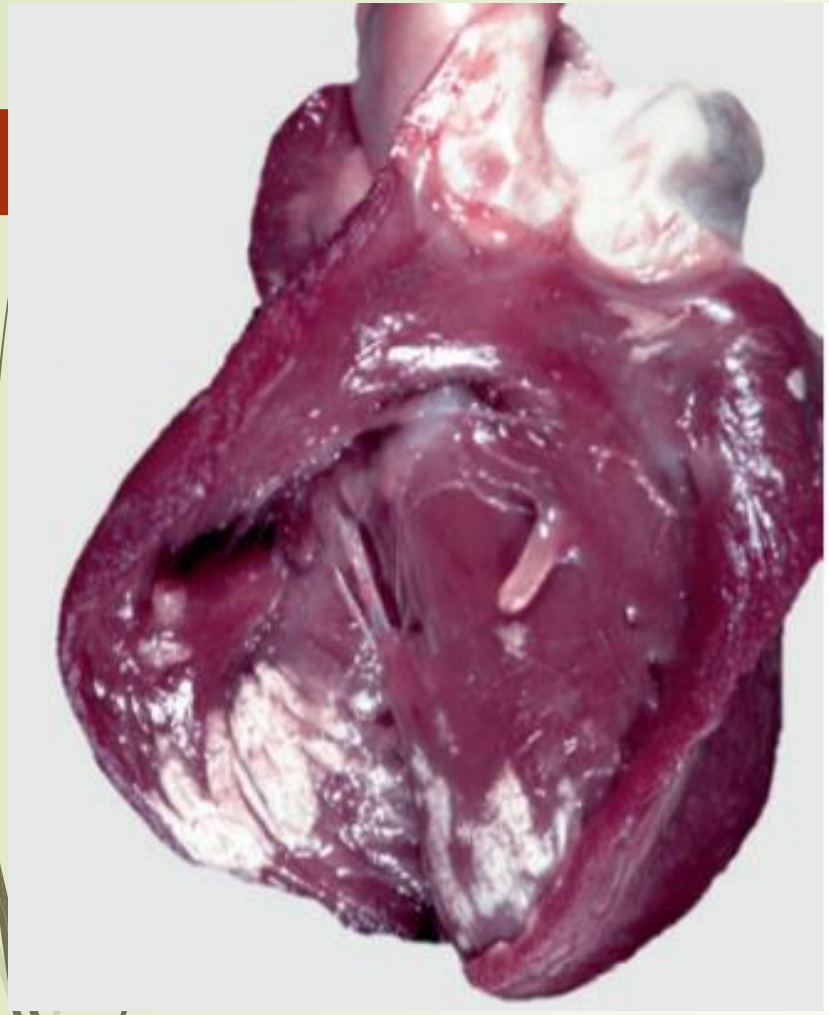
Ex:-Myeloid tumors,demineralization of Bone.

Feature	Dystrophic Calcification	Metastatic Calcification
Definition	Deposits of calcium salts in dead and degenerated tissues	Deposits of calcium salts in normal tissues
Calcium metabolism	Normal	Deranged
Serum calcium level	Normal	Hypercalcaemia
Reversibility	Generally irreversible	Reversible upon correction of metabolic disorder
Causes	Necrosis (caseous, liquefactive, fat), infarcts, thrombi, haematomas, dead parasites, old scars, atheromas, Mönckeberg's sclerosis, certain tumours, cysts, calcinosis cutis	Hyperparathyroidism (due to adenoma, hyperplasia, CRF), bony destructive lesions (e.g. myeloma, metastatic carcinoma), prolonged immobilisation, hypervitaminosis D, milk-alkali syndrome, hypercalcaemia of infancy
Pathogenesis	Increased binding of phosphates with necrotic and degenerative tissue, which in turn binds to calcium forming calcium phosphate precipitates	Increased precipitates of calcium phosphate due to hypercalcaemia at certain sites e.g. in lungs, stomach, blood vessels and cornea

