

Necrosis, Gangrene and Post-mortem Changes

- Sometimes empty spaces but infiltration of neutrophils at periphery.

FAT NECROSIS

Local death of adipose cells in living body.

Etiology

- Trauma
- Increased action of enzymes due to leakage of pancreatic juice.
- Starvation

Macroscopic and microscopic features

- Chalky white mass deposits in organ.
- White opaque firm mass.
- Adipose cell without nucleus.
- Macrophages giant cells contain fat droplets.
- Presence of lime salts in tissues.

Differential features of various types of Necrosis

	Coagulative	Liquifactive	Caseative	Fat
Macroscopic features	1. Organ becomes gray/ white in colour, firm, dense, depressed with surrounding tissue	1. Liquifactive necrosed tissue present in a cavity "Abscess" 2. It contains small/ large amount of cloudy fluid, which is creamy yellow (Pus)	1. Dead tissue looks like milk curd or cottage cheese 2. Tissue dry, firm, agranular, white/ gray/ yellowish in colour	1. Chalky white mass deposits in organ 2. White opaque firm mass
Microscopic features	1. Cellular outline present, which maintains the architecture of tissue/ organ 2. Nucleus absent or pyknotic 3. Cytoplasm becomes acidophilic	1. Areas of liquifactive necrosis stains pink. 2. Infiltration of neutrophils 3. Sometimes empty spaces but infiltration of neutrophils at periphery	1. Disappearance of cells; no cell details/ architecture 2. Purplish granules on H&E staining, blue granules from nucleus fragments, red granules from cytoplasm fragments.	1. Adipose cell without nucleus 2. Macrophages giant cells contain fat droplets. 3. Presence of lime salts in tissues.

(12)

Difference between Dry & Moist Gangrene

S.No. Properties

1. Location

Dry Gangrene

It usually occurs on extremities.
e.g. ear, tail, nail etc.

Moist Gangrene

It usually occurs in internal organs.
e.g. Intestine, lung
Heavy & thick mucus
Mammary gland

2. Etiology

Slow occlusion of blood supply by cold,
tight bandage

sudden occlusion of
blood supply due to
obstruction & clot

3. Demarcation b/w living & dead tissue

There is sharp line
of demarcation

No line of demarca-

4. Consistency

Area is dry, thick
& mummified

Area shows haemor-
& oedema

5. Gas bubbles

less

more

Post-mortem Autolysis and Necrosis

S.No. Post-mortem Autolysis

1. Absence of inflammatory reactions

Necrosis

Presence of inflammatory reactions

2. Autolytic changes are seen uniformly throughout the tissue.

Diffuse or focal adjacent living and dead tissues are seen

- | | Apoptosis is a programmed cell death (programmed) | Necrosis is a premature cell death |
|----|--|---|
| 1. | Apoptosis is a highly regulated timely event | Necrosis is an unregulated random event |
| 2. | Genetically Controlled | Not Genetically controlled |
| 3. | Apoptosis is a pre-planned cell death pathway | Necrosis is not a pre-planned cell death pathway |
| 4. | Apoptotic cell deaths are natural/normal | Necrotic cell deaths are always pathological (not natural) |
| 5. | Apoptotic cell death usually do not require any treatment | Necrotic cell death are not naturals and always require proper treatment |
| 6. | Apoptotic cell deaths are usually beneficial to the organisms | Necrotic cell deaths are always detrimental to the organisms |
| 7. | Apoptotic cell death is initiated by self-generated signals from inside or outside the cells | Necrotic cell death always occurs after signals from external agents such as fungal or bacterial toxins |
| 8. | Shrinkage of cells occurs during apoptosis | Swelling of cells occurs during necrosis |
| 9. | Membrane blebbing occurs during apoptotic cell death | No membrane blebbing but the membrane get disrupted during necrotic cell death |

- 3** Apoptotic bodies are formed during apoptotic cell death
No such necrotic bodies are formed during necrosis
- 4** Usually apoptotic cell death is devoid of any physical symptoms
Severe inflammatory symptoms are evident in the neighboring cells after necrotic cell death
- 5** No inflammation occurs in the surrounding tissues
Cause severe inflammation in the surrounding tissues
- 6** Cells undergoing apoptosis actively take part in cell death pathway
Cells undergoing necrosis do not take part in any events in the death pathway
- 7** An active process hence require energy from ATP molecules
A passive process and do not require ATP
- 8** Since it is an active process, apoptosis does not occur at 40°C
Since it is a passive process, necrosis can also occur at 40°C
- 9** Phagocytosis of the cell remnants are done by the adjacent cells or macrophages
Phagocytosis of the cell remnants are always done by the macrophages
- 10** The integrity of lysosomes are preserved in apoptotic cell death
The integrity of lysosomes are compromised during necrotic cell death, lysosome leakage occurs
- 11** Chromatin condensation is hallmark of apoptosis
No chromatin condensation occurs during necrosis
- 12** Nucleus get fragmented
Nucleus get deorganized

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Apoptosis is a caspase dependent cell death pathway

