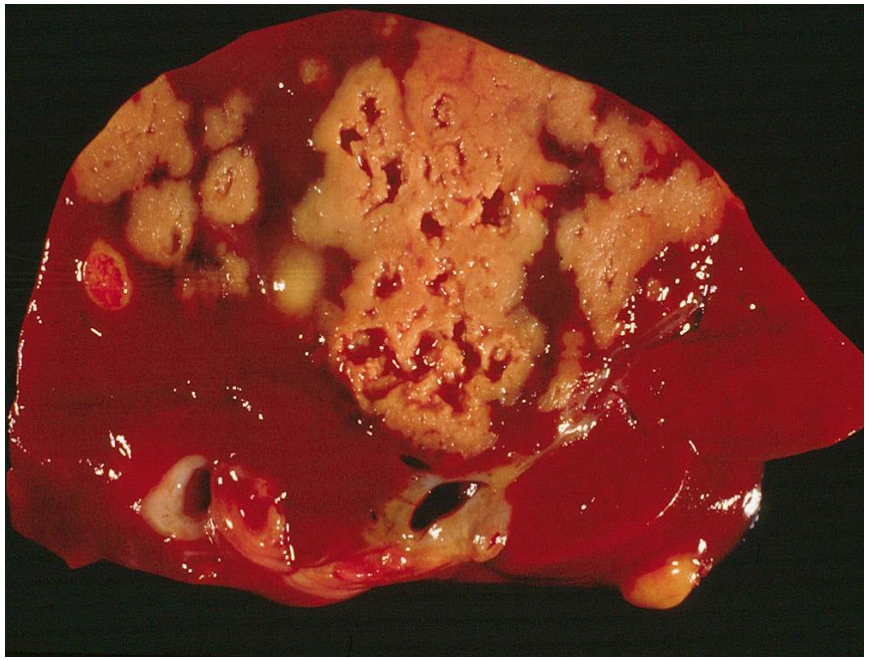
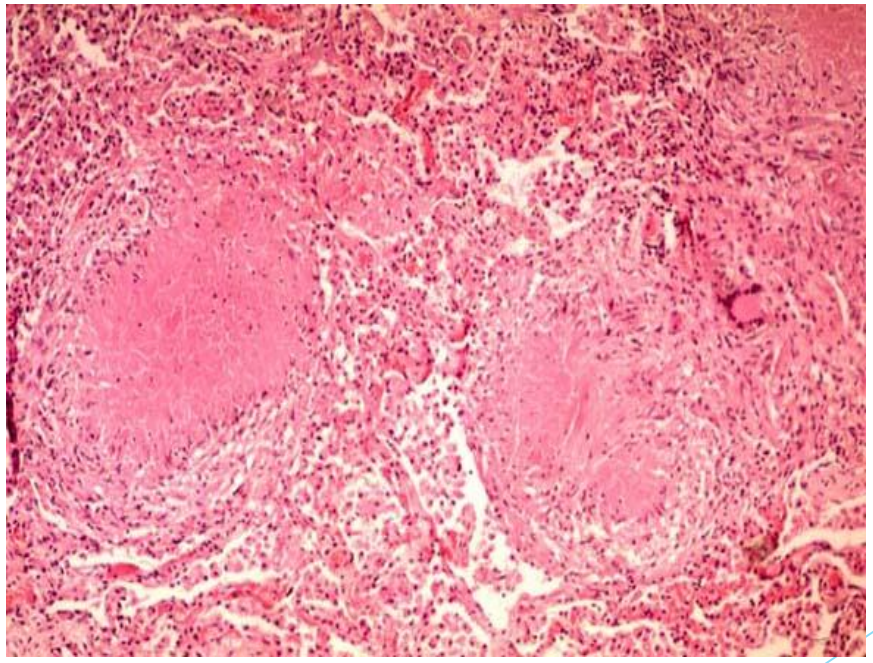
M.J.F. COLLEGE OF VETERINARY AND ANIMAL SCIENCE, CHOMU, JAIPUR

DEPARTMENT OF VETERINARY PATHOLOGY





Necrosis

- Necrosis - Local death of cells or tissues within the living individual
- The death of body as a whole - somatic death
- The tissue fixed immediately in a fixative like formalin is dead but not necrotic
- Cells can be recognized as dead only after they undergo certain morphological changes so
- Necrosis is defined as sum of morphological changes that follow cell death in living tissue or organ due to progressively degradative action of enzymes on lethally injured cells.
- Necrosis occur due to enzymic digestion of a cell and denaturation of proteins
- Digestive enzymes are derived from lysosomes of dead cells- referred as autolysis or lysosomes of infiltrating neutrophils

- Autolysis-(self lysis) Liquefaction/digestion of cells by its own enzymes. Lysis of cells after death due to leakage lysosomal enzymes - acid hydrolases which produce certain changes in the cytoplasm and nucleus. Because of these enzymes cell mem become more permeable and rupture due to anoxia and cessation of circulation.
- In autolysis the changes are more exaggerated than necrosis.
- Autolysis is rapid in organs in which metabolism is active like liver, kidney, adrenals
- In autolysis the whole section will be uniform dead tissue, there is no inflam reaction
- In necrosis there is both living and dead tissue cells and there is zone of inflam reaction

Causes

- **Chemical poisons -** strong acids, alkalis, insecticides, fungicides causing coagulation of proteins
- Toxins of pathogenic organisms- Bact, virus, fungi, protozoa, rickettsiae
- Plant poisons - Plants of senesio - hepatotoxic-hepatic necrosis; mushrooms - contain toxic glycoside Phallin-renal tubular necrosis; Croton oil-necrosis of skin epi
- Animal poisons- bee stings, cantharidin from beetles.
- Disturbances in circulation - Loss of blood supply-Ischemic necrosis; Passive hyperemia-necrosis seen during torsion, volvulus
- Mech. injuries-when tissue is crushed & blood supply is cutoff
- Physical agents-heat, cold, electricity, irradiation-Necrosis

Macroscopic appearance

- Area of necrosis appear white or grey or yellow in color
- Tissue appear as it is cooked
- Stand out distinctly from surrounding normal tissue
- Borders are sharply demarcated by red zone of inflammatory reaction.
- If pyogenic bact present-abscess may form
- Gangrene may supervene if invaded by putrefactive bacteria.

Microscopic change

Cytoplasm of necrotic cells stains more intensely with eosin- increased eosinophilia because -Due to loss of normal basophilia imparted by RNA in cyto & also-Due to increased binding of eosin to denatured i/c protein

Cells have more glassy and homogenous appearance

Cell outlines are indistinct and absent

The cytoplasm appear vacuolated and moth eaten

Nuclear changes: Various degree of changes seen like

Pyknosis- condensation/shrinkage of nucleus

Karyoschisis - cracks appear and nucleus may break at this point

Karyorrhexis - fragmentation of nucleus-scatter in cytoplasm

Karyolysis-Dissolution/disappearance of nucleus leaving nuclear mem which also disappear later stage

Chromatolysis-Disappearance of nucleolus, chromosome and other stainable material

Types of Necrosis

- 1. Coagulative necrosis
- 2. Caseative necrosis
- 3. Liquefactive necrosis
- 4. Fat necrosis: Traumatic, Enzymatic (Pancreatic), Nutritional

