Cell death

1. Necrosis (Homicide)
2. Apoptosis (Suicide)

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1. Necrosis (Homicide)

Pathological aspect of necrosis:

- Severe damage.
- Metabolism stop.
- Structure destroy.
- Function loss.
Definition:

It’s a rapid death of limited portion of an organism and it’s consider to be the final stage of irreversible degeneration or cell injury, or it defined as Localized death of cell or tissue occurring in the living body.
Necrotic Cell is recognized by:

① Ultrastructural changes.

- Margination or progressive loss of nuclear chromatin.
- Focal rupture of the nuclear membrane.
- Breakdown of the plasma membrane.
- Development of flocculent densities in mitochondria.
② Changes in the nucleus.

1. **Pyknosis**: condensation of nuclear chromatin into a dark blue (H&E), “Hyperchromatosis”.

2. **Karyorrhexis**: It means splitting or fragmentation of the nuclear chromatin into tiny basophilic granules as a consequence of nuclear membrane rupture. It is more prominent in nuclei of dead neutrophils in case of “abscesses and purulent exudates”.
3. **Karyolysis:**

- It’s dissolution or lysis of the nuclear chromatin by nucleases enzymes released from leaking lysosomes of dead cells.
③ Changes in cytoplasm staining

1. Eosinophilia: denaturation of basic amino groups results in increased affinity for acidic dyes such as eosin.

2. Lysis of the cytoplasm giving pale vacuolated appearance.

3. Reduce differential staining of nucleus & cytoplasm.

4. Complete loss of the cellular outlines e.g. in case of Tuberculosis “T.B”.
Normal    | Pyknosis   | Karyorrhexis | Karyolysis
Nuclear changes in cell necrosis

- Karyorrhexis
- Karyolysis
- Pyknosis
Kidney, necrosis of tubular cells
Gross Characteristic of necrosis:

1. Loss of color or paleness due to “hemolysis of erythrocytes” in necrotic area.

2. Loss of tensile strength “enzymatic digestion to cytoskeleton, e.g.; cell membrane & intercellular connection”.

3. Necrotic tissues have bad odor or foul smelling due to ”Bacterial colonization”, then bacterial fermentation of protein result in production of hydrogen sulfide & ammonia e.g. in case of Gangrene.
Coagulative Necrosis
Kidney - Gross

Dry gangrene
Nota Bene (NB):

1. If dead tissues are (congested, hemorrhagic or contain hemolyzed blood) necrotic tissues become blackish-red in color.

2. Necrosis in liver & lung appear dark “double blood circulation”.

3. Necrosis in heart, kidneys & muscles appear pale “single blood supply”.

4. A series of chemical changes occur in tissues after death similar to necrosis macro & microscopically called (Postmortem changes & autolysis).
Coagulative necrosis—kidney infarction

This is the typical pattern with ischemia and infarction (loss of blood supply and resultant tissue anoxia). Here, there is a wedge-shaped pale area of coagulative necrosis (infarction) in the renal cortex of the kidney. Microscopically, the renal cortex has undergone anoxic injury at the left so that the cells appear pale and ghost-like. There is a hemorrhagic zone in the middle where the cells are dying or have not quite died, and then normal renal parenchyma at the far right.
Postmortem change:

Generally distinguished from necrosis by being diffuse and not associated with inflammatory response.

Autolysis:

Digestion of cell by enzymes released from lysosomes; occurs after cell dies or it means self digestion by lysosomal enzymes.
Patterns of Tissue Necrosis:

1. Coagulative necrosis
2. Liquefactive necrosis
3. Gangrenous necrosis
4. Caseous necrosis
5. Fat necrosis
6. Fibrinoid necrosis
1. Coagulative (Coagulation) Necrosis:

- Preservation of the structural outline of the dead (coagulated) cell for several days.

- The *most common* form of necrosis (particularly in myocardium, liver, kidney).

- Characteristic of infarcts in all solid organs except in the brain.

- *Myocardial infarction* is a very good example.
Morphology of Coagulative Necrosis:

• **Gross lesions:**
pale color, normal firm texture at the beginning → become soft later due to digestion by macrophages (may lead to rupture of infarcted myocardium)

• **Microscopic lesions:**
1. first few hours → no abnormalities
2. later → progressive loss of nuclear staining, with preservation of cell boundaries cell detail is lost, but architecture preserved.
3. This type of necrosis is frequently caused by lack of blood supply and is exemplified well in infarcts of solid organs, e.g. heart, skeletal muscle and kidney.
4. finally → damaged cells are removed by macrophages
5. The presence of necrotic tissue usually evokes inflammatory response followed by repair.
Kidney Normal

Kidney Coagulation necrosis
Coagulative necrosis of the left ventricular wall
Liver infarct necrosis
Splenic infarcts
2. Caseous (Caseation) Necrosis:

- Result from a mixture of coagulated protein with fat lead to formation of caseous materials resembling cheese.

- Sometimes mixed with blood "hemorrhage" or calcification.

- Dead tissue architecture is completely obliterated (no structure) & cellular outline are not seen.

- Characteristic of *tuberculosis* infection.
Gross lesions:

“Caseous” (Cheese-like) friable yellow-white gross appearance of the central necrotic area which is soft, granular, and a cream-cheesy appearance.

