Necrosis

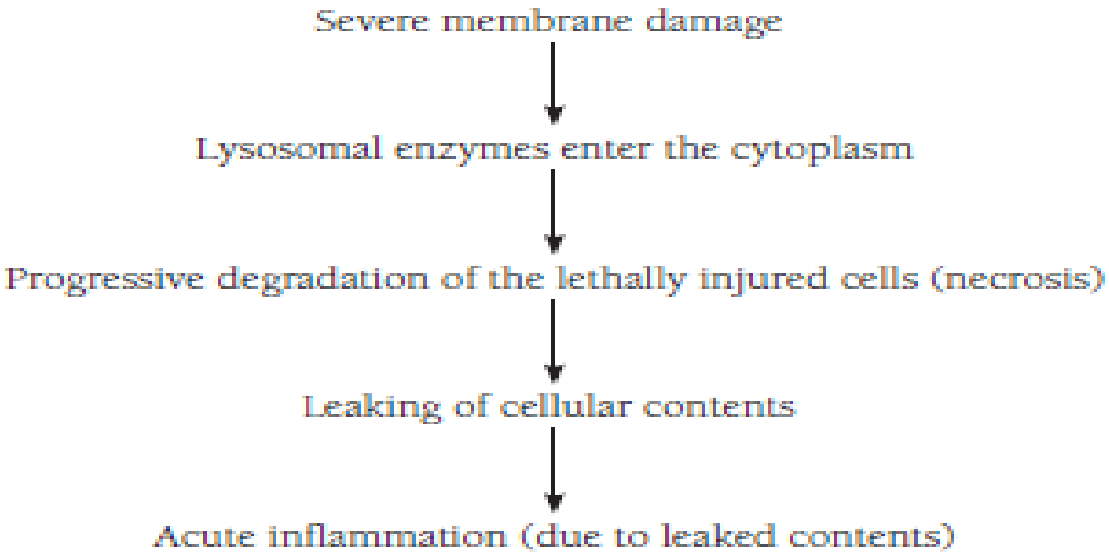
==========

- Necrosis is a localized area of cell death of living tissue followed later by degradation of tissue by hydrolytic enzymes liberated from dead cells; it is invariably accompanied by inflammatory reaction.

Causes of necrosis

==========

- May occur directly when exposed to pathogens or occur after reversible injury
- 1- Obstruction or interruption of blood supply to the cells for reasons:
- A - blockage of the arteries supplying the blood to the cells due to the presence of thrombus or embolus or contract of the arteriole because the neurological effects or the occurrence of external pressure on it and in this case the cellular area fed by this arteriole is suffer from necrosis and the entire necrotic area called infarct
- - hypoxia (less than 2-3 milligrams of oxygen per liter of water) or Anoxia(When oxygen levels are at zero)
- B - the presence of passive hyperemia leads to injury to tissue necrosis directly due to the depletion of oxygen and nutrients, for example, necrosis that occurs when folding or warping or narrowing the intestine
- C- General anemia causes necrosis in several parts of the body due to lack of oxygen and nutrients
- 2- Exposing cells or tissues to various chemical agents such as inorganic toxins such as acids, bases and organic toxins that are sourced from pathogenic organisms
- 3- Exposing the tissue to various physical factors:
- High heat causes inhibition of the action of intracellular enzymes and affects the nature of the cytoplasm
- Freezing affects on capillary blood vessels and ice crystals form in the cells
- trauma and pressure lead to rupture of cells or destruction of blood vessels
- Ionizing radiation, such as X-rays and ultraviolet rays, cause intracellular molecules to be dissolved and free radicals to form.
- 4- Biological factors such as parasites either causes necrosis directly by pressure or by toxins secreted from them or indirectly by pressure on blood vessels
- 5- Spontaneous or induced hypersensitivity against many antigens may lead to immune reactions that end in necrosis, for example, when infected with tuberculosis, a defensive immune protein called tuberculoprotien protein is formed in the body that is derived from toxins secreted by tuberculosis bacilli and leads to necrosis of neighboring cells.



FLOWCHART 1.6. Sequence of events in cellular necrosis.

Macroscopic or Gross appearance

- The necrotic area can be distinguished with the naked eye due to its different color and texture
- The color of the necrotic area depends on the amount of blood in it
- Pale when blood-free and dark when congested or bleeding
- Texture of the necrotic area is Fragile and easy to shatter
- Edges of the necrotic area are sharp
- The necrotic area is surrounded by a red zone that represents an inflammatory reaction in normal nearby tissues
- The necrotic organ may be bad smell or without smell , and this depends on the presence of saprophytic bacteria on the remains of necrotic cells.

Microscopic appearance

- When examining the necrotic area or necrotic cells in the histological section, the following is observed:
- 1- Loss of the general shape of the outlines cells
- 2- Changes in the nucleus
- 3- Presence of changes in the cytoplasm
- 4- Presence of a red inflammation area between the necrotic area and the adjacent normal areas in same tissue

- **First: Changes in the nucleus**:
- 1- pyknosis
- pyknosis is the Thickening of nucleus and is the first response to necrosis
- The size of the chromatin material decreases until the nucleus becomes a small, homogeneous circular mass and basophilic
- The nucleolus, chromatin granules or any structure in the nucleus cannot be distinguished.
- The thickening nucleus is dyed black when dyeing the sections with hematoxylin and eosin pigments because the release the DNA, which attracts a large amount of hematoxylin pigment, so it is colored black

- 2- karyorrhexis
- karyorrhexis is the Rupture of the nucleus into small pieces or very small crumbs
- These pieces may remain in the same position as the original nucleus or spread into the cytoplasm
- 3- karyolysis or chromatolysis
- karyolysis is lysis of the nucleus
- It is the decomposition of the nucleus so that all the internal structures in the nucleus, such as the nucleolus and chromatin, disappear, and only the nuclear membrane remains.
- karyolysis due to DNase activity
- So the nucleus appears under the microscope as an empty hollow ball surrounded by a nuclear membrane.
- 4- Disappearance of nucleus
- All previous changes lead to the disappearance of the nucleus
- The cell appears under the microscope devoid of the nucleus

- **Second: Changes in the cytoplasm**:
- 1- denaturation of cytoplasmic proteins which then bind strongly to the eosin and the cytoplasm become strongly acidophilic , where it is dyed in a dark red color with eosin, and the composition of the cytoplasm is not clear under the microscope
  2- Formation of myelin figures (phospholipid masses derived from damaged cell membranes).

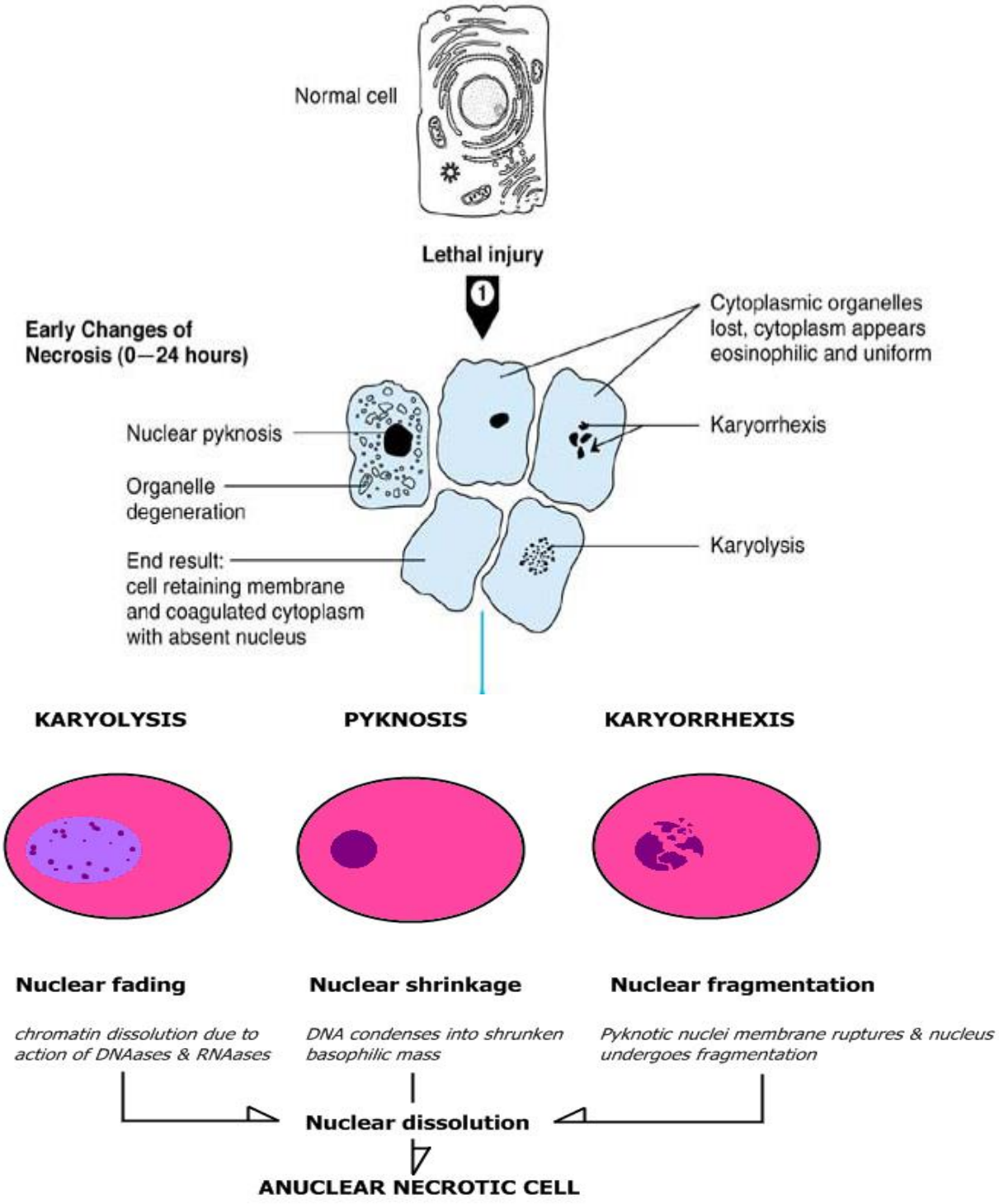
- 3- Cytoplasmolysis
- The cytoplasm of necrotic cells gradually decomposes until all its components disappear

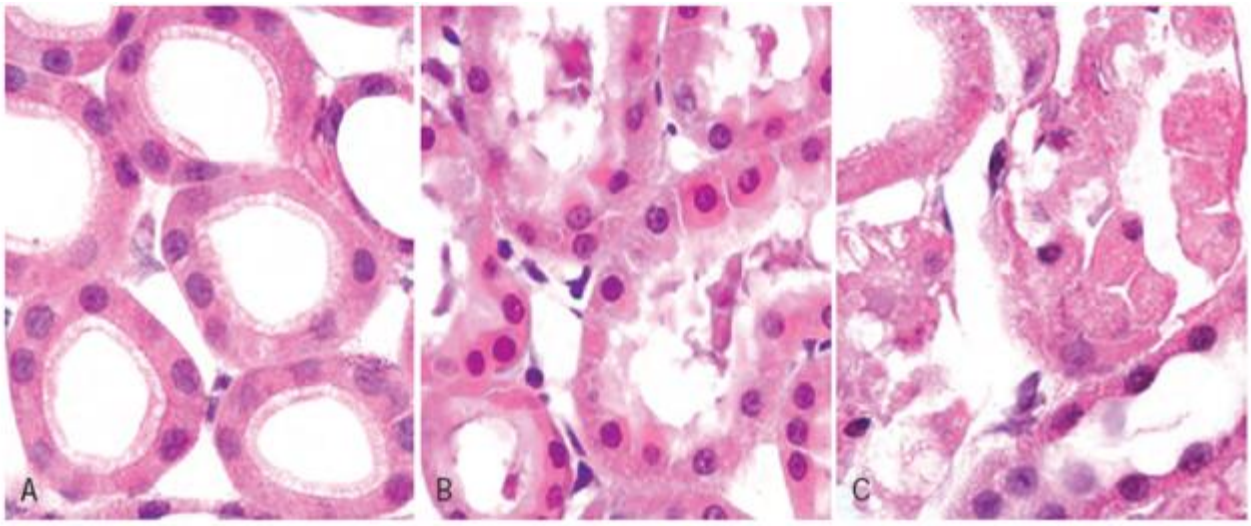
- The death of the cell is not determined by the decomposition of the cytoplasm, but by the presence of the nucleus.
- When all the previous changes are made in the nucleus and cytoplasm, the outlines of the cells or their characteristic external appearance disappear and it becomes

difficult to see the boundaries of the cells and this can be clearly seen in tuberculosis.

