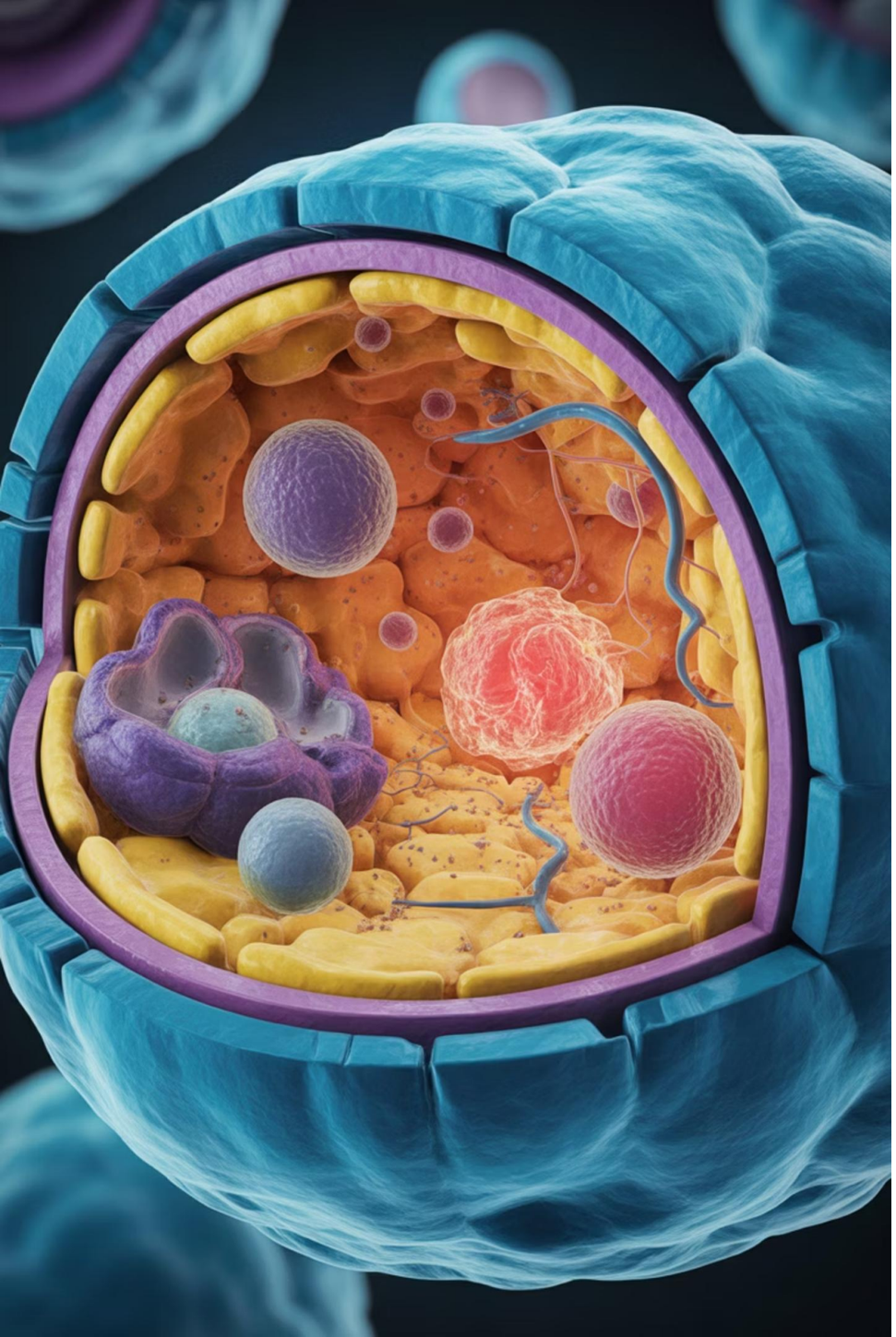

NECROSIS

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Irreversible Cell Injury (Cell Death)

Cell death is a state of irreversible injury. It may occur in the living body as a local or focal change (autolysis, necrosis and apoptosis) and the changes that follow it (gangrene and pathologic calcification), or result in end of the life (somatic death). These pathologic processes involved in cell death are described below.

Understanding Cell Death

Autolysis: Self-Digestion of Cells

Autolysis (self-digestion) is disintegration of the cell by its own hydrolytic enzymes liberated from lysosomes. Autolysis can occur in the living body when it is surrounded by inflammatory reaction but the term is generally used for postmortem change in which there is complete absence of surrounding inflammatory response.