Types of necrosis depend on

- When protein denaturation is primary pattern- Coagulative necrosis develops

-When enzymatic digestion is primary pattern- Liquefactive necrosis prevails

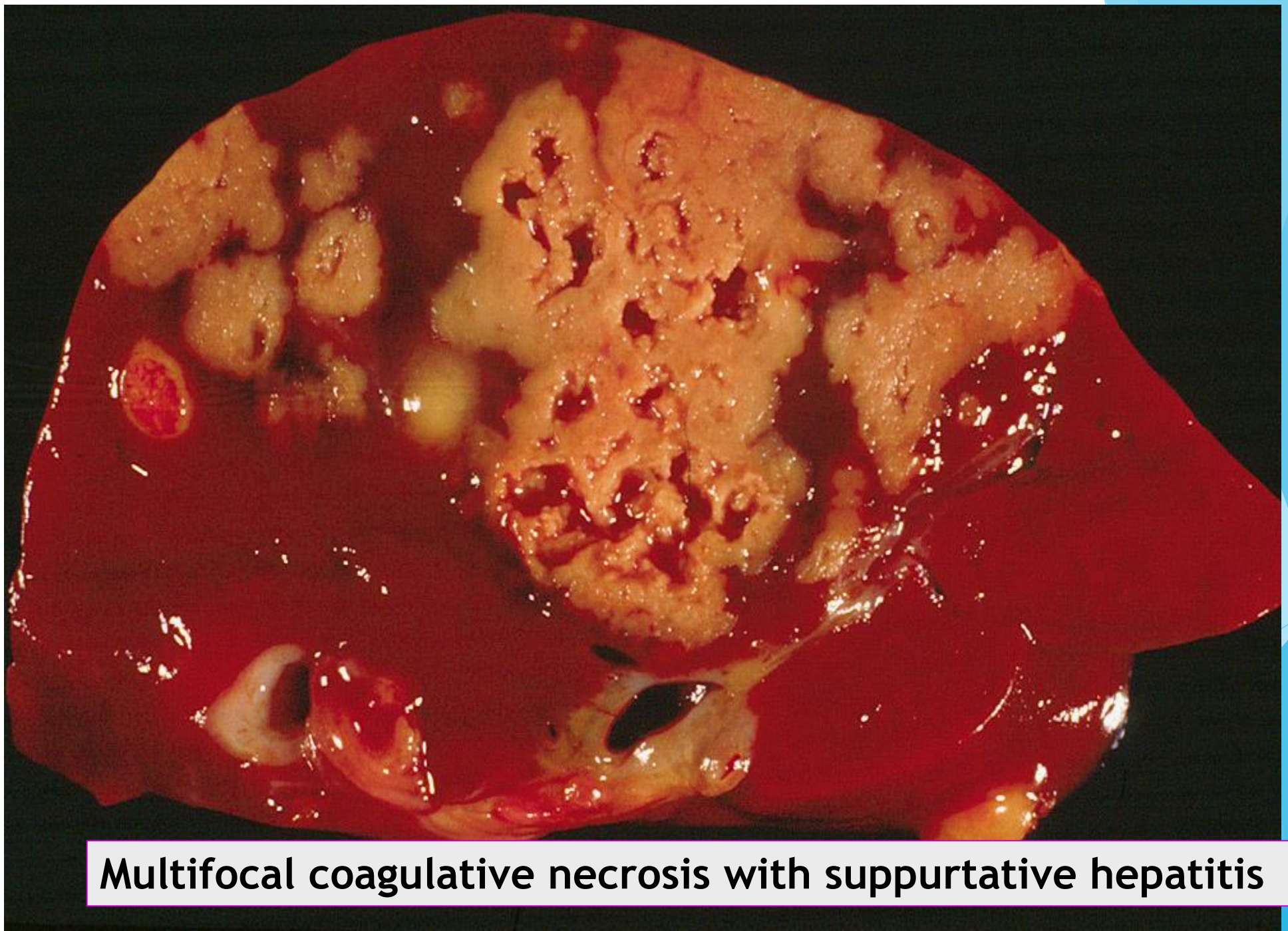
-In special circumstances- caseous or fat necrosis may develop

- The type of necrosis also depend on nature and severity of irritant, duration of irritant and type of tissue and species involved.

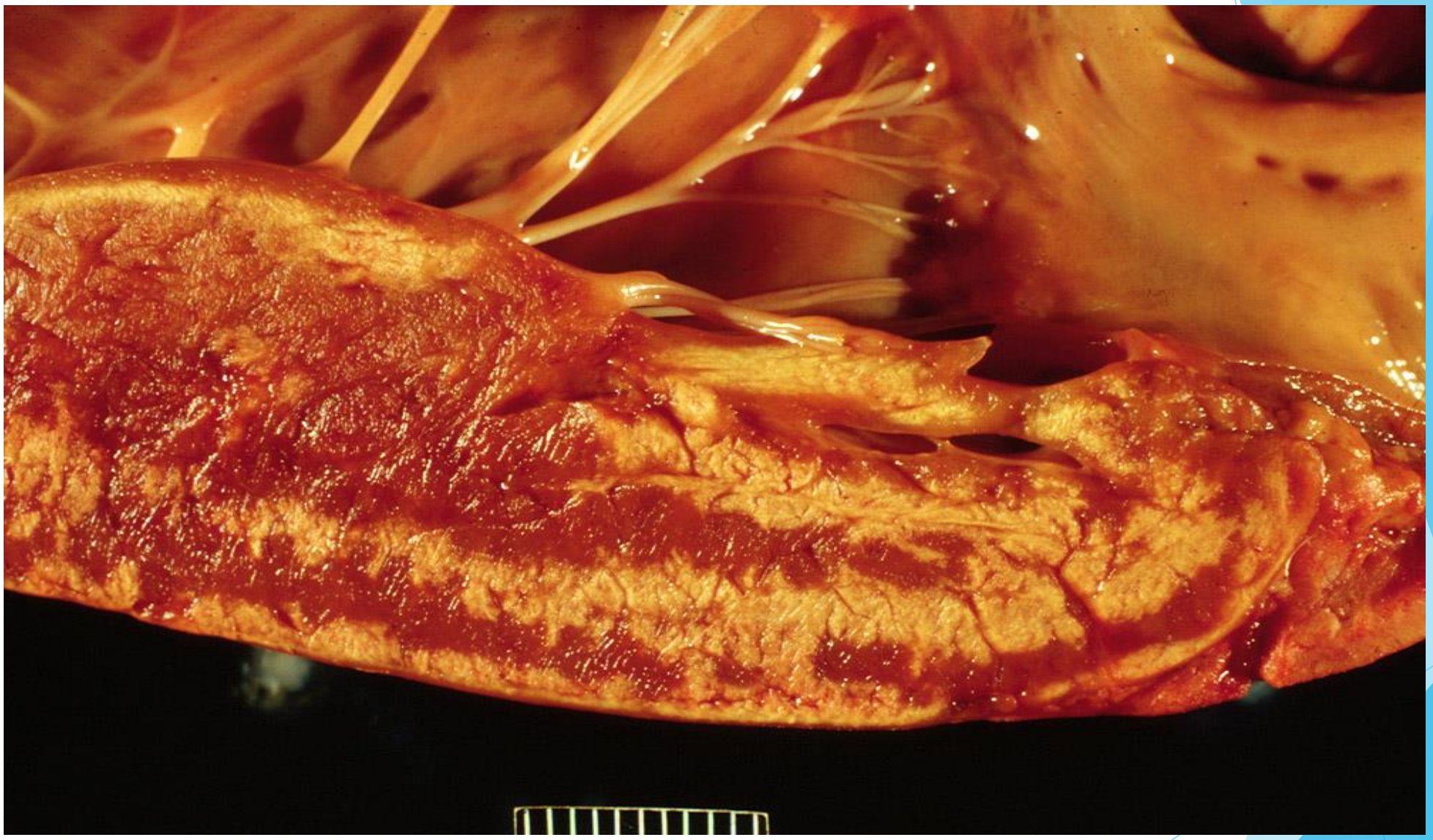
Coagulative necrosis

- Most common type of necrosis.
- Characterized by preservation of basic outline of cell but cellular details are lost, nucleus also is lost.
- That is architectural details are present i.e. basic cellular shape is preserved permitting recognition of cell outline & tissue architecture but cellular details are lost.
- This type of pattern is due to denaturation of structural proteins and enzymic proteins because of cell injury
- This blocks the proteolysis and thus architecture is maintained.