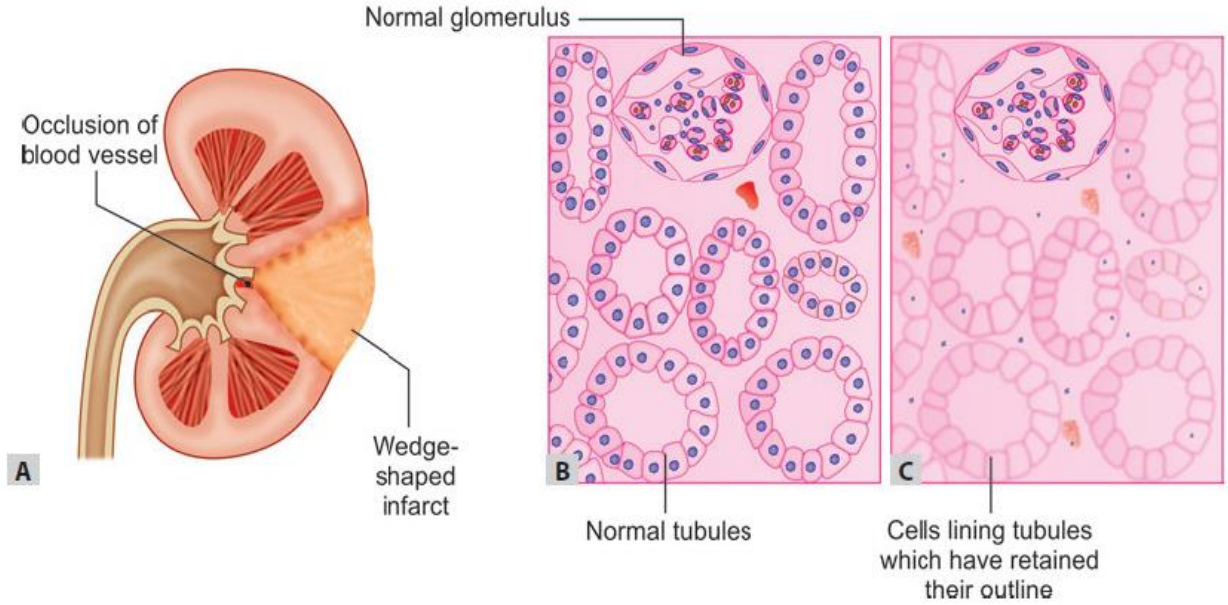
- The necrotic area is surrounded by an inflammatory red band consisting of hyperemia or congestion and inflammatory cells to isolate from the neighboring normal cells, which is considered as a defensive response of the body to isolate the necrotic area

- the necrotic cells are removed by phagocytosis of the cellular debris by infiltrating leukocytes and by digestion of the dead cells by the action of lysosomal enzymes of the leukocytes





A, Normal kidney tubules with viable epithelial cells.
B, Early reversible injury(paranecrosis or prenecrosis) showing surface blebs, increased eosinophilia of cytoplasm, and swelling of cells
C, Necrosis (irreversible injury) of epithelial cells, with loss of nuclei, fragmentation of cells, and leakage of contents.



17A to C: (A) Gross appearance of infarct of kidney; (B) Microscopy of normal kidney parenchyma; (C) Infarcted area of kidney

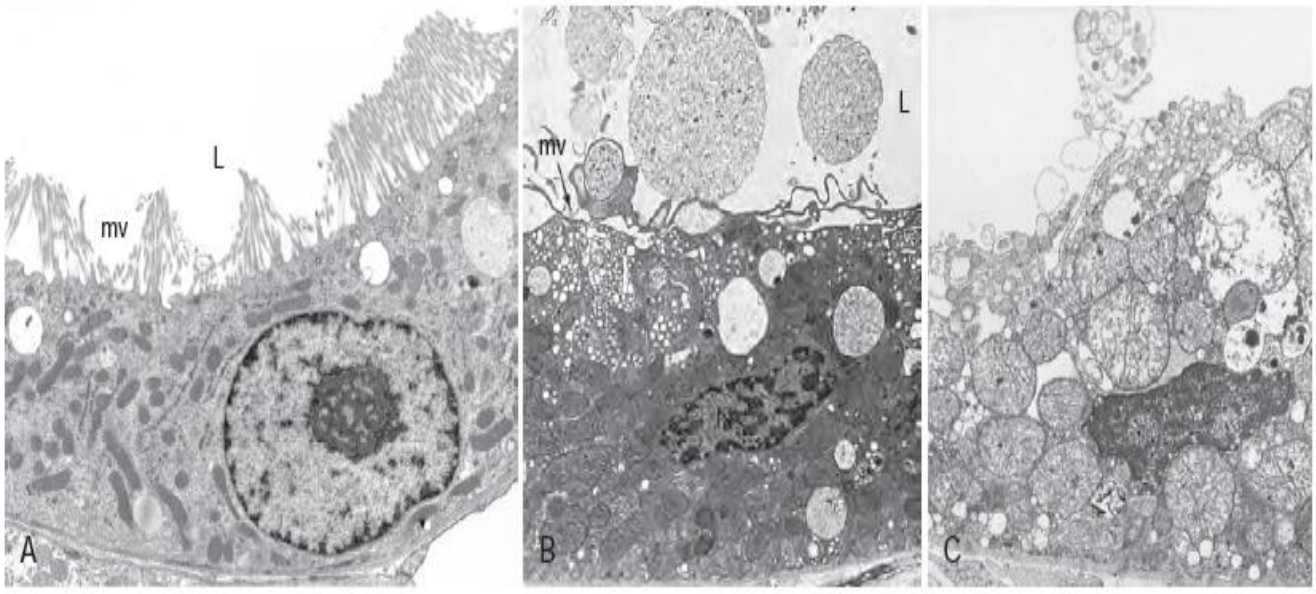
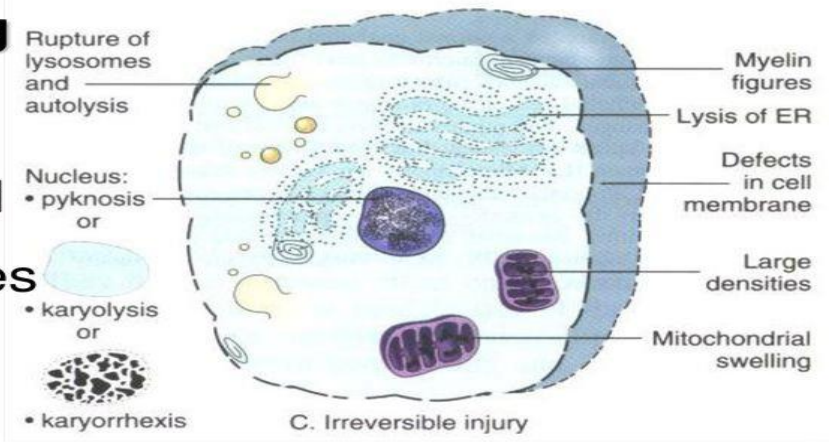


Figure 2-10 Ultrastructural features of reversible and irreversible cell injury (necrosis) in a rabbit kidney. **A,** Electron micrograph of a normal epithelial cell of the proximal kidney tubule. Note abundant microvilli (mv) lining the luminal surface (L). **B,** Epithelial cell of the proximal tubule showing early cell injury resulting from reperfusion following ischemia. The microvilli are lost and have been incorporated in apical cytoplasm; blebs have formed and are extruded in the lumen. Mitochondria would have been swollen during ischemia; with reperfusion, they rapidly undergo condensation and become electron-dense. **C,** Proximal tubular cell showing late injury, expected to be irreversible. Note the markedly swollen mitochondria containing electron-dense deposits, expected to contain precipitated calcium and proteins. Higher magnification micrographs of the cell would show disrupted plasma membrane and swelling and fragmentation of organelles. (**A,** Courtesy Dr. Brigitte Kaisslin, Institute of Anatomy, University of Zurich, Switzerland. **B, C,** Courtesy Dr. M. A. Venkatachalam, University of Texas Health Sciences Center, San Antonio, Texas.)

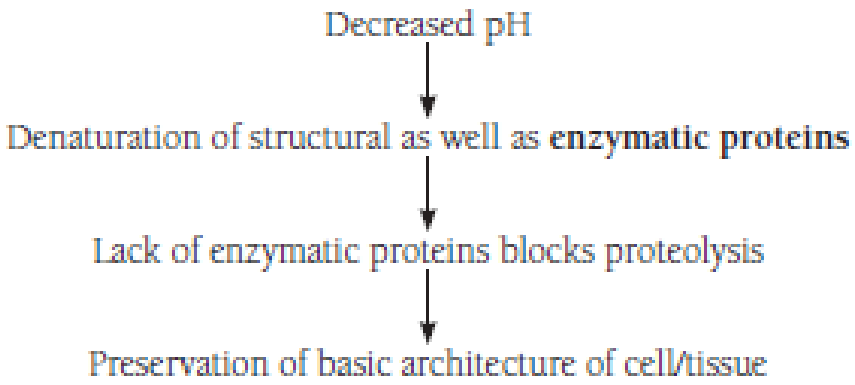
Ultrastructural morphological changes: Necrosis

- **Defects in cell membrane**
- **Mitochondrial swelling** and large densities
- **Swelling of the ER** and detachment of ribosomes
- Appearance of **myelin figures**
- **Rupture of lysosomes**



Types of necrosis

- The type of necrosis that occurs in the tissue depends on several factors:
- 1- Host factors including the nature of the tissue and the type of inflammatory response produced by the host
- 2- The nature of the causative agent and whether toxins or enzymes produce a state
- Each type of necrosis has a distinctive macroscopic and microscopic appearance
- 1- Coagulative n. Or simple necrosis
- All types of necrosis start with this type and then turn into another type or not
- It is the most common pattern of necrosis and is caused by ischemic injury(ischemic necrosis) resulting in hypoxic death of cells in all tissues except the brain , (liquefactive necrosis occurs in the brain). The organs commonly affected are the heart, kidney, and spleen.
  - A localized area of coagulative necrosis is called an **infarct**.
  -.There is preservation of the basic architectural outlines and type of tissue can be recognized but cellular details are lost.



FLOWCHART 1.7. Mechanism of evolution of coagulative necrosis.

causes

- ==========
- Pathological bacterial toxins
- Infarct (local ischemia)
- Exposure to heavy metals and caustic chemicals
- slight burns
- Vitamin A deficiency

- **Gross or Macroscopic appearance**
- ==========
- The necrotic area is dry and hard
- Its color depends on the amount of blood in it, it is gray or yellowish when it is free of blood and dark reddish when there is congestion or bleeding
- Focus of coagulative necrosis in the early stage is pale, firm, and slightly swollen and is called infarct. With progression, the affected area becomes more yellowish, softer, and shrunken

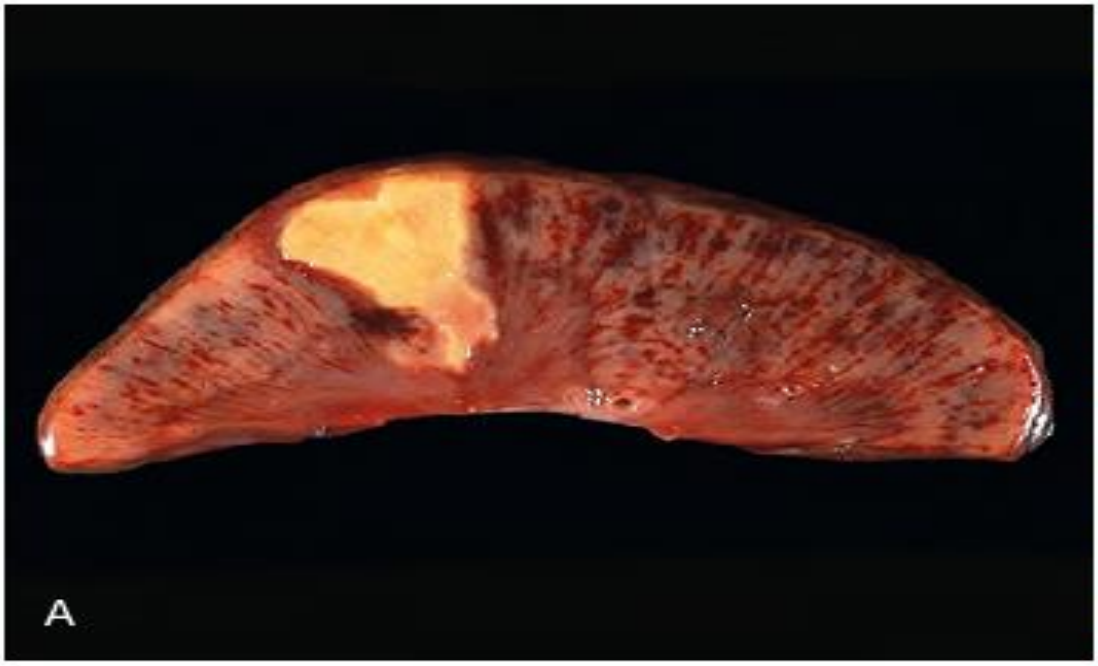
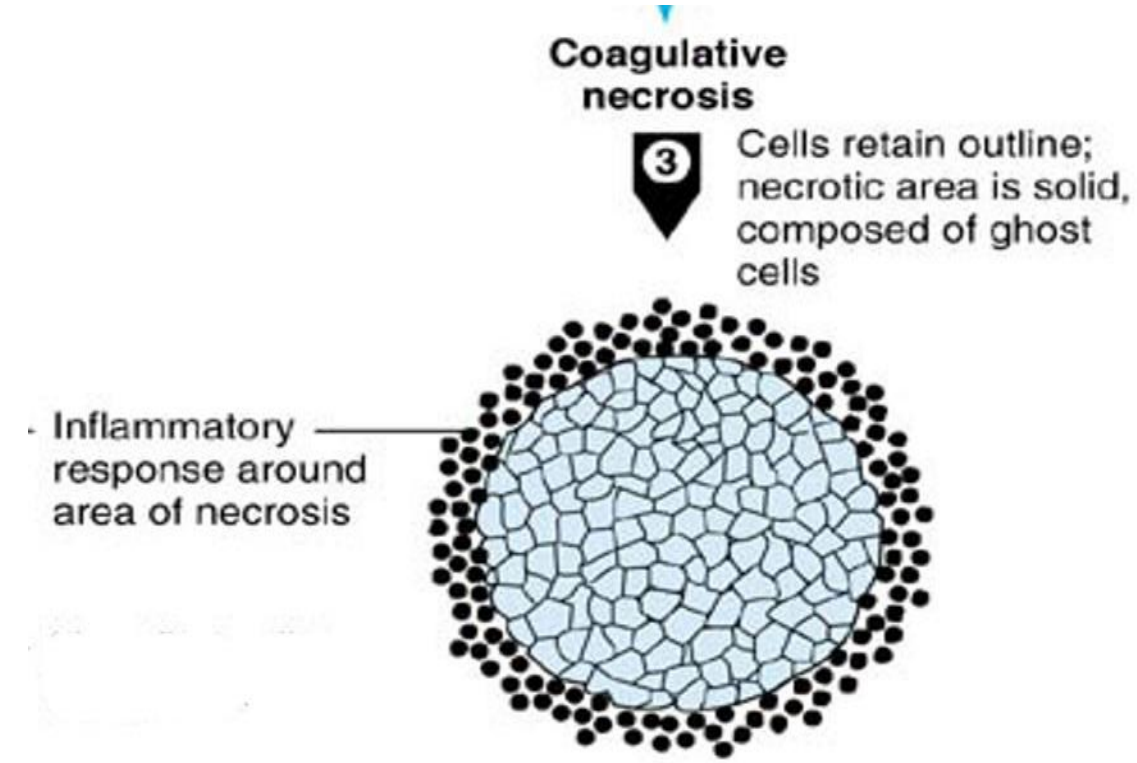