Autolysis: Speed and Characteristics

Rapid Autolysis

Tissues rich in hydrolytic enzymes such as in the pancreas, and gastric mucosa

Intermediate Autolysis

Tissues like the heart, liver and kidney

Slow Autolysis

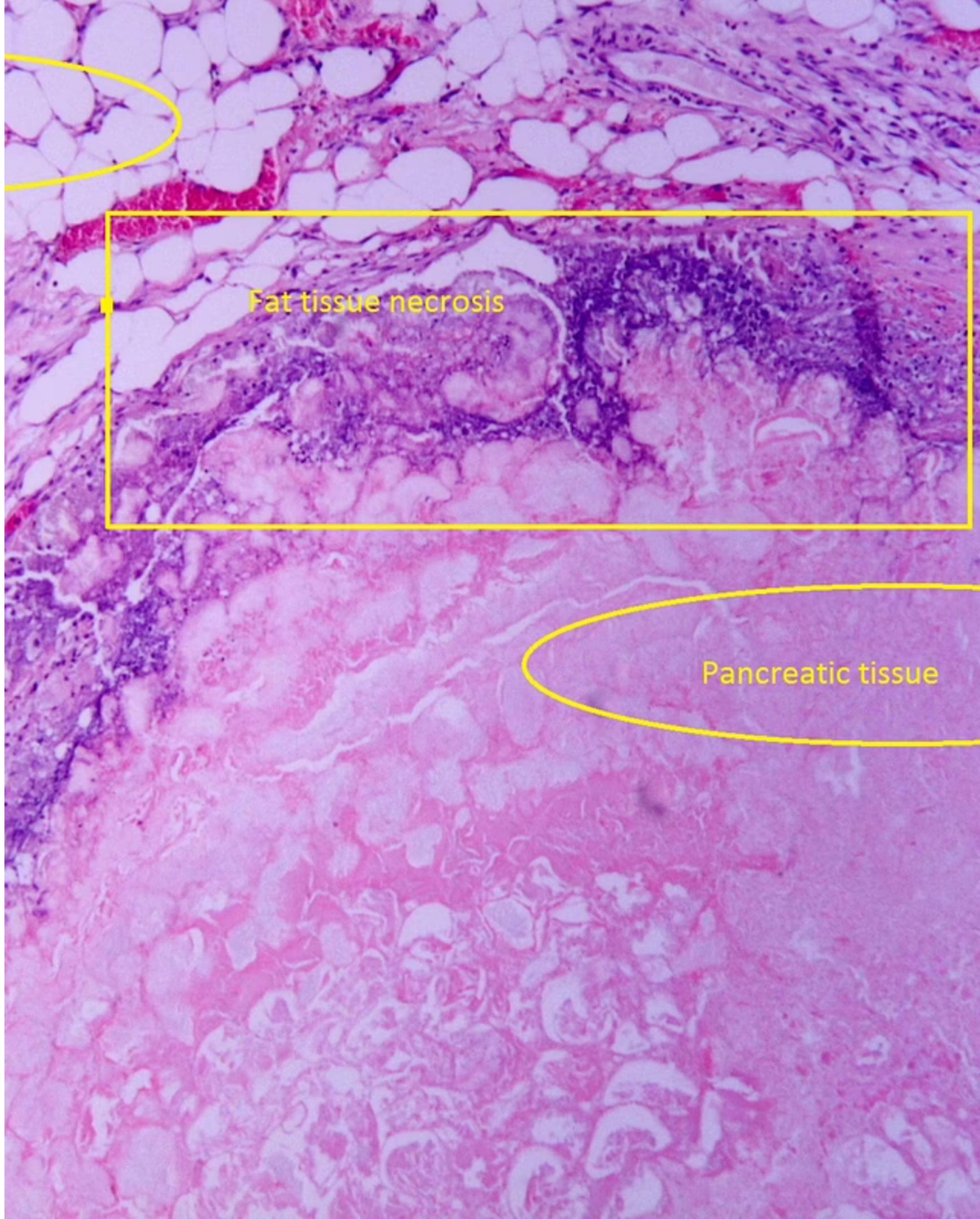
Fibrous tissue

Morphologically, autolysis is identified by homogeneous and eosinophilic cytoplasm with loss of cellular details and remains of cell as debris.