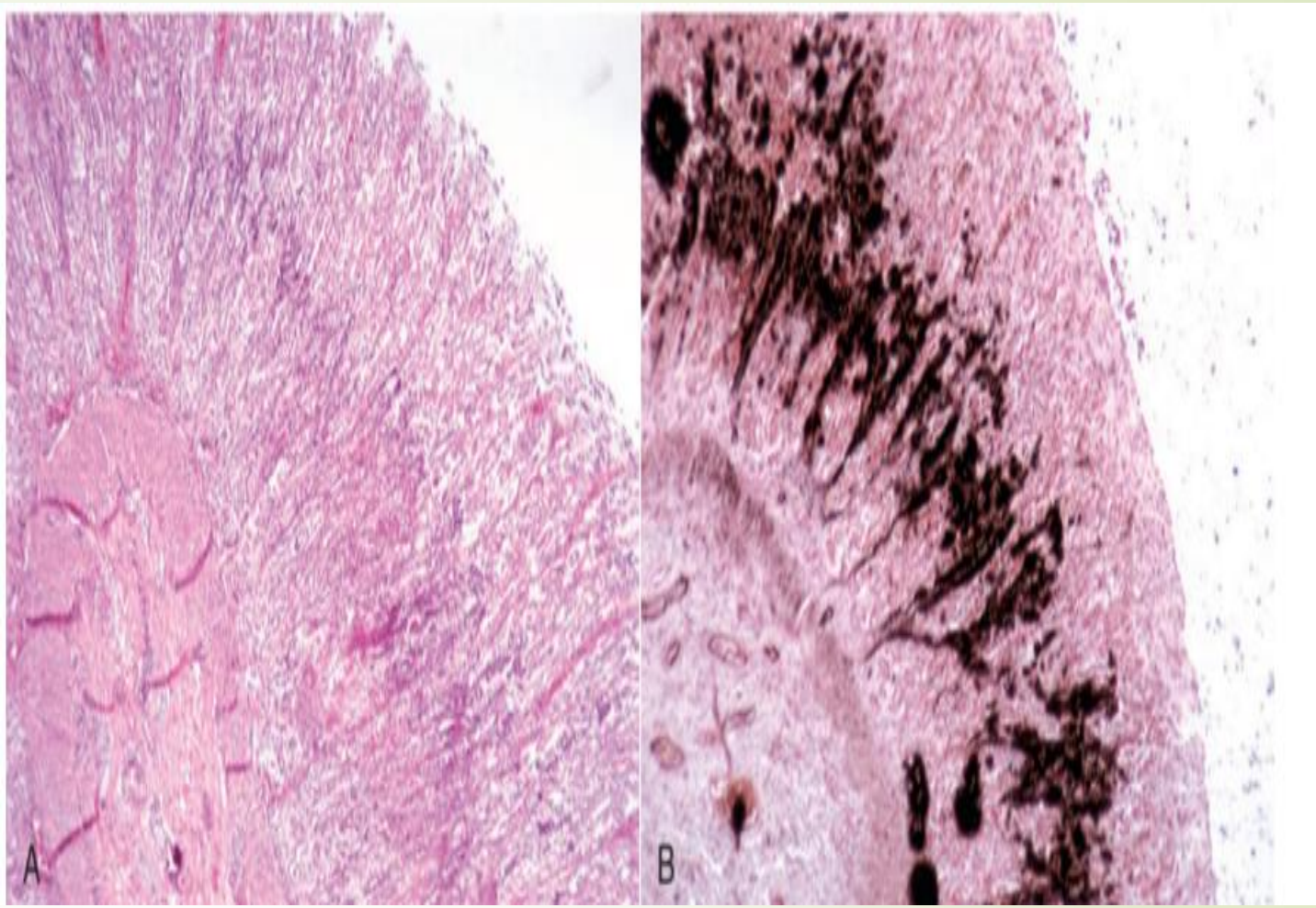
Macroscopic- Appear as white or grayish masses in the tissue .
-when cut,gritty sound is heard and gritty feeling is felt.

Microscopic- Calcium salt that are deposited as granules or spheres take a BLUE stain with hematoxylin.

Stain:- H&E Staining- Calcium takes blue colour
Silver impregnation method- Von kossa technique producing black colour
Alizarin red S- produces red staining



Calcification, Vitamin E or Selenium Deficiency, Heart,Lamb. The chalky white lesions are areas of myocardial necrosis that have been calcified



Calcification, Stomach, Dog. A band of calcification is in the middle of the gastric mucosa. A, The calcium salts are basophilic (stained blue with hematoxylin). H&E stain. B, The calcium salts are black with the von Kossa technique for mineralization.

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THANKYOU