Figure 2-11 Coagulative necrosis. **A,** A wedge-shaped kidney infarct (yellow).

- **Microscopic appearance**
- ==========
- The general shape of the tissue is clear, but the details of the cells in the necrotic area are not clear.
- Where the cytoplasm appears to be clot-grainy and pale or dyed red.
- The nucleus suffers one or all stages of necrosis from thickening, rupture, decomposition or complete disappearance
- increased eosinophilic of the cytoplasm and decreased basophilic of the nucleus are observed.
- the necrotic area is infiltrated by inflammatory cells and the dead cells are phagocytosed leaving granular debris and fragments of cells

- Myocardial infarction is an excellent example in which acidophilic, coagulated enucleate cells are seen



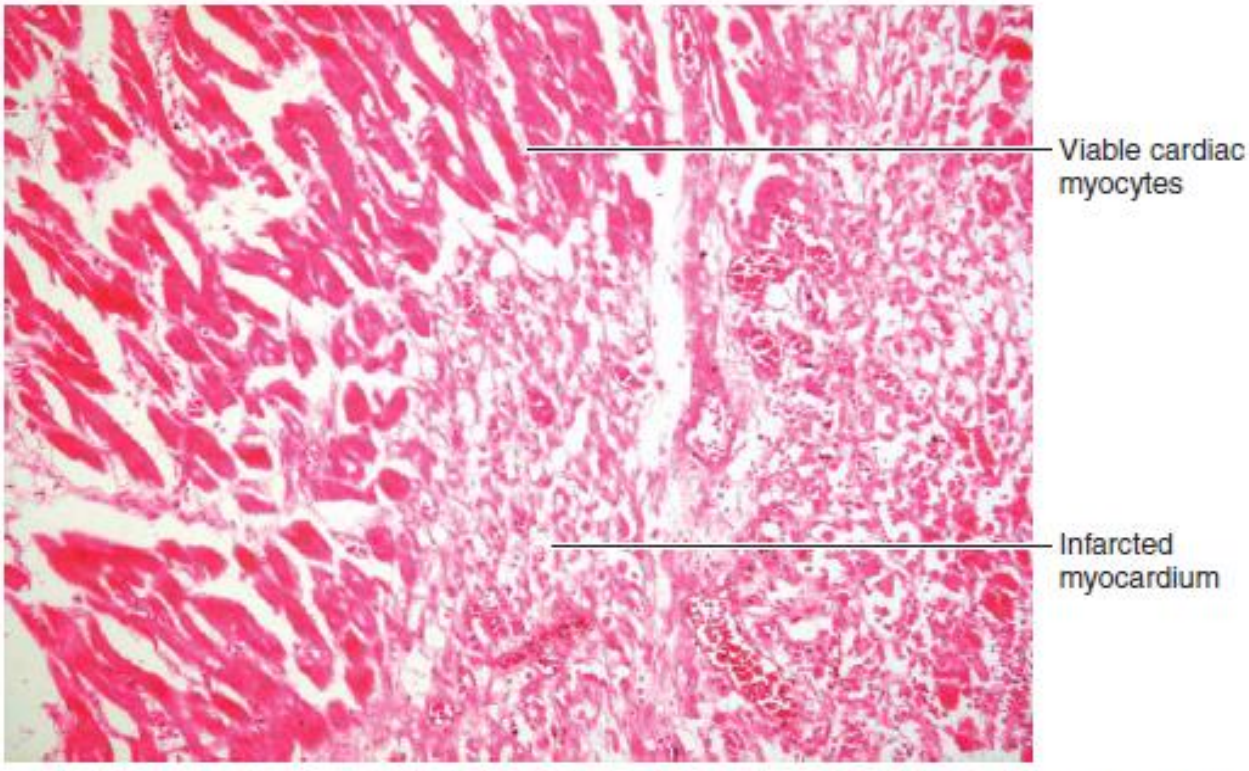
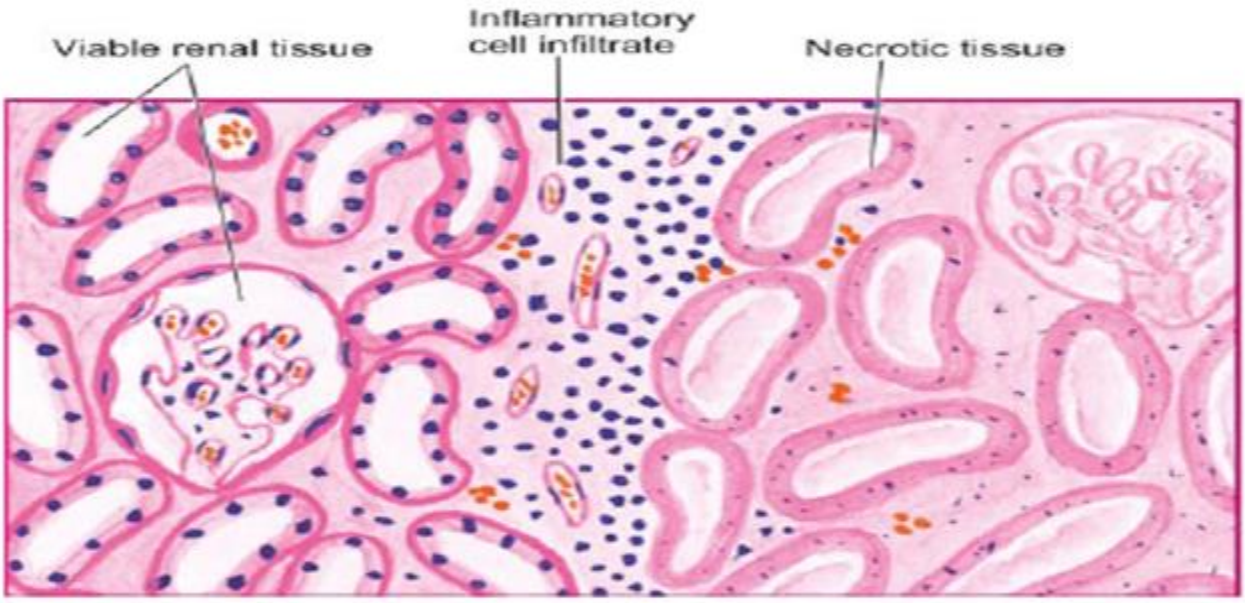


FIGURE 1.7. Infarcted myocardium surrounded by viable cardiac myocytes (H&E; 100×).



Coagulative necrosis in infarct kidney. The affected area on right shows cells with intensely eosinophilic cytoplasm of tubular cells but the outlines of tubules are still maintained.
The nuclei show granular debris.
The interface between viable and non-viable area shows chronic inflammation and proliferating vessels.

- **Prognosis**
- ----------
- In the advanced stages of this necrosis, the following changes may be observed:
- The necrotic area can act as irritant, resulting a fibrous reaction surrounding it containing neutrophils.
- Calcification may occur in the necrotic area due to cell death and Obstruction of blood supply
- The necrotic area may be replaced with fibrous tissue composed of neutrophils, fibrous connective tissue and capillary blood vessels
-

2- Caseous necrosis (caseous= cheese-like)

- This type of necrosis is most common cause is tuberculosis.its found in the centre of foci of granuloma of tuberculous infections.
- It combines features of both coagulative and liquefactive necrosis.

- It is characterized by the disappearance of tissue details and the necrotic area appear to have granular a cheesy tan to white appearance.
-This begins as infection is recognized by the body and macrophages begin walling off the microorganisms or pathogens. As macrophages release chemicals that digest cells, the cells begin to die. As the cells die they disintegrate but are not completely

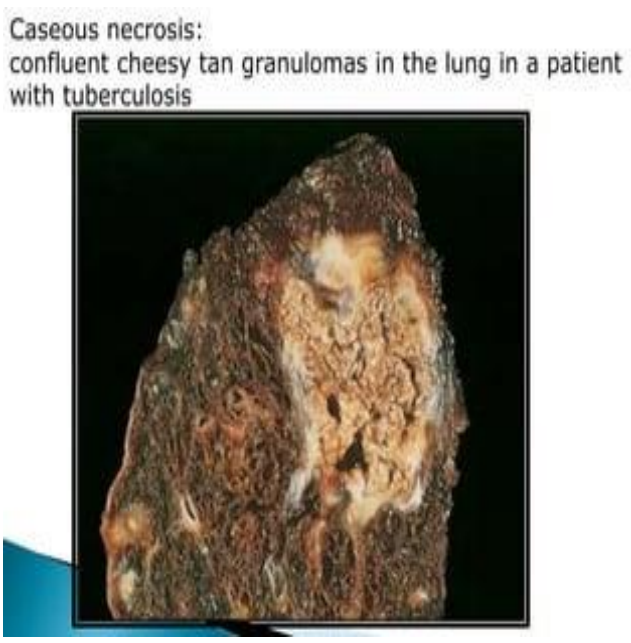
digested and the debris of the disintegrated cells clump together creating soft granular mass that has the appearance of cheese. As cell death begins, the granuloma forms and cell death continues the inflammatory response is mediated by a type IV hypersensitivity reaction.

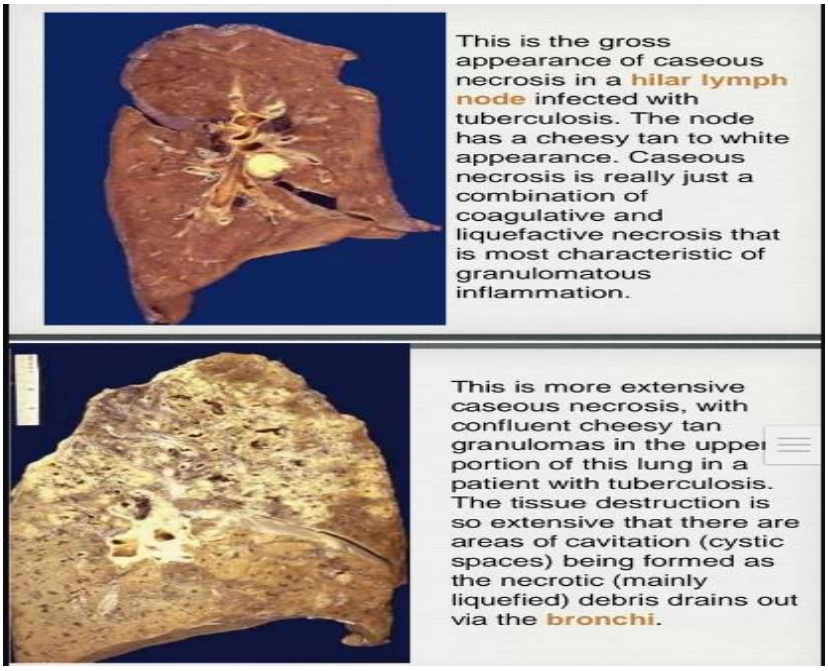
- **causes**
- ----------
- Tuberculosis (TB) is the most common cause of caseous necrosis. TB is a bacterial disease of the lungs (pulmonary). It can also spread to other organs and systems throughout your body

-It can also be caused by syphilis and certain fungi:

- Histoplasmosis: A respiratory illness caused by a fungus in the soil. Like TB, it can spread to other parts of your body.
- Syphilis: A sexually transmitted infection that leads to degeneration of nervous system.