Necrosis

Localized tissue death with degradation

Necrosis is defined as a localized area of death of tissue followed by degradation of tissue by hydrolytic enzymes liberated from dead cells; it is invariably accompanied by inflammatory reaction. Necrosis can be caused by various agents such as hypoxia, chemical and physical agents, microbial agents, immunological injury, etc.



Two Essential Changes in Necrosis

Two essential changes characterise irreversible cell injury in necrosis of all types:

1

Cell digestion by lytic enzymes

Morphologically this change is identified as homogeneous and intensely eosinophilic cytoplasm. Occasionally, it may show cytoplasmic vacuolation.

2

Denaturation of proteins

This process is morphologically seen as characteristic nuclear changes in necrotic cell. These nuclear changes may include: condensation of nuclear chromatin (pyknosis) which may either undergo dissolution (karyolysis) or fragmentation into many granular clumps (karyorrhexis).

Classification

Five Types of Necrosis

Morphologically, there are five types of necrosis: coagulative, liquefaction (colliquative), caseous, fat, and fibrinoid necrosis.

1. Coagulative Necrosis

This is the most common type of necrosis caused by irreversible focal injury, mostly from sudden cessation of blood flow (ischaemia), and less often from bacterial and chemical agents. The organs commonly affected are the heart, kidney, and spleen.

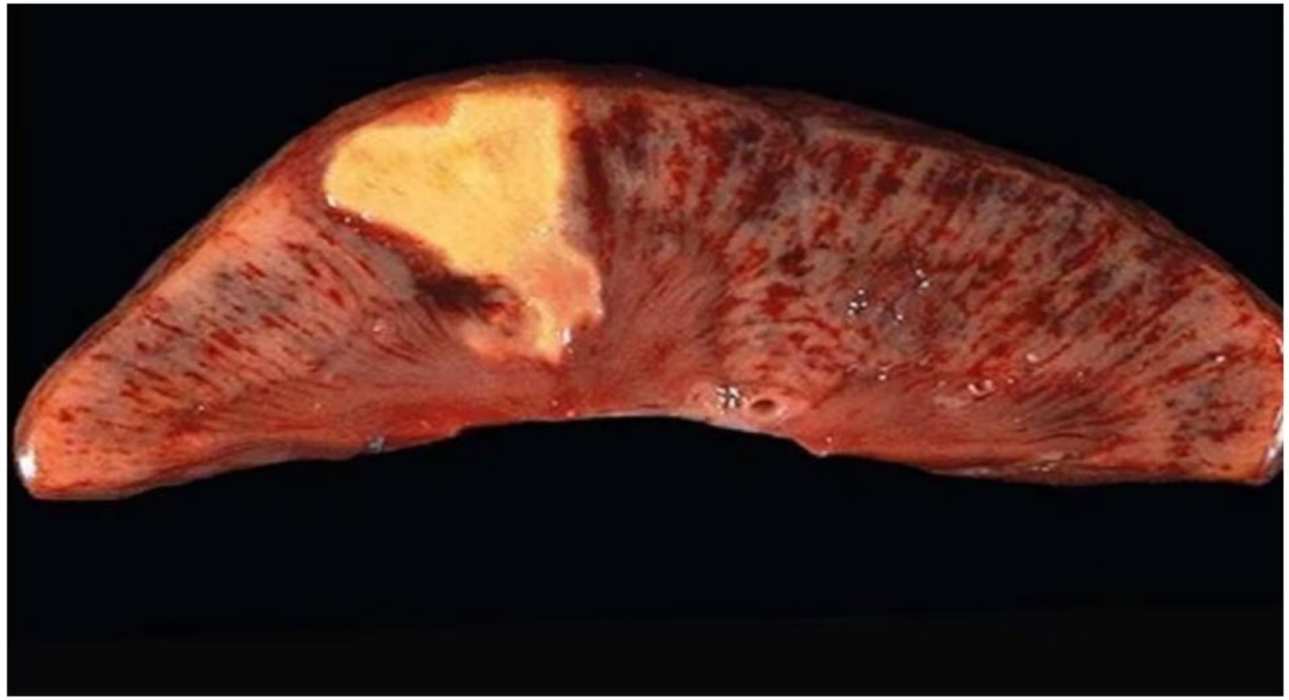
Gross Appearance

Foci of coagulative necrosis in the early stage are pale, firm, and slightly swollen. With progression, they become more yellowish, softer, and shrunken.