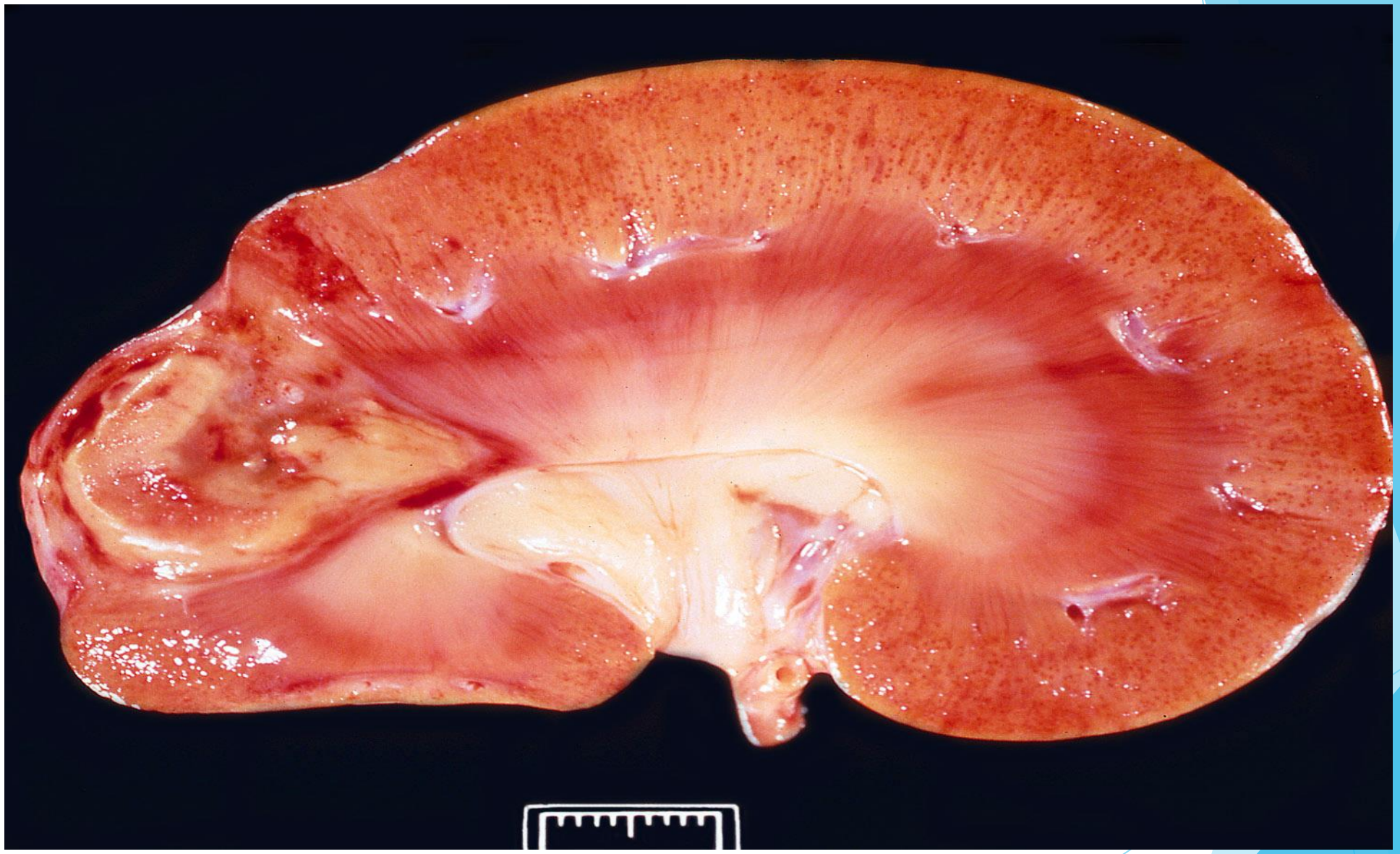
- This results when severe ischemia or hypoxic death of cells in liver, kidney, heart and adrenal gland,
- Fusobacterium necrophorus common cause of necrosis in cattle
- Muscular dystrophy associated with vit E defi. in cattle & sheep
- Renal tubular necrosis in mercury, uranium & thallium poisoning
- Grossly- necrotic area is firm, dry in consistency, grey white cooked appearance,
- **Microscopically**- Cellular details are lost.
- No attraction for neutrophils because the autolytic enzymes are destroyed.
- Dead material remains for long time.
- Removed by fragmentation and phagocytosis of cellular debris.



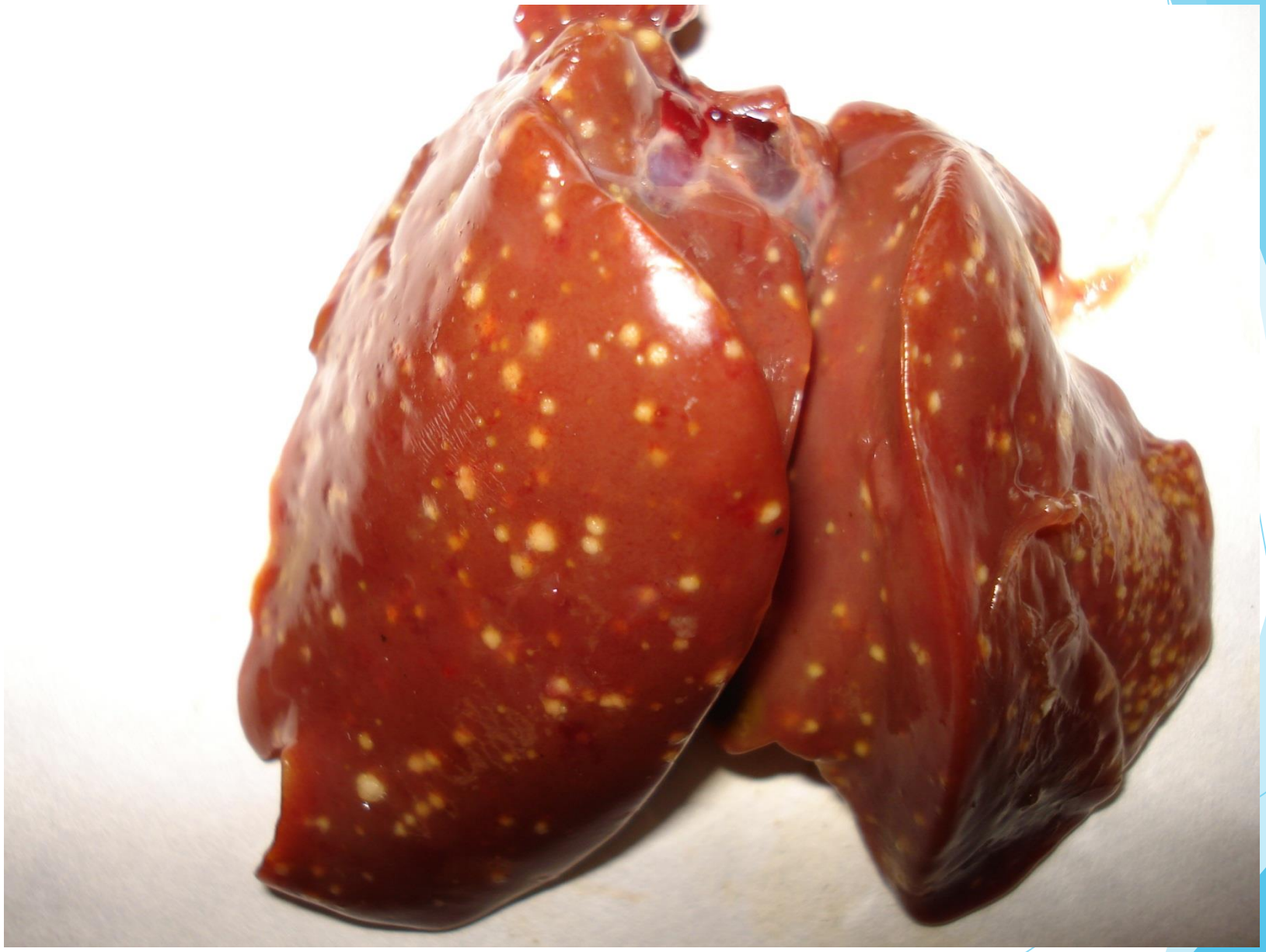
Multifocal coagulative necrosis with suppurtative hepatitis