- **Macroscopic appearance or Gross examination**
- ==========
- the necrotic areas like dry cheesy white (caseous) or yellowish and granular. This appearance is partly attributed to the histotoxic effects of lipopolysaccharides present in the capsule of the tubercle bacilli, *Mycobacterium tuberculosis*.
- foci of necrosis as dry or wet nature and crumbles easily.





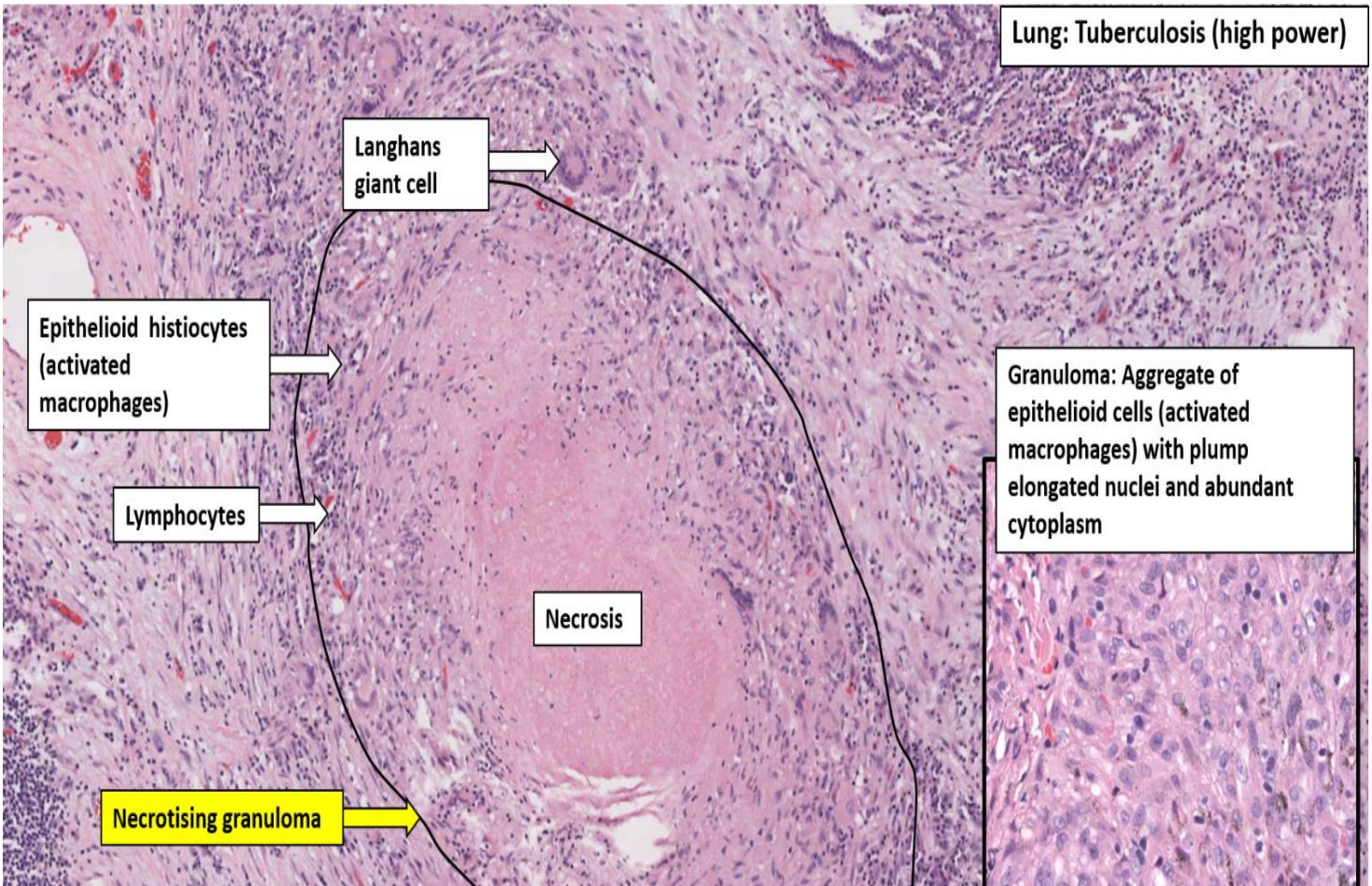
- **Microscopic appearance or examination**
- ==========

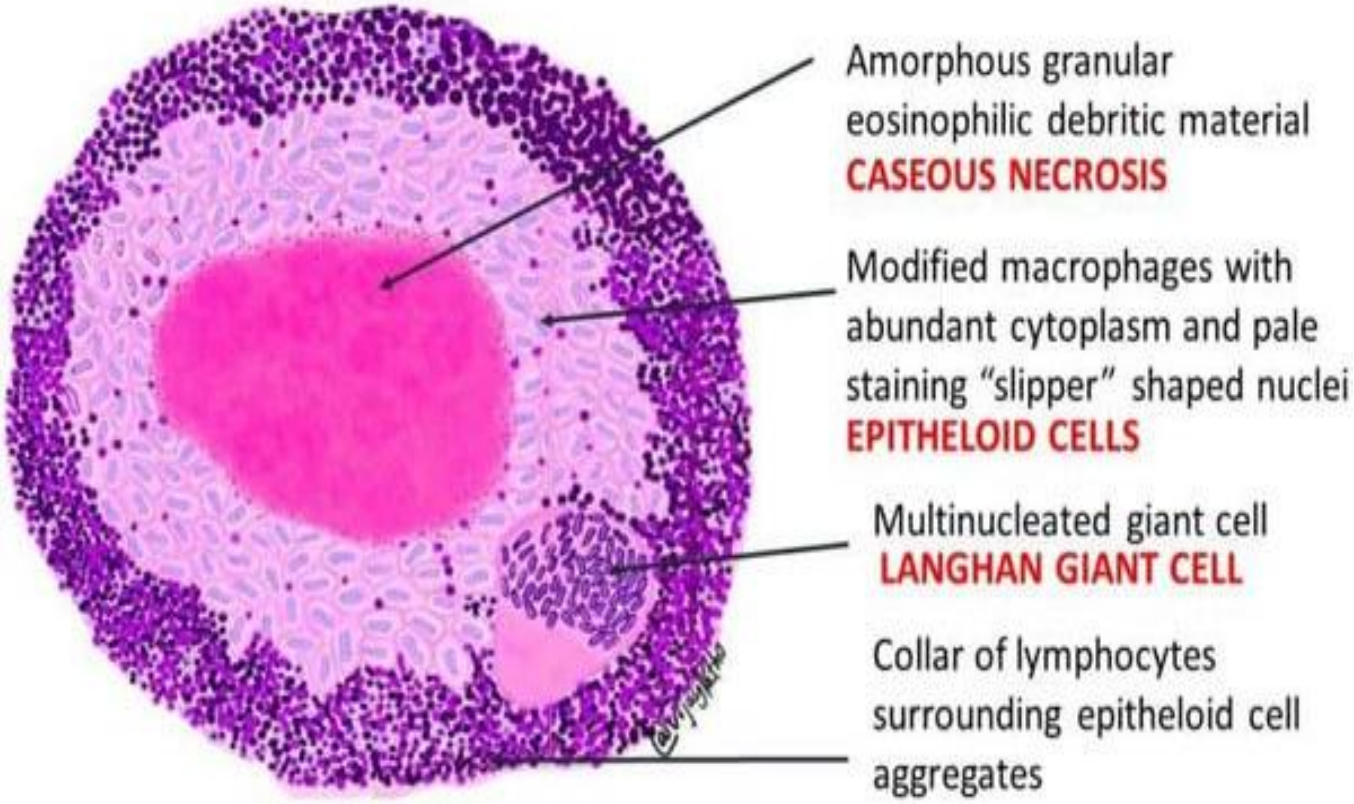
-The necrotic area is clearly determined on the normal area in same tissue with or without a fibrous capsule

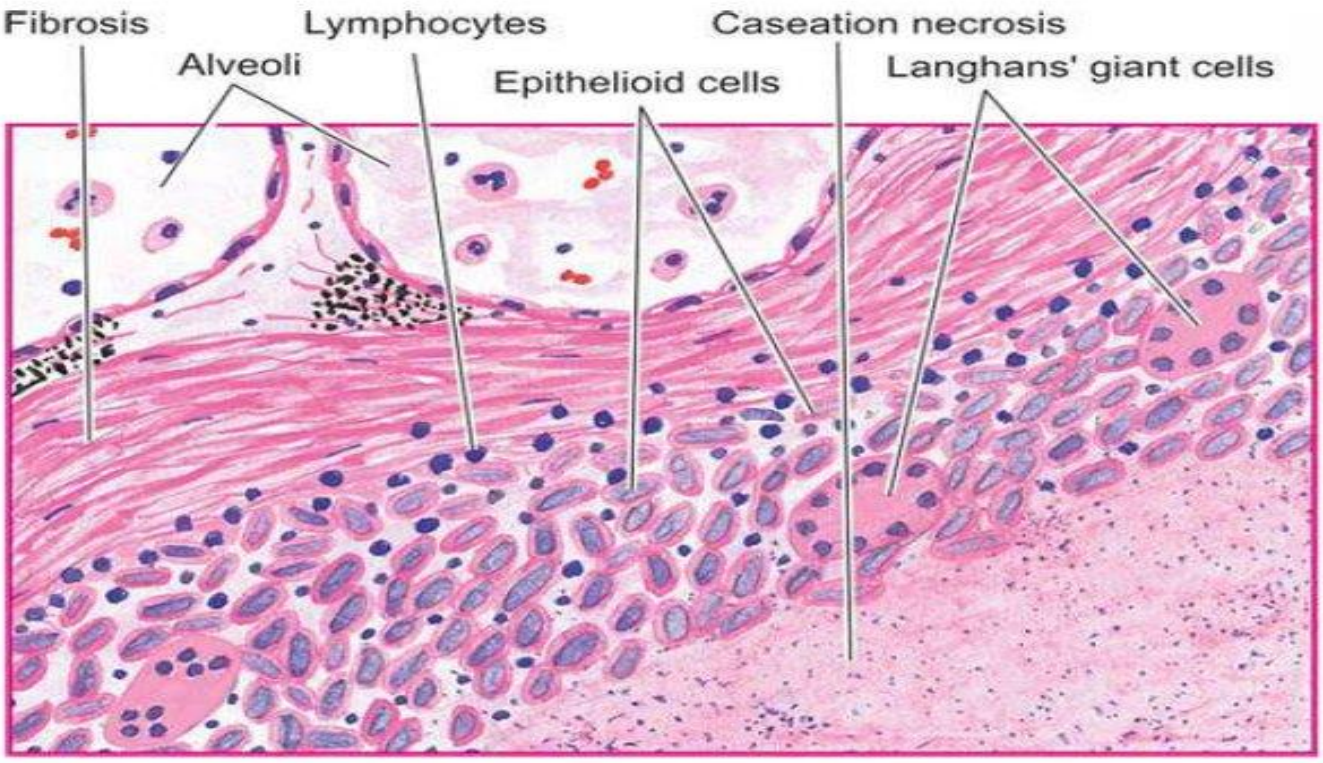
- Loss of cellular and structural details of tissue in the necrotic area
- Necrotic tissue appears as amorphous ,eosinophilic and granular and is surrounded by a distinct inflammatory reaction called granulomatous reaction consist of a fibrous capsule with fibroblasts , large number of epithelioid cells (modified macrophages having slipper-shaped vesicular nuclei), multinucleated Langhans giant cells (**formed by the fusion of epithelioid cells (macrophages), and contain nuclei arranged in a horseshoe-shaped pattern in the cell periphery)** ,foreign body type or foreign body giant cells (fused macrophages giant cell) and peripheral mantle of lymphocytes.in addition to the bacteria
- Neutrophils are rarely noticed
- take a pigmented purple when dyeing the sections with hematoxylin and eosin, because of mixing of blue chromatin granules from the nucleus with granules derived from the cytoplasm

-when the tissue destruction is so extensive that there are areas of cavitation (also known as cystic spaces)

- In some cases, Dystrophic calcification may occur in the necrotic area due to calcium deposition in it.