Microscopic Features

The cell type can still be recognised but their cytoplasmic and nuclear details are lost. The necrosed cells are swollen and appear more eosinophilic than the normal, along with nuclear changes described above. The necrosed focus is infiltrated by inflammatory cells and the dead cells are phagocytosed leaving granular debris and fragments of cells.

Coagulative Necrosis: Kidney Infarction



Organ: kidney

Diagnosis: infarction

Lesion: Gross appearance of kidney infarction (coagulative necrosis)

Affected area is triangular in shape. It is pale, dry and opaque. It is surrounded by hyperemic area.

2. Liquefaction (Colliquative) Necrosis

Liquefaction or colliquative necrosis occurs commonly due to ischaemic injury and bacterial or fungal infections. It occurs due to degradation of tissue by the action of powerful hydrolytic enzymes. The common examples are infarct brain and abscess cavity.

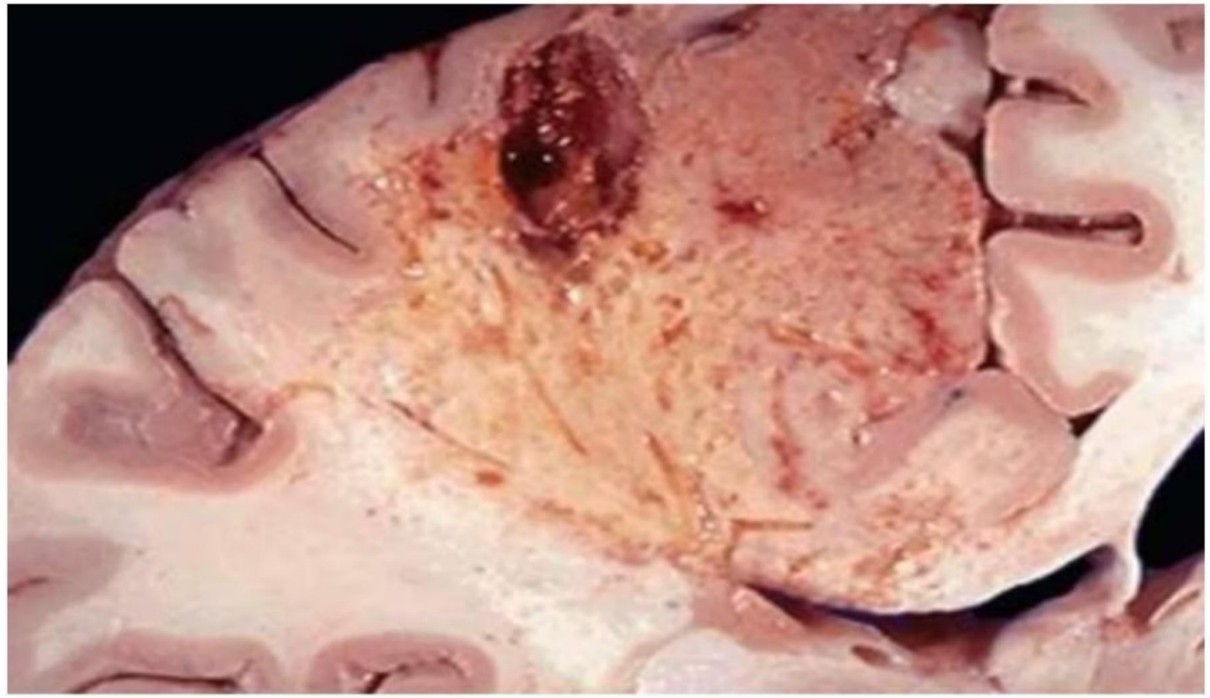
Gross Appearance

The affected area is soft with liquefied centre containing necrotic debris. Later, a cyst wall is formed.

Microscopic Features

The cystic space contains necrotic cell debris and macrophages filled with phagocytosed material.

Liquefactive Necrosis: Brain Tissue



Organ: brain

Diagnosis: liquefactive necrosis

Lesion: softening of white matter

Loss of brain tissue with activated microglia accumulation

3. Caseous Necrosis

Caseous necrosis is found in the centre of foci of tuberculous infections. It combines features of both coagulative and liquefactive necrosis.