Bov w/ white muscle disease



Renal infarction with sequestrum



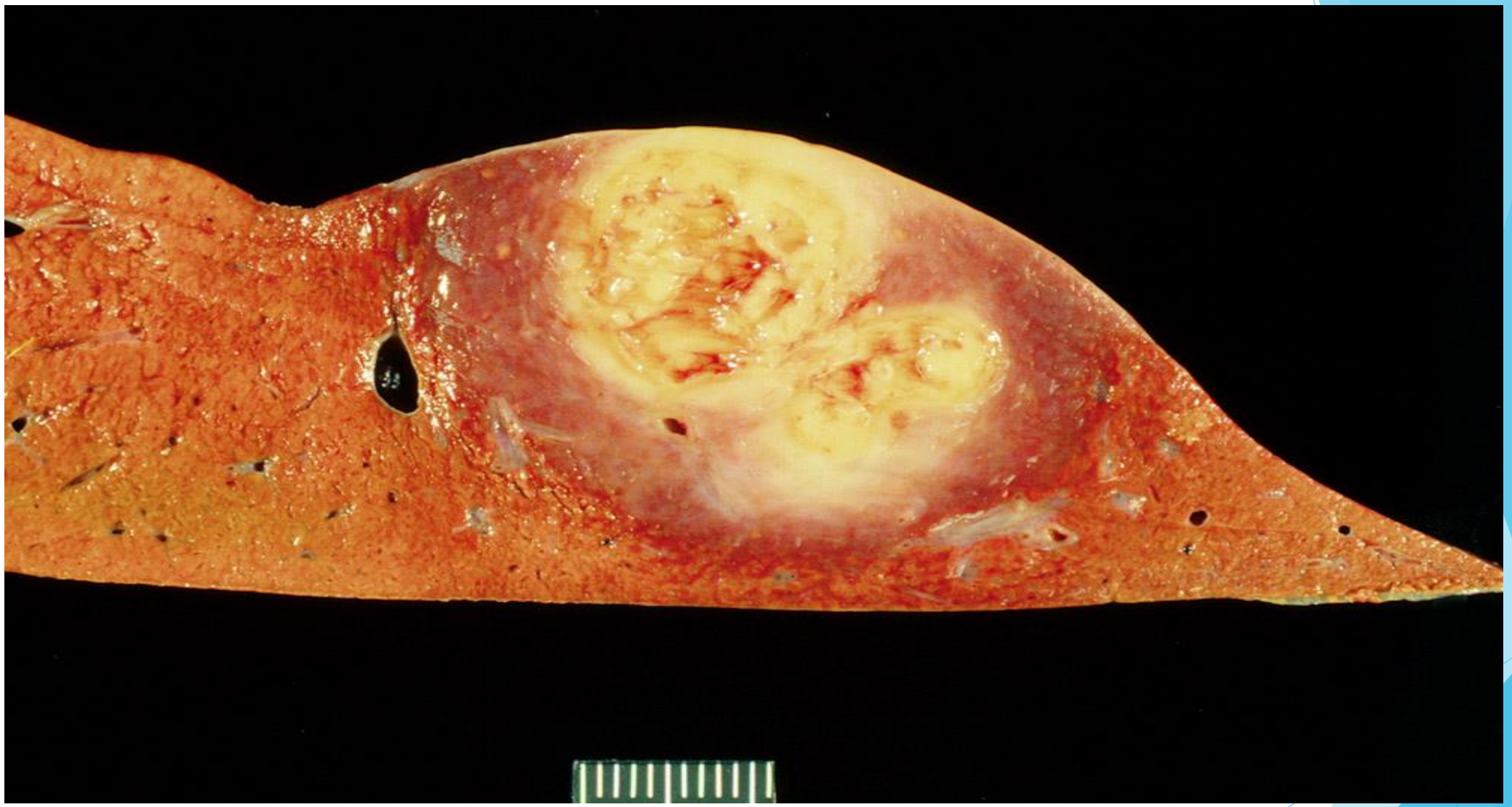
Liquefactive necrosis

- Characterized by disintegration of necrotic material into liquid mass where cellular and structural details are lost
- Due to enzymic digestion of cells by autolytic & heterolytic enzymes from lysosomes - action of hydrolytic enzymes
- Characteristically seen in focal bact infections by pyogenic bact. or local abscess or in areas of suppuration
- Accumulation of neutrophils due to stimuli by the pyogenic bacteria.
- Chemicals like turpentine cause accumulation of neutrophils and suppu inflam.
- Also cha. seen in ischemic destruction of brain tissue. For unknown reasons hypoxic death in CNS produce lique necrosis. Nervous tissue is normally soft and has less structural support and high lipid and water content so autolytic enzymes in the cells easily convert into liquid or semisolid mass.

Macroscopic appearance

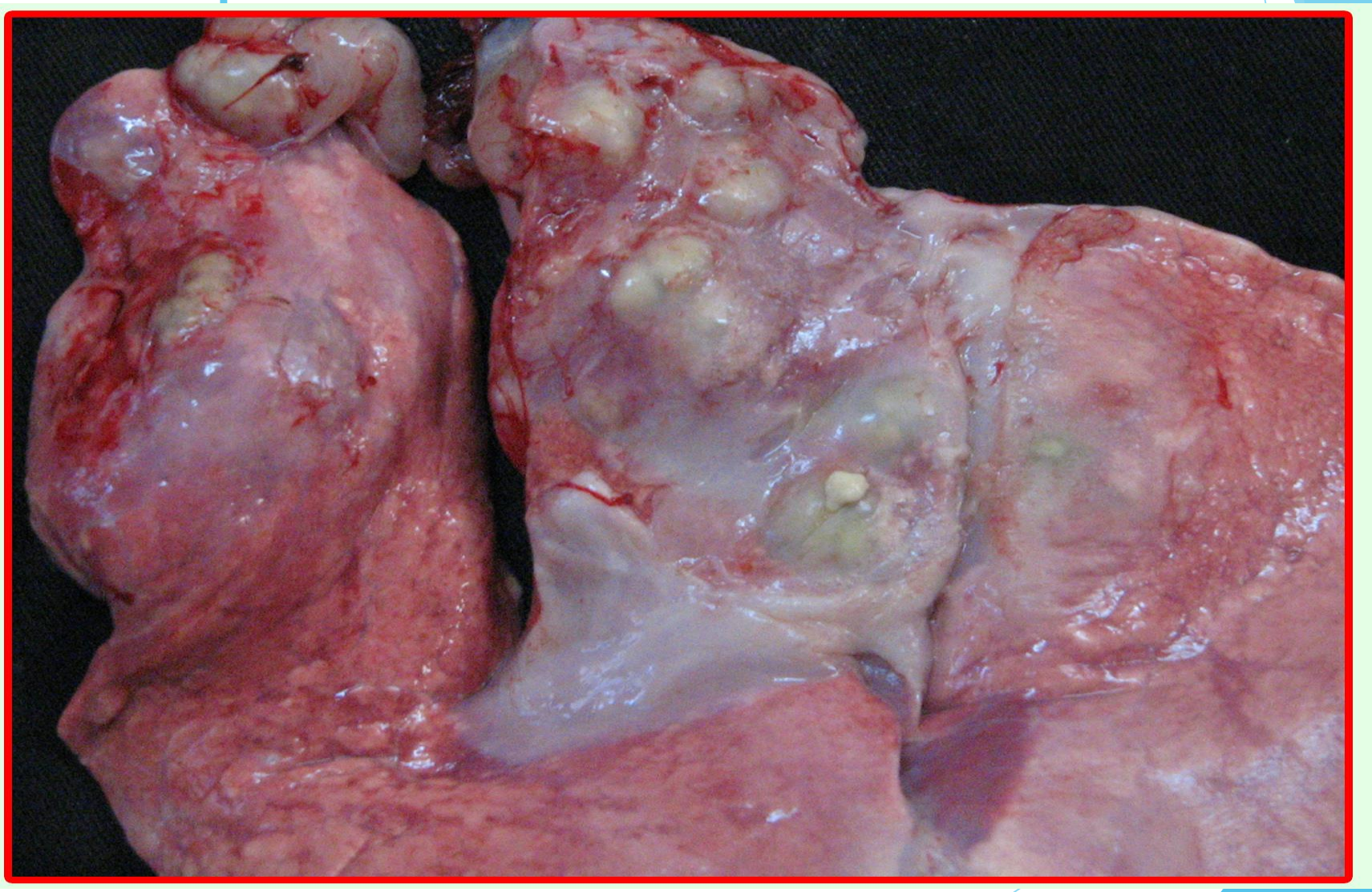
- **Consistency:** Tissue in area of necrosis is liquefied, watery, tenacious or semi solid.
- **Color:** white, green, yellow or red.
- If longstanding then formation of connective tissue around the mass.