Amorphous granular eosinophilic debritic material
CASEOUS NECROSIS
Modified macrophages with abundant cytoplasm and pale staining "slipper" shaped nuclei
EPITHELOID CELLS
Multinucleated giant cell
LANGHAN GIANT CELL
Collar of lymphocytes surrounding epitheloid cell aggregates


Fibrosis
Alveoli
Lymphocytes
Epithelioid cells
Caseation necrosis
Langhans' giant cells

- **prognosis**
- ----------
- Cheesy necrosis is a permanent change and its severity depends on the severity of the disease

-treatment for TB is usually effective and most people have a good outcome. Without treatment, half of people with TB will die from the disease

3-Fatty necrosis

- It necrosis of the fatty tissue in the body by the action upon fat by digestive enzymes(lipase)

-In fat necrosis the enzyme lipase releases fatty acids from triglycerides. The fatty acids then complex with calcium to form soaps. These soaps appear as white chalky deposits.

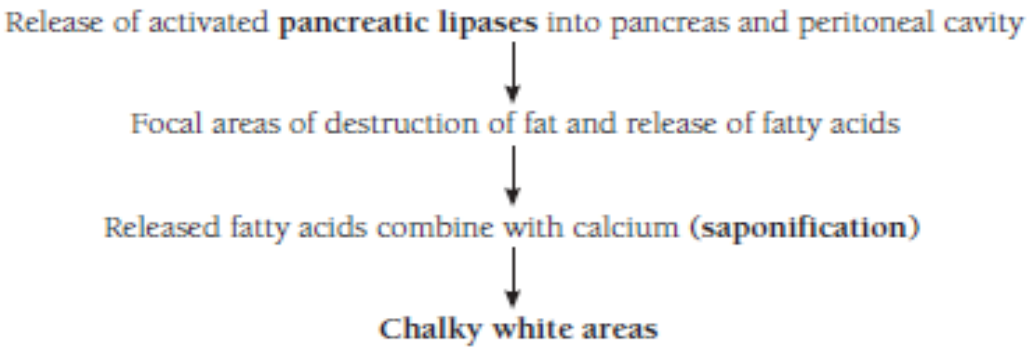
- **Types of fatty necrosis**:
- 1- Pancreatic fat necrosis or Enzymatic fat necrosis

-which is a complication of acute hemorrhagic pancreatitis, a severe inflammatory disorder of the pancreas. Its may be occur in chronic pancreatitis and pancreatic tumors .

- It refers to a focal area of fat destruction that converts adipocytes to necrotic cells with shadowy outlines and basophilic calcium deposits, surrounded by an inflammatory reaction

-it resulting from release of activated pancreatic lipases into the substance of the pancreas and the peritoneal cavity. The pancreatic enzymes leak out of acinar cells and liquefy the membranes of fat cells in the peritoneum. The released lipases split the triglyceride esters(into glycerol and free fatty acids) contained within fat cells. The fatty acids, so derived, combine with calcium to produce grossly visible chalky-white areas (fat saponification or soap formation or calcium soaps)

- Vessels are eroded, with resultant hemorrhage
- It is observed in adipose tissues adjacent to the pancreas, such as interstitial adipose tissue of the pancreas and fatty tissue of the mesentery (mesenteric fat necrosis).
- Calcium is absorbed inside the lymphatic vessels, while fatty acids combine with calcium, sodium and potassium salts to form a soap-like substance or soap
- Macroscopically: necrotic adipose tissue appears as yellowish-white lumps
- Foci of calcification may be observed ,its result from connection of fatty acids with calcium.
- Bone tissue formation may be observed due to metaplasia of connective tissue.



FLOWCHART 1.10. Mechanism of evolution of enzymatic fat necrosis.

- 2- Lipid traumatic Necrosis (Traumatic fat necrosis**)**
- It occurs due to the resulting from trauma directly on the fatty tissue during accidents, work or exercise
- which occurs after a severe injury to tissue with high fat content such as the breast, fatty tissue under the skin, and around the vagina as a result of the obstruction of blood from the cells to this tissue

-there are different stages of fat necrosis. As the fat cells die, they release their contents, forming a sac-like collection of greasy fluid called an oil cyst. Over time, calcifications (small deposits of calcium) can form around the walls of the cyst.

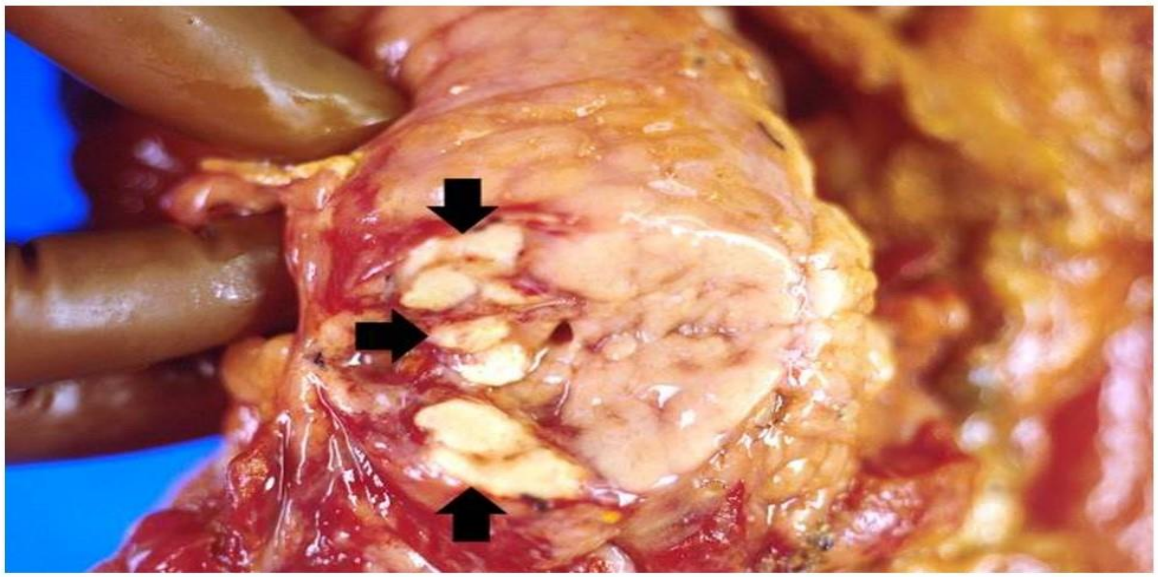
- Macroscopically: Necrotic adipose tissue appears as a yellowish-white and solid mass
  - Formation of calcium soaps imparts the necrotic foci firmer and chalky white appearance.

- 3- Fat Food or nutritional necrosis
  - It is observed in cases of severe weakness(Asthenia) and starvation, as in the case of stomach and intestinal infections, or due to debilitating diseases such as pulmonary tuberculosis.
- It can be observed in any part of the body but usually occurs in the fatty tissue found in both the mesentery and around the kidneys.
- Macroscopically: the necrotic fatty tissue appears white and solid

- **Microscopic appearance** for all type fatty necrosis
- ==========
- Fat cells appear to be replaced either by a homogeneous granulated substance of a pink blue color when dyed with hematoxylin and eosin or by clear crystals that appear in the form of crystalline needles for cholesterol.
- An acute or chronic inflammatory reaction may be observed between necrotic adipose tissue and normal adjacent tissue, which contains a lot of inflammatory cells, mostly large microphages.
- When fat necrosis occurs in acute pancreatitis, large numbers of neutrophils are observed in necrotic adipose tissue.

-Formation of calcium soaps is identified in the tissue sections as amorphous, granular and basophilic material

- Focal or diffuse calcification or bone tissue formation may be observed in the necrotic fat



gross photograph of the pancreas from this case shows white nodules (arrows) in the pancreas and the adjacent mesenteric fat tissue.

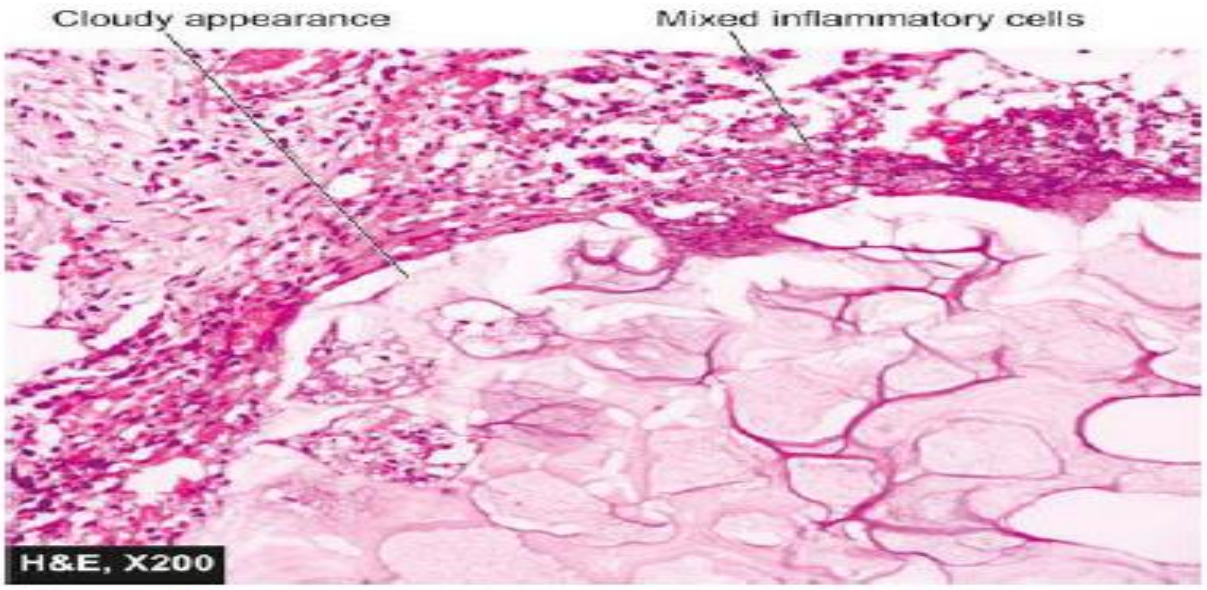
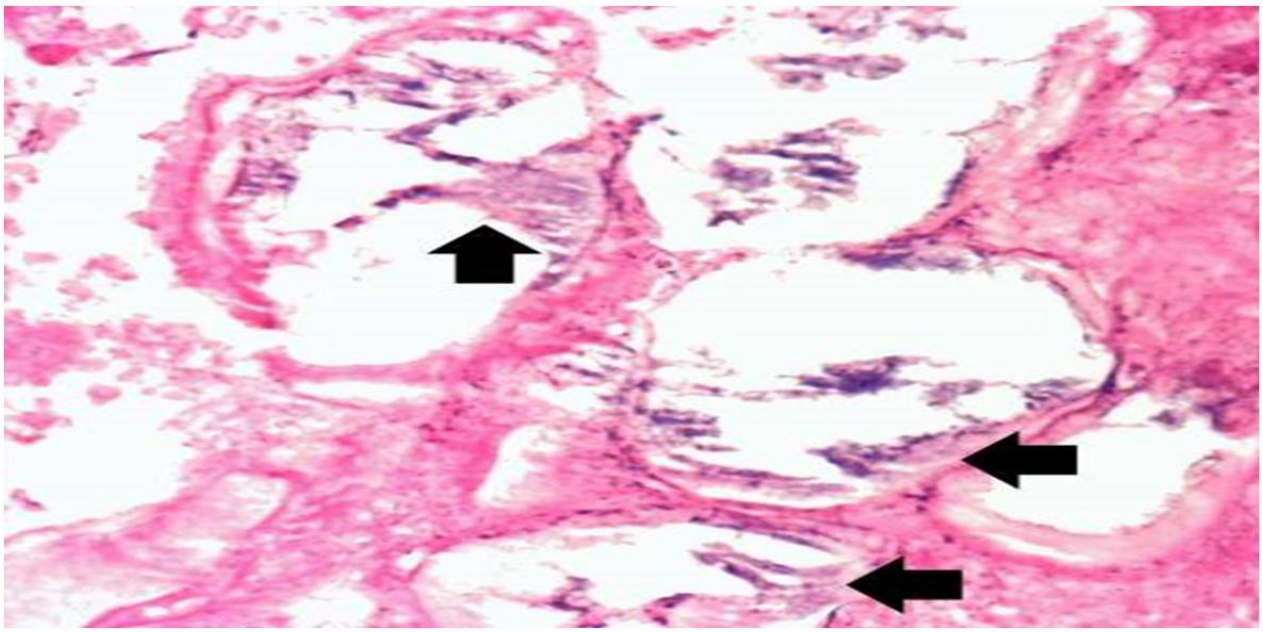


Figure 2.24 Fat necrosis in acute pancreatitis. There is cloudy appearance of adipocytes, coarse basophilic granular debris while the periphery shows a few mixed inflammatory cells.