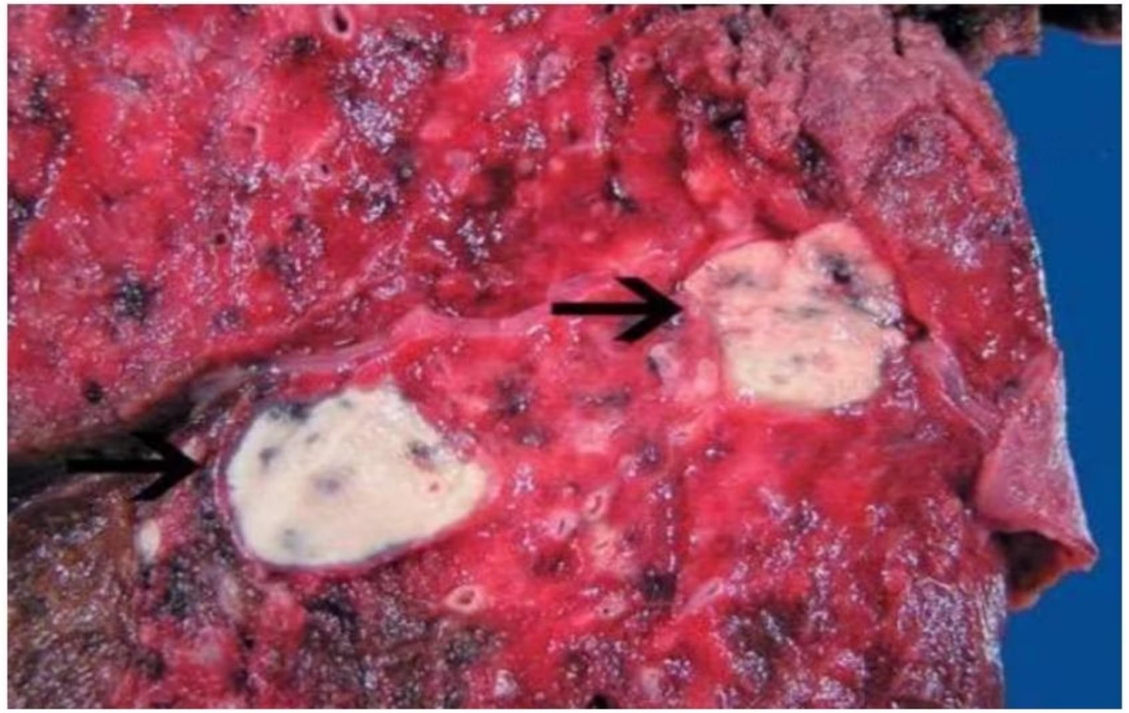
Gross Appearance

Foci of caseous necrosis, as the name implies, resemble dry cheese and are soft, granular and yellowish.

Microscopic Features

The necrosed foci are structureless, eosinophilic, and contain granular debris. The surrounding tissue shows characteristic granulomatous inflammatory reaction.

Caseous Necrosis: Pulmonary Tuberculosis



- Organ: lung
- Diagnosis: caseous necrosis of the lung due to pulmonary tuberculosis
- Lesion: Gross section

  The soft, cheese-like nature white pale in color in the center of granuloma.

4. Fat Necrosis

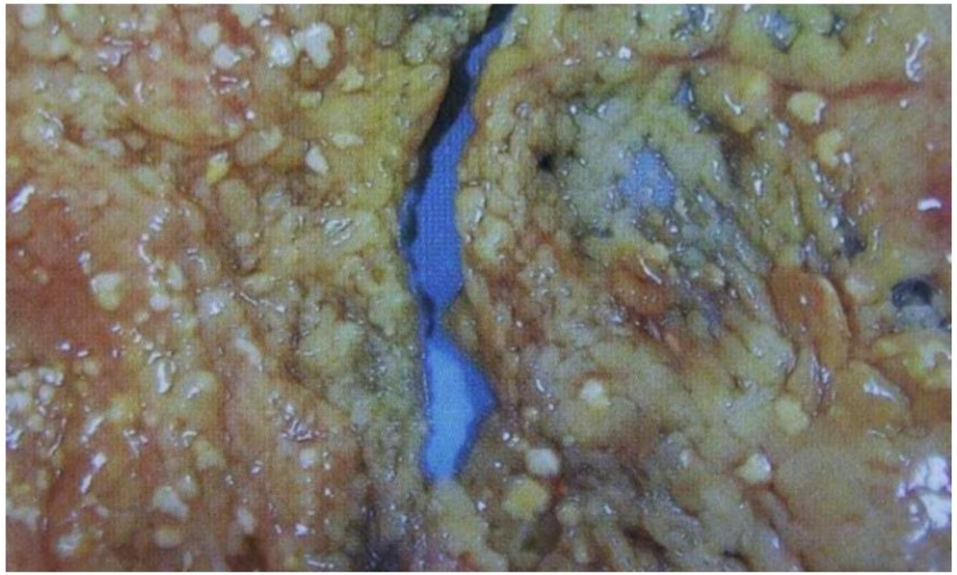
Fat necrosis is a special form of cell death occurring at two anatomically different locations but morphologically similar lesions. These are: following acute pancreatic necrosis, and traumatic fat necrosis commonly in breasts.