It is associated with CO, cynide poisoning in brain. Thiamine defi in cats, Vit E defi in chicks, Mouldy corn poisoning in horses.



Focal chronic suppurative hepatitis (Liver abscess)

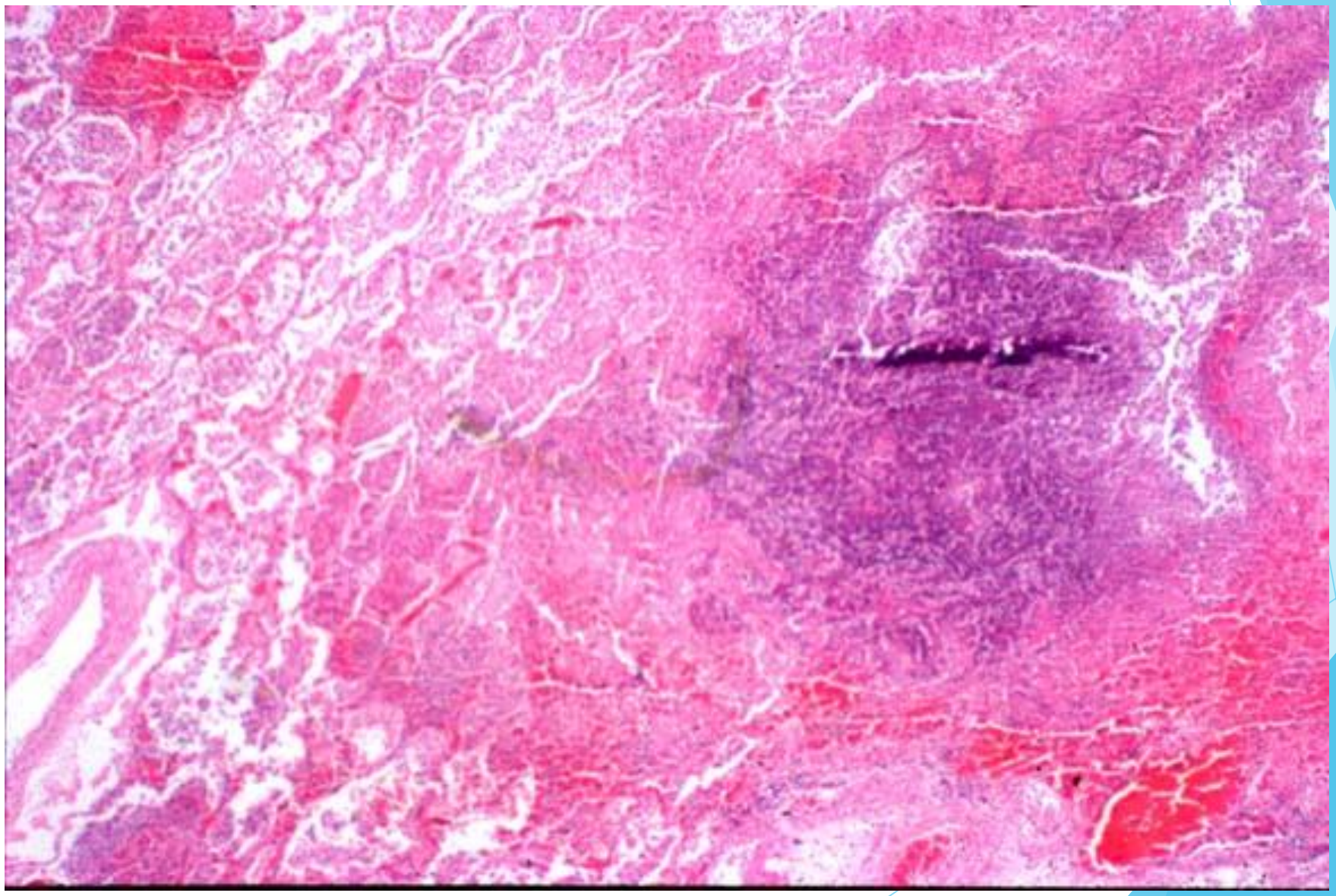
Suppurative pneumonia



Microscopic appearance

- No architectural details nor cellular details are seen
- Dead tissue is homogenous and stains pink with eosin
- Necrotic mass is surrounded by large number of neutrophils.
- Necrotic mass is surrounded by zone of acute or chronic inflam. depending upon the duration
- In brain neutrophils are not present unless bacteria are present

Abscess (liquefactive necrosis) of lung
The abscess cavity, filled with purulent exudate,



Caseous necrosis

- Caseous means white and cheesy
- Characterized by conversion of dead tissue into homogenous granular mass resembling cheese
- Absence of both structural and cellular details
- Characteristic of mycobacterium sp bacteria.

Seen in tuberculosis, oesophagostomiasis,

caseous lymphadenitis and addison’s disease.

Cheesy appearance is due to capsule of mycobacteria which contain lipopolysaccharides

Macroscopic appearance

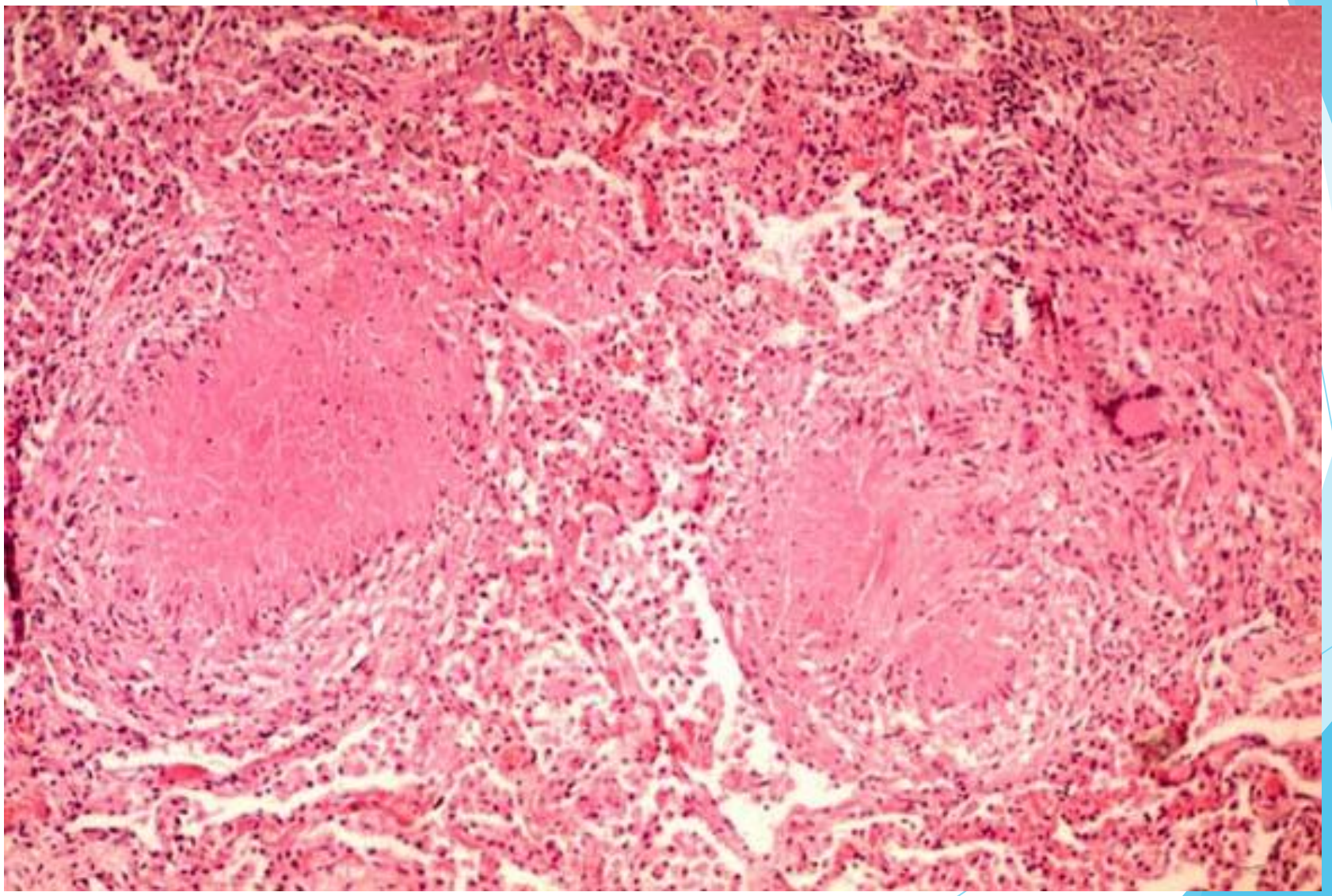
- Appearance : granular, amorphous, cheesy like
- Consistency : dry and creamy.
- Calcium salts are deposited in the tissue
- Mass may be covered by a connective tissue capsule.