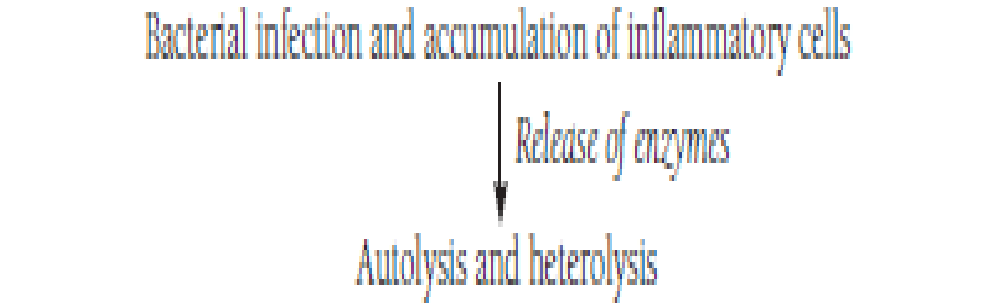
photomicrograph demonstrates fat necrosis in the interlobular spaces of the pancreas. Note the granular blue-staining calcium deposits-calcification (arrows) within the fat cells, The necrotic adipocytes are devoid of nuclei. Hematoxylin and eosin stain;

4-Liquefactive necrosis (Abscesses or pus) or colliquative necrosis

- **Liquefactive necrosis is** characterized by digestion of the dead cells, resulting in transformation of the tissue into a liquid viscous substance.
- It is seen in focal bacterial or, occasionally, fungal infections, because microbes stimulate the accumulation of leukocytes and the liberation of enzymes from these cells.

-The necrotic material is frequently creamy yellow because of the presence of dead leukocytes and is called **pus**.

- **Liquefactive** necrosis begins in the form of Coagulative necrosis and then turns into an abscess in response to the activity of some autolytic enzymes.



FLOWCHART 1.8. Mechanism of evolution of liquefactive necrosis.

- **causes**
- ----------

-It is usually associated with bacterial or fungal infections because microbes stimulate the accumulation of leukocytes and liberation of enzymes from these cells

- Suppurative infections characterized by the formation of pus (liquefied tissue debris and neutrophils) by heterolytic mechanisms involve liquefactive necrosis .its based on the activity of autolatic enzymes that are released by neutrophils at necrosis sites where bacteria that induce pus.

- Ischemic injury to the central nervous system (CNS) characteristically results in liquefactive necrosis. After the death of CNS cells, liquefaction is caused by autolysis, for unknown reasons, hypoxic death of cells within the central nervous system often manifests as liquefactive necrosis. In the central nervous system, autolysis enzymes in cells decompose necrotic nervous tissue, not neutrophils, so neutrophils are not observed in necrosis in nervous tissue.

- Nerve tissue necrosis occurs at the sites of infarction and trauma damage, as well as in cases of hypoxia, carbon oxide and cyanide poisoning.

- Liquefactive necrosis is most commonly seen in organs that have a high-fat and low protein content (eg, the brain), or those with a high-enzymatic content (eg, the pancreas), and typically causes gangrene of intestine and limbs and hypoxic death in brain.

- Lack of a proper collagenous connective tissue framework in an organ also aids to this type of necrosis.

- **Macroscopic appearance**
- ==========
- The organ–cellular architecture is lost, and the tissue is digested and converted into a liquefied mass, which appears creamy yellow, white, red or green in colour and is called ‘pus’
- The texture of the necrotic area may be liquid or semi-solid
- The necrosis area may be surrounded by a range of chronic inflammation and connective tissue when it remains for a period of time
-

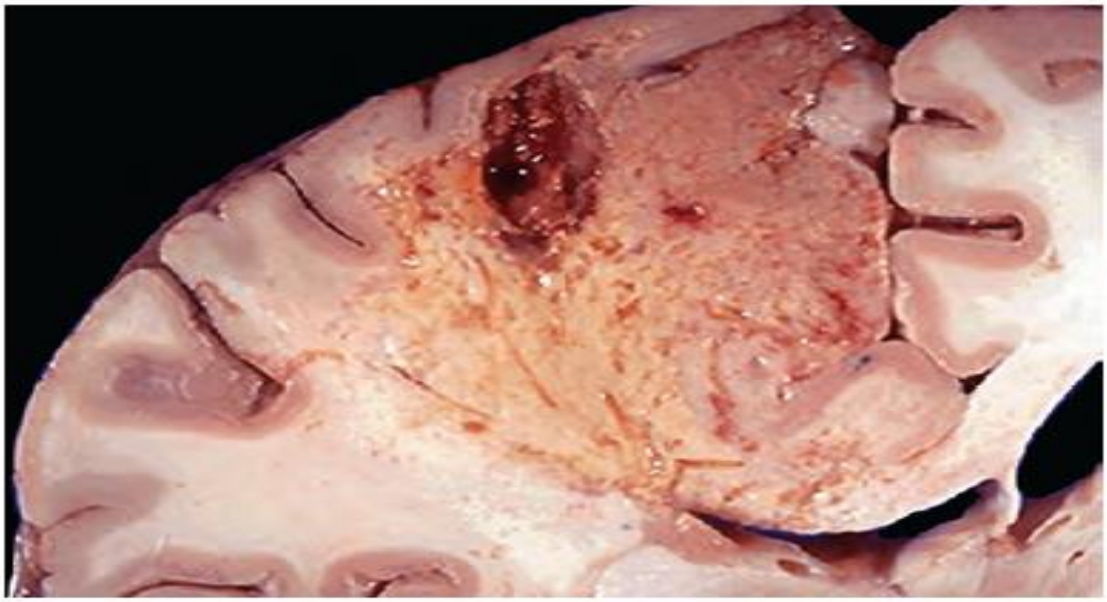
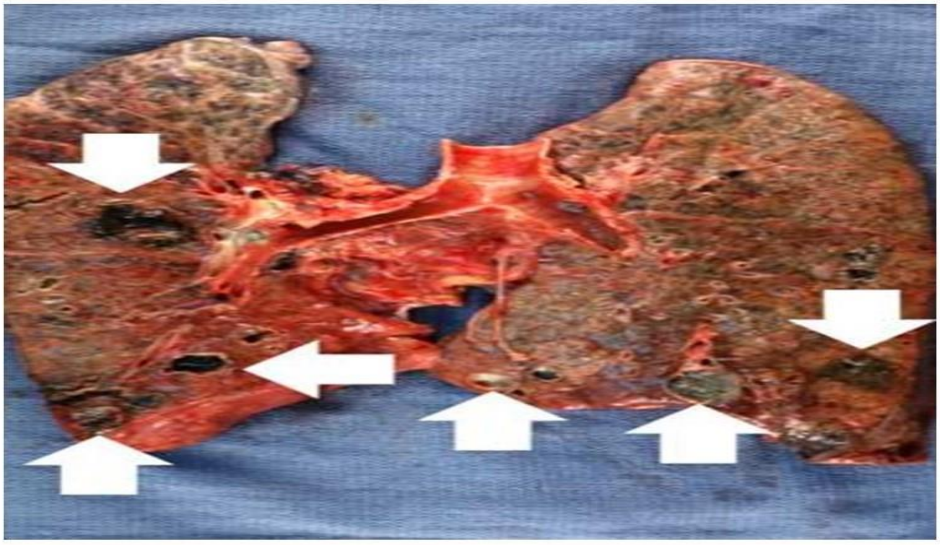
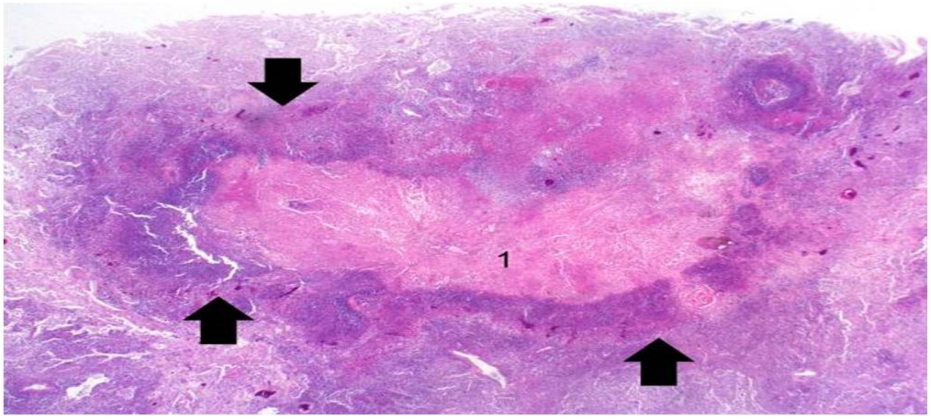


Figure 2-12 Liquefactive necrosis. An infarct in the brain, showing dissolution of the tissue.

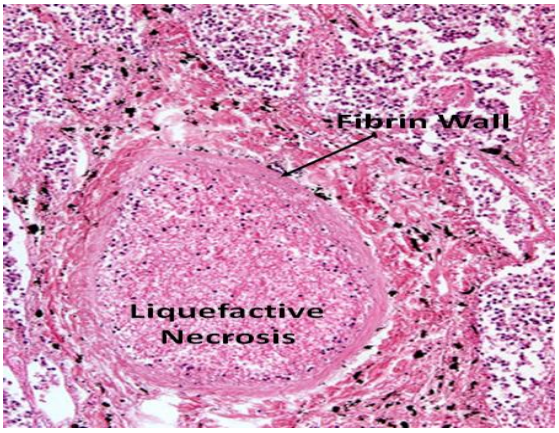


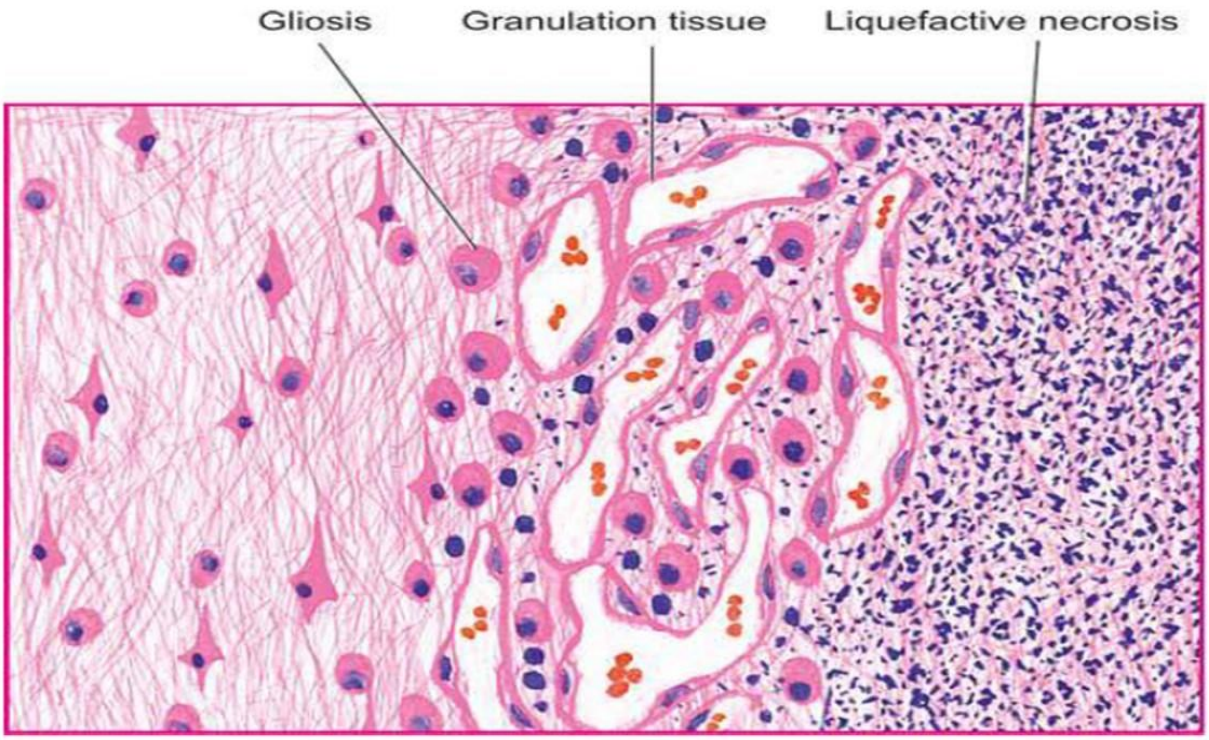
gross photograph of the lungs. Note the abscesses (arrows) especially in the lower lobes.