Microscopic lesions:

- Structureless amorphous granular eosinophilic debris surrounded by granuloma (aggregations of macrophages)
- Loss of cellular outlines & differential staining.
A tuberculosis lung with a large area of caseous necrosis.
Caseous necrosis in the lung

Granuloma

Giant cells
Caseous necrosis

- Caseous materials
- Giant cells
- Granuloma
Lymphocytes

Epithelioid cells

Giant multinucleated cell (Langhans)

Caseous necrosis
Lung and bronchial lymph node, caseous necrosis
3. Liquefactive (Liquefaction) Necrosis:

- Complete digestion of the dead cells with rapid dissolution “dead tissues undergo liquefaction”.
- The necrotic area is soft and filled with fluid e.g. abscess: in localized bacterial infections
- Characteristic of bacterial and some fungal infection → accumulation of white blood cells “dead neutrophils”.
- Also seen in hypoxic cell death in the central nervous system (brain, because its lacks supporting stroma)
- **NO cell structure remains.**
Causes of liquefactive necrosis:

1. In the brain due to high lipid content & low coagulated protein content.

2. In case of abscesses, neutrophils in the necrotic tissues extrude their lysosomes containing “hydrolytic enzymes” which degraded & liquefy the necrotic tissues as well as themselves “heterolysis”.
**Gross lesions:**

1. Consist of cavity containing yellow to white, opaque fluid.
2. Area of L. N. in the brain will be demarcated by a zone of inflammatory cells.
3. The wall of the cavity is irregular.

**Microscopic lesions:**

1. Necrotic area appear as empty space → no distinct outline
2. Pink staining “eosinophilic” amorphous protenicious materials of liquefactive necrosis found within the space.
3. Abscess is a localized collection of “pus” consist mainly of dead neutrophils & necrotic debris.
Brain Abscess, Liquefactive necrosis
Old infarct showing dissolution of tissue
Stroke - Liquifactive necrosis
Cerebral Infarction (Stroke)

Hemorrhagic Necrosis
Brain, normal

Brain, liquefaction necrosis
Coagulative necrosis

Liquefactive necrosis
4. Fat necrosis:

- It describes focal areas of fat destruction.
- Occurs in the abdominal cavity or under the skin “subcutaneous”.

**Causes of fat necrosis:**

1. **Pancreatic or “Enzymatic” fat necrosis:**

   Typically seen in:

   *Acute Pancreatititis or in case of pancreatic neoplasms.*

   Release of pancreatic lipases \(\rightarrow\) liquefy fat cells & hydrolyze triglyceride esters \(\rightarrow\) released fatty acids + calcium \(\rightarrow\) **Fat saponification.**
2. **Traumatic fat necrosis:**

- Occur outside the abdominal cavity.
- Result from mechanical trauma to subcutaneous adipose tissue e.g.:

Fat necrosis of subcutaneous & muscular area of the back region after prolong recumbence (bedridden patients).
subcutaneous fat necrosis
**Grossly:**
- The affected area become opaque, solid or slightly granular, white and chalky.

**Microscopical lesions:**
- Shadowy outlines of necrotic fat cells with basophilic calcium deposits or pinkish color depending on the present of sodium or potassium, surrounded by an inflammatory reaction.
Foci of fat necrosis with saponification in the mesentery.
fat necrosis next to pancreas
Acute pancreatitis.
Special types of coagulative necrosis

Gangrene:

**Definition:** necrosis of big tissue with superadded putrefaction, black, foul-smelling appearance or define as a necrotic tissue invaded by a saprophytic bacteria. It occurs in necrotic tissues which are exposed to air-borne saprophytes (bacteria) such as skin, lung, intestine and mammary glands.

Necrosis of big tissues \{ putrefactive
Or organ \{ organisms infection \{ black green appearance

(black or green due to breakdown of hemoglobin and reaction with H$_2$S produced by the bacteria).

Fe + H$_2$S \rightarrow FeS ( Black or Green color).
Types of gangrene:

a. Dry gangrene:

- Conditions only occur on the skin (fingers and toes) surface in which there is little fluid in the necrotic tissue following arterial obstruction with the presence of saprophytic organism.
- There is a line of demarcation of between the viable tissue and dark tissue.

Usual causes of ischemia (Loss of blood supply):

1. Freezing, vasoconstriction (frost bite).
2. Vasoconstriction due to poisonous venom.
3. Tight bandage and cast.
Dry gangrene
Inflammatory line of demarcations
b. **Wet (Moist) gangrene:**

- Condition due to arterial and venous obstruction occur; it occurs in tissues which are filled with blood at the time of their death such as the lung, intestine, mammary glands, appendix and uterus.
- Wet swollen, foul-smelling, black or green contain gas bubbles and has much hemorrhage.
- Rapidly fatal because of systemic toxemia rupture of the affected organs.

**Significance of wet gangrene:**

Gangrenous tissue produces severe toxins which tends to absorbed into the blood circulation resulting in toxemia and death.
Causes of wet gangrene:

1. Gangrene in the lung is associated with acute aspiration pneumonia due to inhalation of irritant oral medication.

2. The intestinal gangrene is associated with twists or torsions that result in blockage of the vascular supply or blockage of the venous drainage.
Moist gangrene
Moist or wet gangrene in an enlarged appendix
c. Gas gangrene:

- Occur in deep contaminated wounds.
- Considerable muscle damaged by gas formation bacteria.

Characterized by swollen obviously, gas bubbles formation. The infection rapidly spreads and associated with severe toxemia.

Only occasionally in civilian practice but is a serious complication of war wounds.
Gas gangrene in thigh region
Gas gangrene in due to IM injection
Consequences of necrosis:

① Acute or chronic inflammation.

② Immunological reactions to sub cellular components released by dead tissue or self-antigens altered by denaturation.

③ Lysis and absorption.

④ Ulceration and cavity formation.

⑤ Organization convert to connective tissue.

⑥ Encapsulation and/or calcification.