Microscopic changes

- The cells are not totally liquefied nor outlines are preserved.
- Cellular and architectural details are lost.
- Distinctive amorphous granular debris seen.
- Calcification is very common.
- The caseous mass is enclosed within a granulomatous inflammatory wall (encapsulation)

Miliary tuberclesis

A low power view demonstrating caseating granulomas. Giant cells are present



Fat necrosis

- Death of the adipose tissue within the living individual.
- Three types of fat necrosis:
- Pancreatic fat necrosis
- Traumatic fat necrosis
- Nutritional fat necrosis

Pancreatic fat necrosis

- Death of adipose tissue in the vicinity of pancreas due to action of lipases.
- Caused by some injury to pancreas or its duct
- Powerful lipases release from pancreas destroy the pancreatic substance as well as adipose tissue in and around pancreas & throughout peritoneal cavity
- Lipases liquify the fat tissues and hydrolyze into F. acids and glycerol. F. acids combines with calcium to produce grossly visible chalky white areas (fat saponification)

Gross Appearance

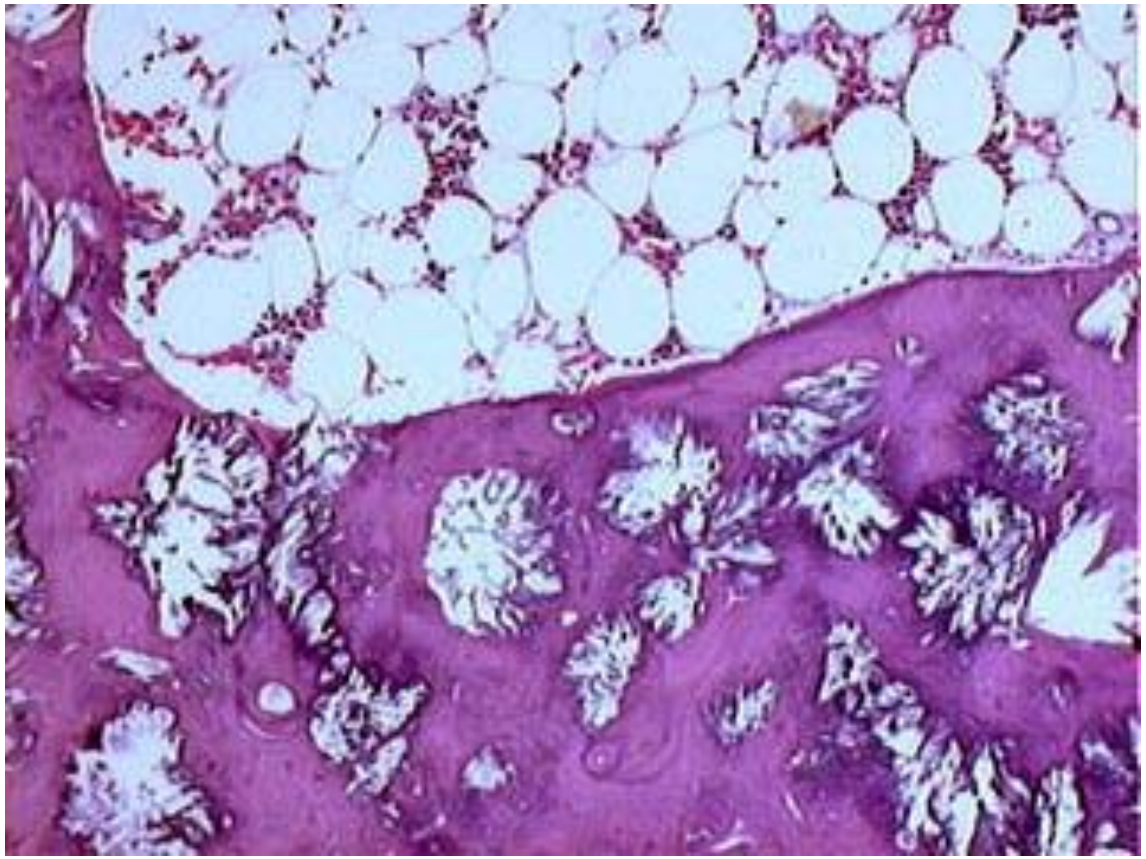
- White or yellowish white, chalky, firm, opaque masses may undergo calcification
- Inflammatory zone is seen at junction of necrotic and living tissue
- The metaplasia of adipose tissue occur. The adipose tissue may undergo metaplasia and form bone seen in abdominal fat of pig and cattle.
- **Microscopically** –adipose cells contain pink slight granular material with clefts of f. acids crystals.
- there are foci of shadow outlines of fat cells and inflammatory zone.

Traumatic fat necrosis

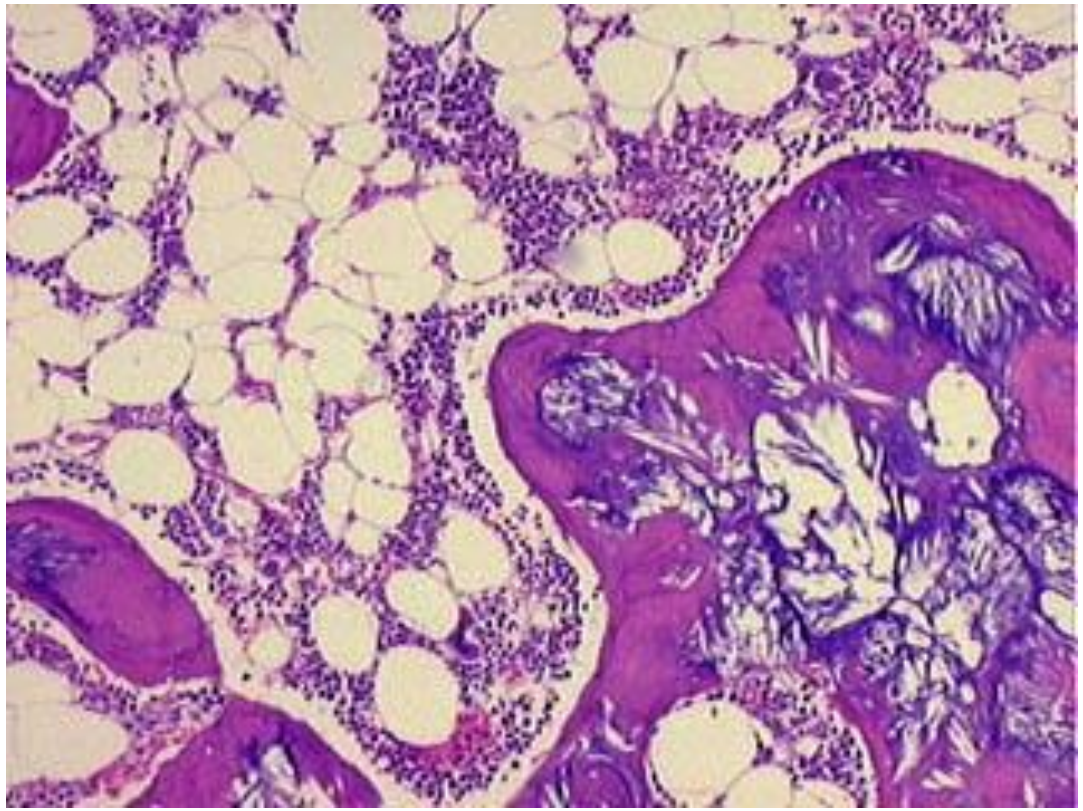
- Death of adipose in an area due to traumatic or mechanical injury during working, fighting, exercising , dog bites, parturition.
- Occurs in subcutaneous tissue.
- Macroscopically opaque chalky appearance.
- Microscopically zone of inflammation.