- **Microscopic appearance**
- ==========
- Necrotic tissue appears as spaces containing pus and its edges made up of necrotic cells
- The center of necrotic tissue may contain a pink protein precipitate
- Pus contains necrotic cell debris and macrophages filled with phagocytosed material , large number of dead and decomposed neutrophils .
- The components of pus are surrounded by an inflammatory wall composed of fibroblasts , white fibers, capillary blood vessels , a number of neutrophils and gliosis (proliferating glial cells) in the case of brain and proliferating fibroblasts in the case of abscess cavity.
- Calcification may be observed in the center of the lesion or the necrotic area

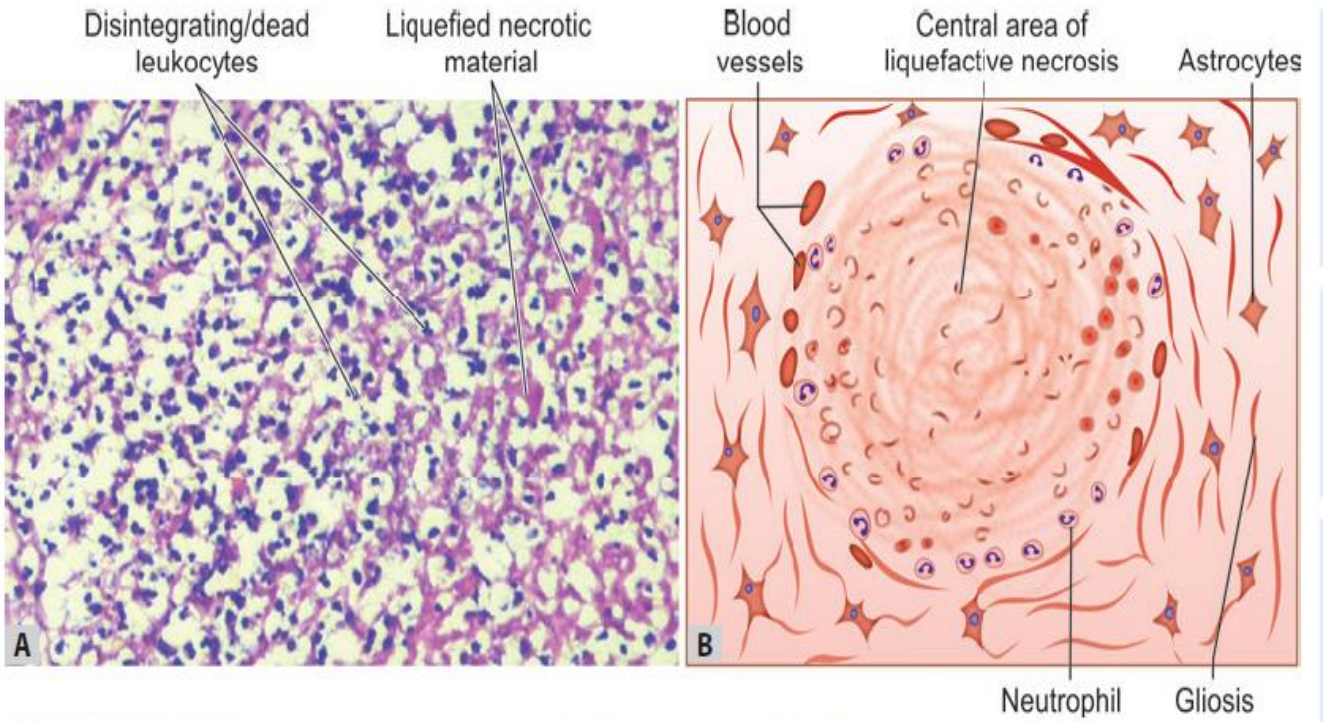


photomicrograph of lung tissue containing a large abscess. The center of the abscess contains necrotic debris (1) and there is a rim of viable inflammatory cells (arrows) surrounding this abscess.





Liquefactive necrosis brain. The necrosed area on right side of the field shows a cystic space containing cell debris, while the surrounding zone shows granulation tissue and gliosis.



Figs 1.18A and B: Microscopic appearance of an abscess consisting of liquified necrotic cell debris and dead/disintegrating neutrophils. (A) Hematoxylin and eosin; (B) Diagrammatic appearance of brain abscess

- **Prognosis**
- ==========
- **Liquefactive** necrosis is a form of autolysis and should be distinguished from inflammation and tissue reaction against bacteria.

5-Gangrenous necrosis

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- This is a clinical term, not a specific pattern of necrosis. It is usually used in context of the lower limbs, which have lost their blood supply and have undergone necrosis,

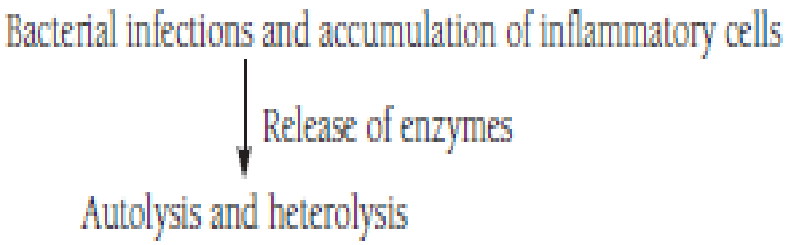
Types of the gangrenes

Dry gangrene – When characterized primarily by coagulative necrosis without liquefaction and dead necrotised tissue remains uninfected.

Wet gangrene- When complicated by infective heterolysis and consequent liquefactive necrosis.

Gas gangrene – Wet gangrene infected by one of the gas forming Clostridia

- initially coagulative (dry gangrene), and later liquefactive due to secondary bacterial infection and immigrating leukocytes (wet gangrene)



FLOWCHART 1.9. Mechanism of evolution of gangrenous necrosis.

Dry gangrene

- Dry gangrene is a form of coagulative necrosis that develops in ischemic tissue, undergoes infarction because of the supply arterial obstruction.
- It is not a disease in itself, but a symptom of other diseases
- his term is used when there necrosis of limbs particularly lower leg and necrosis involving entire thickness of the bowel wall or abdominal viscera (in other locations, this same type of necrosis is called an infarction).
- Dry gangrene is often due to peripheral artery disease, but can be due to acute limb ischemia. As a result, people with atherosclerosis of anteries supplying limb and diabetes commonly have dry gangrene.
-
- High level of blood sugar can damage blood vessels, causing blood flow to a part of the body to stopped .
- Dry gangrene is not accompanied by bacterial infection because the limited amount of oxygen in the rotting tissue restricts bacterial growth and the bacteria fail to survive.
- Over time, dry gangrene may develop into wet gangrene if bacterial infection develops in dead tissue.

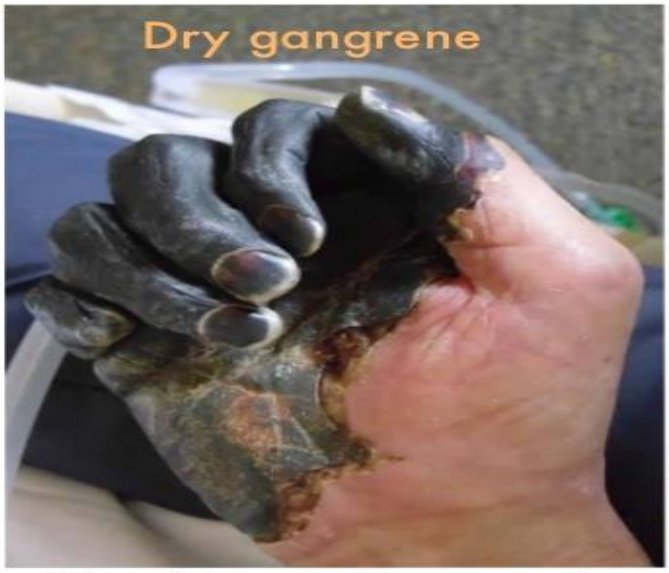
Macroscopic or Gross appearance

==========

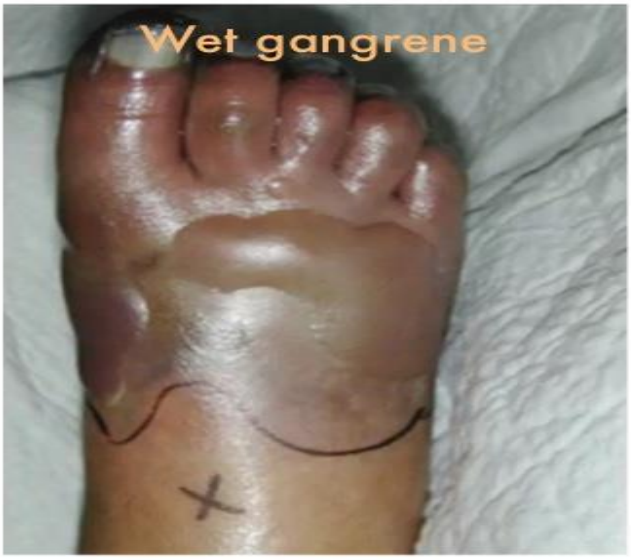
- The necrotic area is dry and the skin that looks brown to purplish blue or black. Dry gangrene may develop slowly

- The line of demarcation usually present between noramal tissue and gangrenous tissue, with eventual falling off the gangrenous tissue if it is not removed surgically, a process called autoamputation

- Black colour is due to release of haemoglobin from the haemolysed RBC's. This is again acted upon by the hydrogen disulfide produced by bacteria which results in the formation of black iron sulphide, and thus makes the damaged part dry, shrunken, dark black in color as well as with musty smell.



Line of demarcation present between healthy tissue & gangrenous tissue.



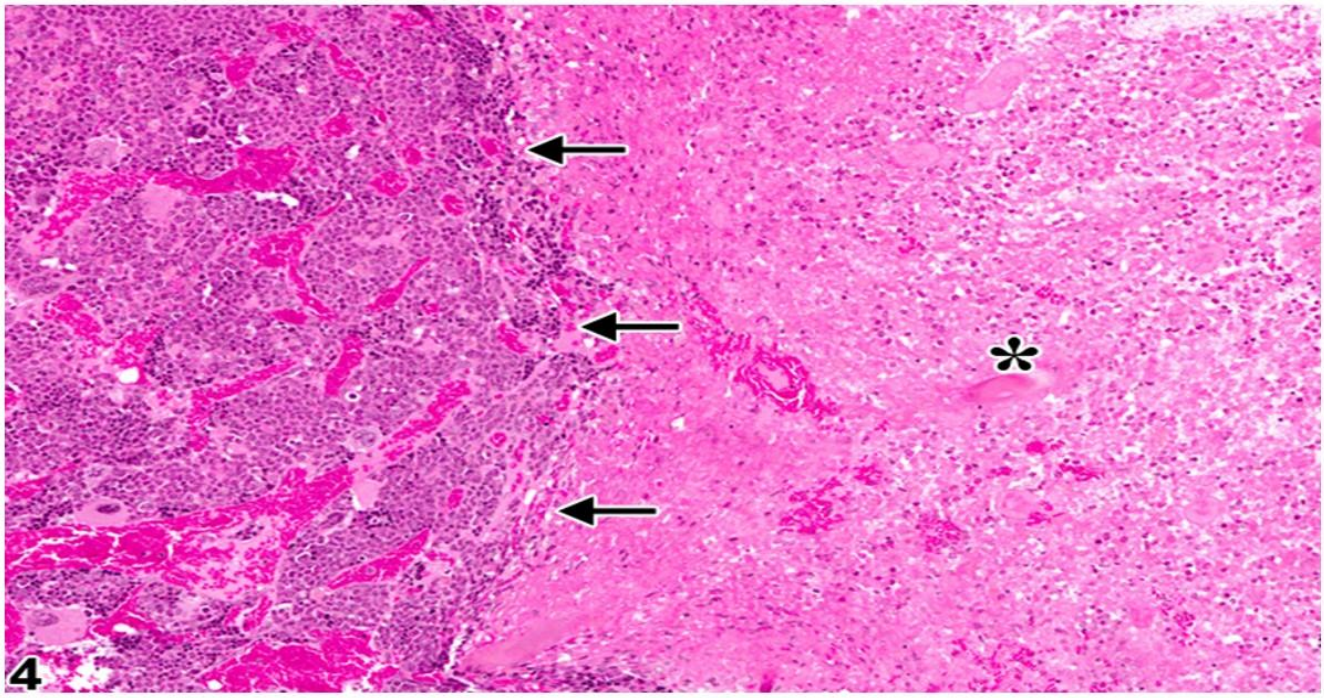
Line of demarcation absent between healthy tissue & gangrenous tissue.

Microscopic appearance

==========

- Line of demarcation usually forms between healthy and gangrenous tissue. its formed by the body in an attempt to limit the spread of gangrene and isolate it.

- This line consists of neutrophils, phagocytes and other leukocytes, and large amount of hydrolytic enzymes that decompose necrotic tissue along the line of



Bone marrow in a male B6C3F1 mouse from a chronic study (higher magnification of Figure 3), showing the area of necrosis (asterisk) and the line of demarcation (arrows) between the viable cells and the area of necrosis.

- **prognosis**

- Dry gangrene leads to the separation of the affected part from the body, such as the lower limbs such as the foot or fingers, which leads to the formation of permanent defect.

Wet gangrene or infectious gangrene

==========

- When bacterial infection is superimposed there is more liquefactive necrosis because of the actions of degradative enzymes in the bacteria and the attracted leukocytes (giving rise to so-called **wet gangrene**).

Wet gangrene typically occurs in

-Diabetic foot –High glucose content in the necrosed tissue favours bacterial growth.

-Bed sores –In bed ridden patients at the pressure on the sites like sacrum, buttocks and heel

-Also in several organs like bowel , lung, mouth, etc.

- There are two types of them

- 1- Internal gangrene

- Occurs in internal organs such as intestine due to trauma or burns

- Wet gangrene develops more often from the venous blood blockage and also occurs if there is both venous and arterial blood blockage., where coagulative necrosis occurs, then Liquefactive necrosis, then rotting of the tissue necrosis occurs due to the presence of saprophytic bacteria.

- Affected part is stuffed with blood which favours rapid growth of putrefactive bacteria Infection spreads rapidly into the variable tissue adjacent to necrosis.

- Even the toxic products formed by the bacteria are absorbed in the circulation causing systemic manifestations like high fever, toxaemia later leading to death.

- **Macroscopic appearance**

- Affected organ is edematous with a dark color.