> In the case of pancreas, there is liberation of pancreatic lipases from injured or inflamed tissue that results in necrosis of the pancreas as well as of the fat depots throughout the peritoneal cavity, and sometimes, even affecting the extraabdominal adipose tissue.

Fat necrosis hydrolyses neutral fat present in adipose cells into glycerol and free fatty acids. The damaged adipose cells assume cloudy appearance. The leaked out free fatty acids complex with calcium to form calcium soaps (saponification).

Fat Necrosis: Pancreas

Gross Appearance



Fat necrosis appears as yellowish-white and firm deposits. Formation of calcium soaps imparts the necrosed foci firmer and chalky white appearance.

Microscopic Features

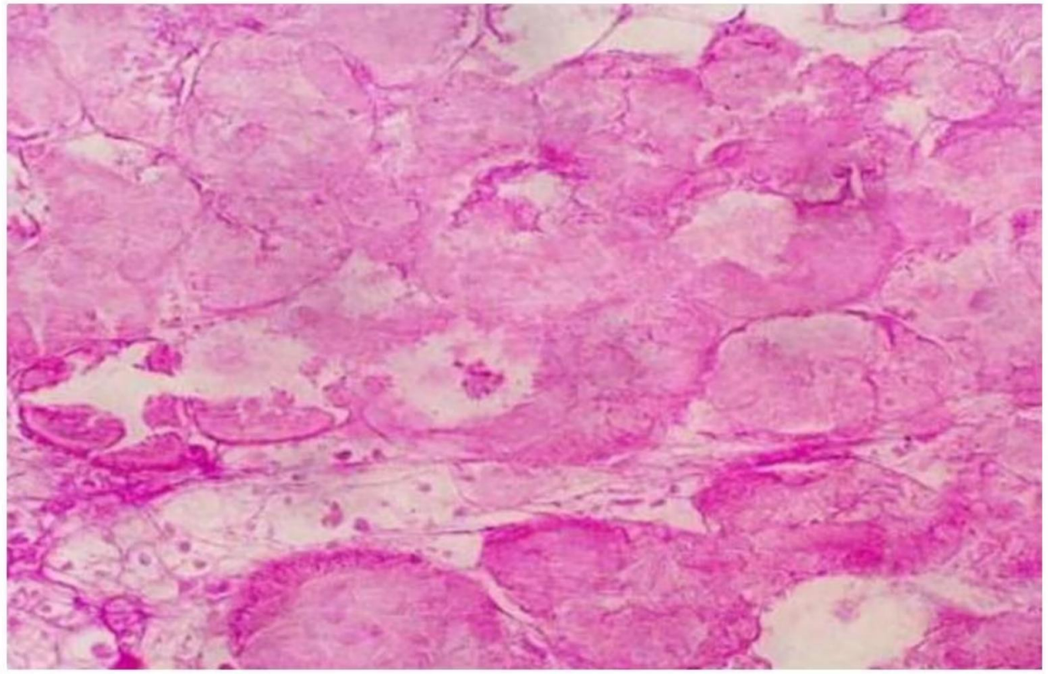
The necrosed fat cells have cloudy appearance and are surrounded by an inflammatory reaction.

Organ: pancreas

Diagnosis: fat necrosis

Lesion: The areas of white chalky deposits represent foci of fat necrosis with calcium soap formation (saponification) at sites of lipid breakdown.