Nutritional fat necrosis

- Necrosis of fat tissue is associated with extreme emaciation and debility. Occur in starving & debilitated animals in diseases like TB & JD
- Common in abdominal fat (mesentric, omental, perirenal)
- Microscopically adipose cells has clefts and crystals



Photomicrograph of adipose tissue showing necrosis and calcification (40x, H&E stain).



Photomicrograph of adipose tissue showing necrosis and calcification (100 x, H&E stain).

Sequalae of necrosis

- Liquefaction & removal- by neutrophils, blood and lymph when area is small
- Liquefaction & formation of cyst- when area is large. The necrotic tissue is converted into fluid by cellular enzymes and connective tissue wall is formed due to irritating nature of fluid
- Liquefaction & abscess formation -when pyogenic bact invade the necrotic tissue
- Encapsulation without liquefaction- when enzymes capable of liquefaction are absent and C.T. wall is formed as necrotic tissue acts as to irritant
- Sloughing & desquamation- when external surfaces are involved or in dig tract or burns involve the skin
- Organization of necrotic tissue- when invaded by new blood vessels, fibroblasts & macrophages- area is replaced by new fibro vascular tissue
- Calcification-may occur in TB
- Metaplasia- occur in necrotic tissue-in fat necrosis appearance of bone in abdo fat in of pigs
- Gangrene-invaded by saprophytic organisms
- Death- when moist gangrene is present. Also occur if vital organ like heart or brain is involved

Apoptosis

- Distinctive and imp method of cell death-Different from necrosis
- Meaning is Apo-away from; Ptosis- Falling
- This is form of cell death designed to eliminate unwanted host cells through activation of coordinated, internally programmed, series of events brought about by a set of gene products
- It is a programmed cell death in several imp physio & patho processes like
- Programmed destruction of cells during embryogenesis & organogenesis
- Hormone dependent physiological involution of endometrium during menstrual cycle & involution of lactating breast (M.gland) in man & animals
- Death of neutrophils in acute inflam
- Deletion of auto reactive B & T cells- removal of self reactive B & T cells during their maturation in thymus or B. M or bF in poultry. Any developing T or B cells that express receptor for self antigen undergo apoptosis
- Cell deletion in prolif population in intestinal crypt epi or cell death in tumors
- A variety of injurious stimuli that cause necrosis but when given in low doses produce apoptosis
- Apoptosis usually involve single cell or small cluster of cells appear

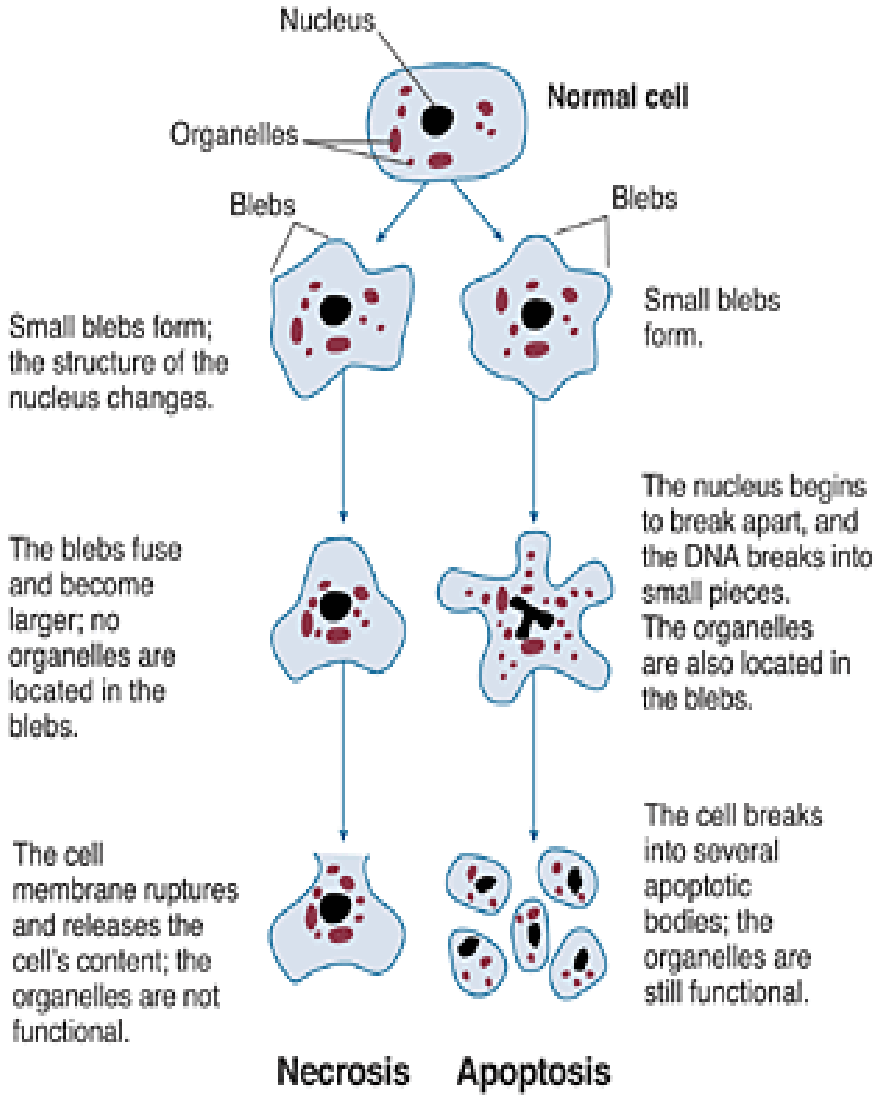
  as round or oval masses and stain intensely eosinophilic

Morphological changes cha. of Apoptosis

- Apoptosis usually involve single cell or small cluster of cells appear as round or oval masses and stain intensely eosinophilic. Cha. Changes are
- **Cell shrinkage- cell is smaller in size, cyto become dense, organelles tightly packed**
- **Chromatin condensation- most cha. feature- Nuclear chromatin is condensed & aggregates periphery under the nuclear mem. The nucleus may break up producing two or more fragments- reflected as fragmentation of DNA in to nucleosome sized particles**
- **Formation of cytoplasnic blebs (buds) & apoptotic bodies- The apoptotic cell rapidly shrink & show extensive surface blebing & finally undergo fragmentation into number of mem bound bodies composed of cytosol & tightly packed organelles**
- **Phagocytosis of apoptotic bodies by nearby healthy cells or macrophages. As phagocytic bodies are quickly extruded & phagocytosed & degraded within lysosomes even significant apoptosis may not be visible microscopically**
- Apoptosis does not produce inflam & this makes difficult to detect under microscope

Morphological features:

- Cell shrink
- Nuclear chromatin condensation & fragmentation.
- mitochondria break down
- Cytoplasmic budding & apoptopic bodies formation
- phagocytosis