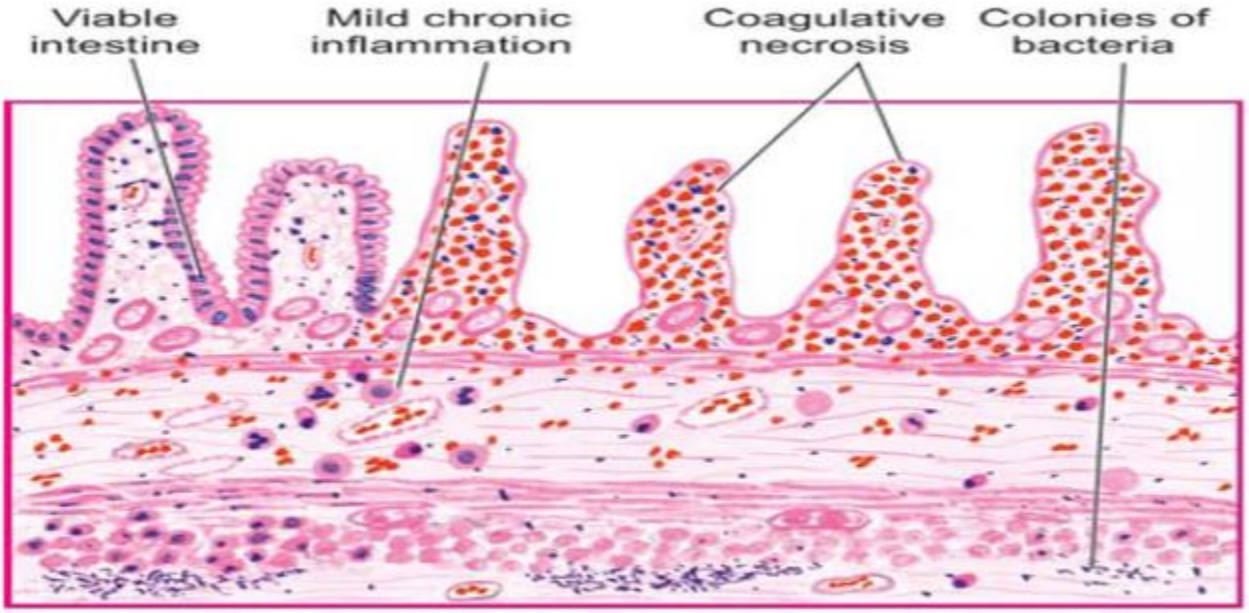
- Swelling of the tissues with musty smell.

• **Microscopic appearance**

- The lesion begins in the form of coagulative necrosis and then develops into Liquefactive necrosis.

- The presence of saprophytic bacteria in the necrotic area

-The Line of demarcation between the necrotic area and the normal adjacent tissues is absent .



Wet gangrene of the small bowel. Microscopy shows coagulative necrosis of the affected bowel wall while the junction with normal intestine is indistinct and shows an inflammatory infiltrate

- Wet gangrene may lead to the breakdown of necrotic tissue proteins and the formation of deadly metabolites

- The bacteria can enter the blood, release toxins and cause sapremia .

• If the organ affected by wet gangrene is not removed surgically, the result is death

• 2- Gas gangrene

-It is a type of wet gangrene

- It is usually caused by a type of Clostridium bacteria (Gram positive anaerobic bacteria). It is often found in the soil

- These environmental bacteria enter the muscles through **a contaminated** wounds during accidents or wars or as a complication of operation on colon which normally

contains Clostridia , later these bacteria multiply in necrotic tissues and secrete toxins .

- These toxins destroy nearby tissues and generate gas at the same time. The gases consist of 5.9% hydrogen, 3.4% carbon dioxide, 74.5% nitrogen and 16.1% oxygen

- Gas gangrene can cause gas bubbles to form when they enter the bloodstream and cause blockage and then death

- Gas gangrene usually affects muscle tissue cause extensive necrosis and massive edema.

- The surface of the skin looks natural at first. As the condition progresses, the skin becomes pale and then turns gray or purple-red, and bubbles may appear in the affected skin that make a crackling sound when pressed due to the presence of gas inside the tissues.

Morphology

– the affected part is edematous, swollen and has crepitations due to accumulation of gas in tissues

- Later the tissue becomes dark black and through breach in the skin, gas escapes with foul smelling distinctive odour

Microscopically

-Muscle fibres undergo coagulative necrosis with liquefaction

- Many Gram positive bacilli can be identified

- At the periphery, a zone of leukocytic infiltration, oedema and congestion are found

- Capillary and venous thrombosis can be seen

prognosis

-Invasive gangrene is an emergency that must be treated immediately, without which the patient dies within 48 hours

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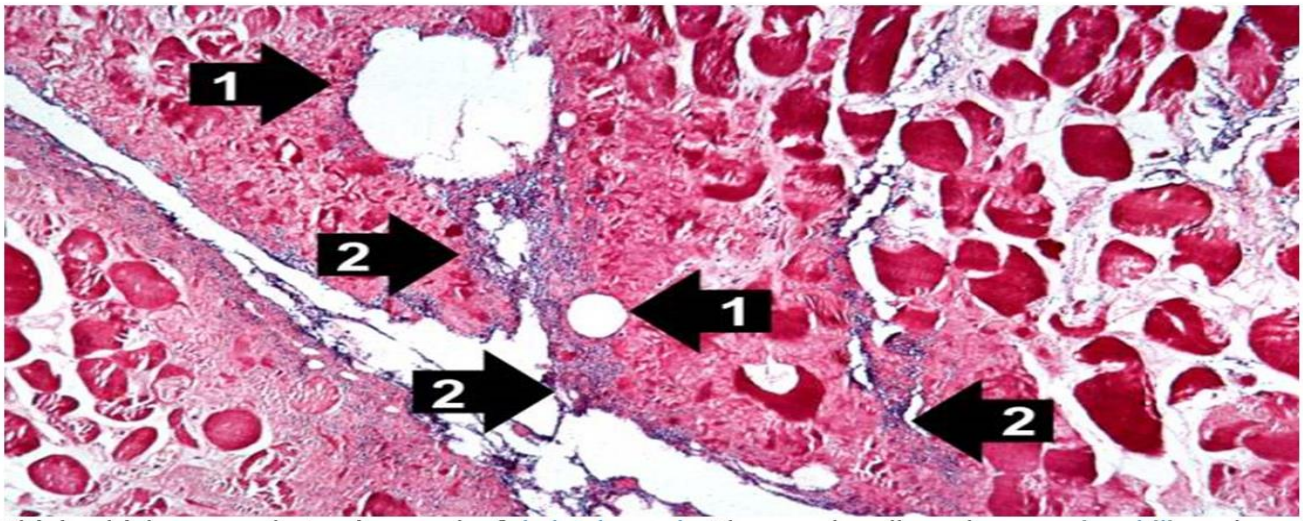

This is a high-power photomicrograph of skeletal muscle. The muscle cells are hypereosinophilic and most do not contain nuclei, indicating that these cells are dead or dying. The round clear spaces (1) in this tissue correspond to gas accumulations prior to death. In between the bundles of muscle cells, accumulations of small dark blue-staining bacterial organisms can be seen (2). Also note that there is no inflammatory response in this tissue.

Table I Differences in features of dry gangrene, wet gangrene, and gas gangrene

Feature	Dry gangrene	Wet gangrene	Gas gangrene
Site	Commonly limbs	More common in bowel	Limbs
Mechanism	Arterial occlusion	More commonly venous obstruction	Gases produced by *Clostridium* bacteria
Macroscopy	Organ dry, shrunken, and black	Part moist, soft, swollen, rotten, and dark	Organ red, cold, pale, numb, shriveled up, and auto-amputation
Putrefaction	Limited due to very little blood supply	Marked due to congestion of organ with blood	Marked due to bacteria and infiltration of gases produced by them in tissues
Line of demarcation	Present at the junction between healthy and gangrenous parts	No clear-cut line of demarcation	No clear-cut line of demarcation
Bacteria	Bacteria fail to survive	Numerous present	Major cause
Prognosis	Generally better due to little septicemia	Generally poor due to profound toxemia	Generally poor due to quick spread to the surrounding tissues

Fibrinoid necrosis

Fibrinoid necrosis is associated with vascular damage (caused mainly by autoimmunity, immune-complex deposition, infections) and the exudation of plasma proteins (such as fibrin). This pattern typically occurs due to a type 3 hypersensitivity, where an immune complex is formed between an antigen (Ag) with an antibody (Ab). The Ag-Ab complex may be deposited in the vascular walls causing inflammation, complement being activated,

and phagocytic cells are recruited, which could be releasing oxidants and other enzymes causing further damage and inflammation. Fibrin, a non-globular protein involved in the clotting of blood, is leaked out of the vessels. The results create an amorphous appearance that is bright pink in an H&E stain. The pathologists call this appearance 'fribinoid' which means fibrin-like.

Gross appearance: usually not grossly discernible.

Microscopic appearance: an amorphous appearance that is bright pink in an H&E stain. The deposition of fibrinoid are surrounding the blood vessels. Inflammation should be present.

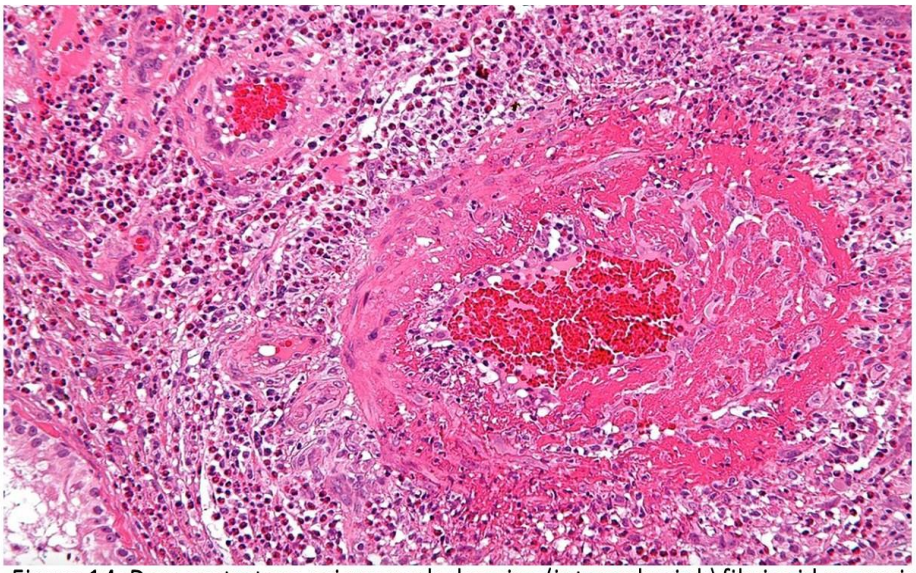

Figure 14: Demonstrates a micrograph showing (intensely pink) fibrinoid necrosis (large blood vessel - right of image) in a case of vasculitis. H&E stain was used.

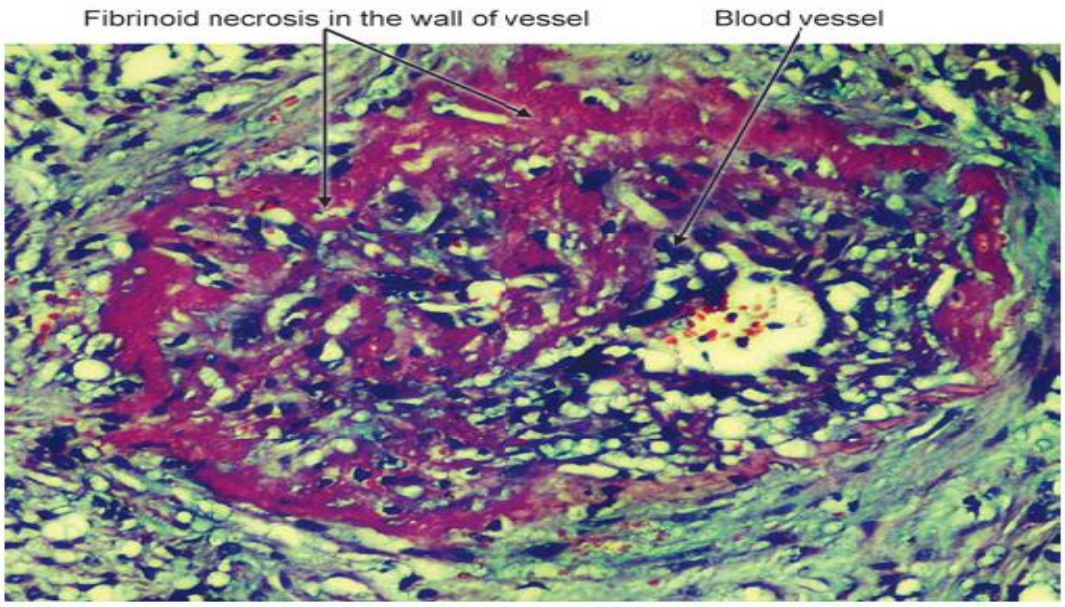

Fig. 1.22: Fibrinoid necrosis in the wall of blood vessel