Fat Necrosis: Adipose Tissue



Organ: adipose tissue

Diagnosis: fatty necrosis

Lesion

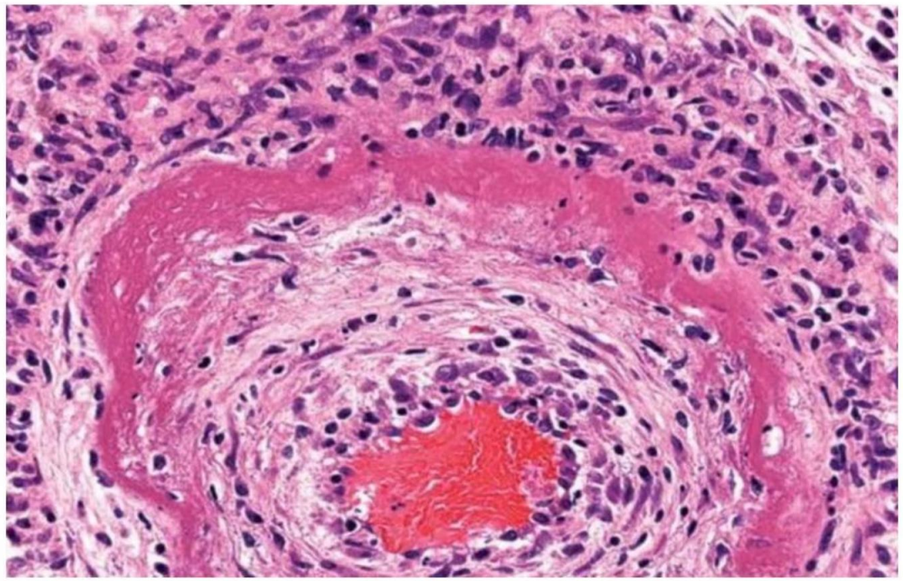
Fatty tissue change in to soapy material replace the fatty tissue surrounding by some normal fatty cells (adipocyte).

5. Fibrinoid Necrosis

Fibrinoid necrosis is characterised by deposition of fibrin-like material which has the staining properties of fibrin. It is encountered in various examples of immunologic tissue injury (e.g. in immune complex vasculitis, autoimmune diseases, Arthus reaction etc), arterioles in hypertension, etc.

Microscopically fibrinoid necrosis is identified by brightly eosinophilic, hyaline-like deposition in the vessel wall. Necrotic focus is surrounded by nuclear debris of neutrophils (leucocytoclasis). Local haemorrhage may occur due to rupture of the blood vessel.

Fibrinoid Necrosis: Artery



Organ: artery

Lesion:

- The deposited a bright pink and amorphous materials that has leaked out of vessels, called fibrinoid (fibrin-like).
- The wall of the artery shows a protein deposition and inflammation.

Diagnosis: Fibrinoid necrosis

Massive Necrosis

Gangrene

Massive necrosis of body surface or organs with a passage to the body surface with putrefaction superadded is known as gangrene.

Classification of Gangrene

1. Dry Gangrene

Dry gangrene occurs in the extremities due to occlusion of large artery with intact venous returns. The necrotic area is well demarcated black and mummification.

2. Moist Gangrene

Blockage of venous return and artery supply→massive necrosis followed by liquefaction caused by bacterial enzyme→purplish black color with foul-smelling.

3. Gas Gangrene

A serious complication of war wounds. Deep contaminated wound (massive necrosis) + clostridia group bacterial infection→gas production through the action of saccharolytic and proteolytic enzyme released from bacteria.

Necrosis vs Gangrene

Necrosis	**Gangrene**
Involve the soft organ that rich in blood supply ex: intestine, lung	Involve the solid organ that low blood supply ex: foot
Not prominent	Line of defense (inflammation reaction) is more prominent
To much gas and bacteria	Few
Light red	Dark red
Petrification odor is high	Low
Organ texture is spongy	Leathery and shrinking

Necrosis vs Apoptosis: Key Differences

Feature	Necrosis	Apoptosis
Cell size	Enlarged (swelling)	Reduced (shrinkage)
Nucleus	Pyknosis → karyorrhexis → karyolysis	Fragmentation into nucleosome size fragments
Plasma membrane	Disrupted	Intact; altered structure, especially orientation of lipids
Cellular contents	Enzymatic digestion; may leak out of cell	Intact; may be released in apoptotic bodies
Adjacent inflammation	Frequent	No
Physiologic or pathologic role	Invariably pathologic (culmination of irreversible cell injury)	Often physiologic; means of eliminating unwanted cells; may be pathologic after some forms of cell injury, especially DNA and protein damage