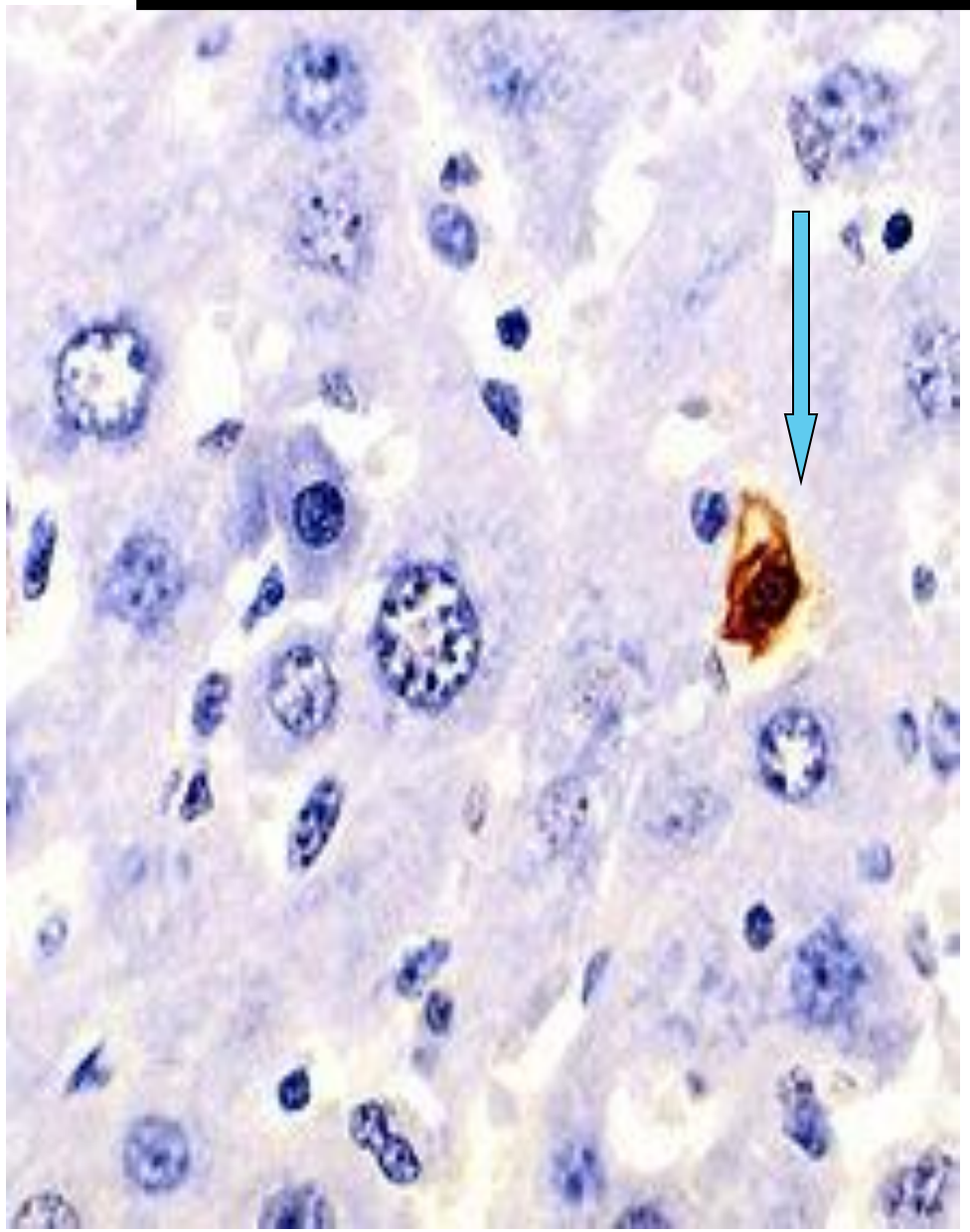


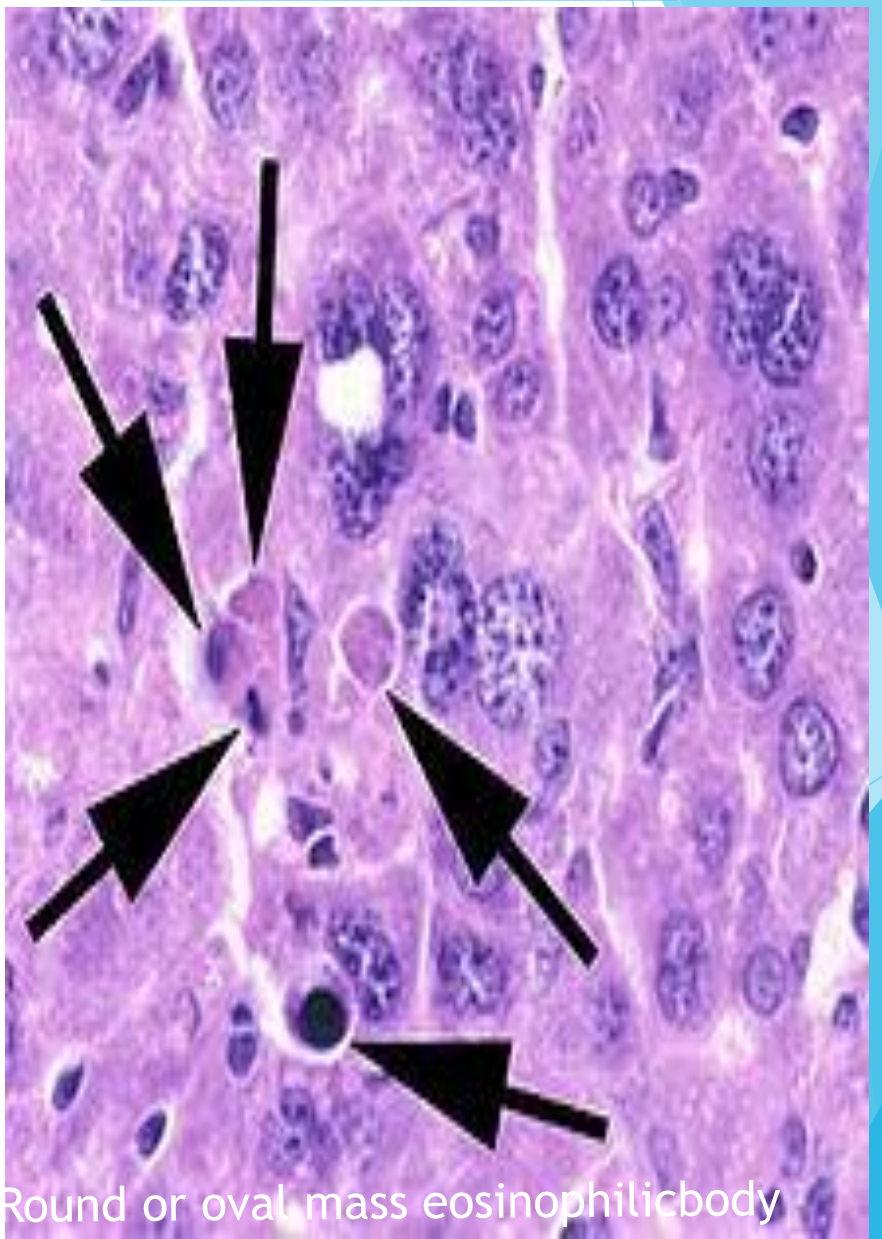
Apoptosis Vs necrosis

Apoptosis	Necrosis
1. Fragmentation of genomic DNA into a 200 bp fragments	1. No fragmentation of DNA
2. Condensation of chromatin and formation of apoptotic body	2. No condensation of chromatin and no formation of apoptotic body
3. Initiated by a signal transduction Process	3. Initiated by direct cell damage mostly physical
4. active process: requires macromolecule synthesis	4. passive process:do not require macromolecule synthesis
5. Does not cause inflammation	5. Cause inflammation

Apoptotic body

(mouse liver)





Round or oval mass eosinophilicbody