Necrosis is caspase independent cell death pathway

- 23 Activation and participation of many Caspase enzymes are involved in apoptosis
- 24 Externalization of phosphatidyl serine from inner to the outer leaflet of plasma membrane occurs
- 25 DNA fragmentation is pre-lytic (before cell lysis) in apoptosis
- 26 DNA is fragmented between nucleosomes and hence a ladder like pattern is formed after the agarose gel electrophoresis of total DNA extract
- 27 Release of cytochrome C and AIF from the mitochondria to the cytoplasm of cells occurs
- 28 pH of the cells changes to acidic during apoptosis
- 29 Apoptosis ends in fragmentation of cells into smaller bodies (apoptotic bodies)
30. Integrity of mitochondria usually lost during initial phases of apoptosis.
- No Caspase enzymes are involved in necrosis
- No such flipping of plasma membrane occurs during necrotic cell death
- DNA fragmentation is post lytic (after cell lysis) in necrosis
- DNA fragmentation is random and hence not ladder but a smear like pattern is formed after agarose gel electrophoresis of total DNA extract
- No such events are reported in necrosis
- There is no change in the pH of the cells during necrosis
- Necrosis ends in total lysis of the cells
31. Integrity of mitochondria usually maintained during the initial phases of necrotic cell death.

Necrosis, Gangrene and Post-mortem Changes

- Necrosis of muscles
- Presence of Gram positive rod shaped Clostridia
- Dissolution of muscle fibers due to saprophytes/ toxins of the organism.

Differential features of various types of Gangrene

	Dry	Moist	Gas
Macroscopic features	1. Dry, fragmented crusts like lesions on tail, scrotum, ear 2. Hoof becomes detached due to necrosis and gangrene, sloughing, exposing the red raw surface. 3. Blackening of the affected area.	1. Greenish or bluish discoloration of the affected organ. 2. Dissolution of affected part into fragments 3. Presence of foreign material like milk, fiber, oil, etc.	1. Oedema of Muscles in affected part particularly thigh region. 2. Blackening of muscles due to production of H_2S by bacteria and its chemical reaction with iron of free hemoglobin producing iron sulphide. 3. Presence of gas in the area giving crepitating sound on palpation
Microscopic features	1. Necrosis and invasion of saprophytes in skin of tail, ear or scrotum	1. Necrosis and invasion of saprophytes 2. Presence of foreign material like milk, fibers, oil, etc.	1. Necrosis of muscles 2. Presence of Gram positive rod shaped Clostridia 3. Dissolution of muscle fibers due to saprophytes/ toxins of the organism

POST-MORTEM CHANGES

Alterations in cells/ tissues occur after death of animal. The degree of such alterations and their speed depends upon the environmental temperature, size of animal, species of animal, external insulation and nutritional state of the animal. The postmortem changes occur rapidly in high environmental temperature, large animal, fur/ wool bearing and fatty animals.

Autolysis: Autolysis is the digestion of tissue by its own enzymes and is characterized by uniform destruction of cells without any inflammatory reaction. After death, a state of hypoxia occurs leading to decreased ATP. The cell organelles

APOTOSIS

Def: → It is a genetically programmed type of cell death, which is designed to eliminate unwanted host cells without inciting inflammatory process. It occurs through activation of a coordinated, internally programmed series of events brought about by a set of gene products.

→ Apoptosis is responsible for programmed cell death in several physiological & pathological conditions such as:

- (i) Programmed destruction of cells during embryogenesis
- (ii) Hormone dependent physiological involution as involution of endometrium during menstrual cycle.
- (iii) ~~Death of neoplastic~~ certain pathological conditions such as irradiation and viral infections.

→ Apoptosis usually involve single cells or cluster of cells that appear in H&E stained sections as round or oval masses of intensely eosinophilic cytoplasm and dense chromatin nuclear fragments.

→ following ^{morphological} changes occur in cells during apoptosis:

1. cell shrinkage: The cell is smaller in size, cytoplasm becomes dense and organelles are tightly packed.

2. chromatin condensation: It is the most characteristic feature of apoptosis.

→ The nuclear ~~neocentri~~ chromatin gets condensed and aggregates peripherally under the nuclear membrane into well defined dense masses of various shape and size.

→ Apoptosis is generally synonymously used with "programmed cell death," but apoptosis cannot be prevented by Cycloheximide or actinomycin D while programmed cell death is prevented by these chemicals.

3. Fragmentation of DNA

4. formation of cytoplasmic buds & apoptotic bodies:

The apoptotic cells shrink rapidly, formation of buds which gets fragmented into a number of membrane bound apoptotic bodies ; These bodies are composed of fluid portion of cytoplasm (cytosol) and tightly packed ~~granules~~ organelles with or without nuclear fragments.

5. Phagocytosis of apoptotic cells : It is done by macrophages or nearby healthy cells.

A characteristic differential feature of apoptosis in contrast to necrosis is absence of inflammation in apoptosis.

Mechanism of Apoptosis

It involves four components:

1. Signalling: Apoptosis is triggered by a variety of stimuli which are transmitted via plasma membrane and initiate a death cascade. There is extrinsic & intrinsic signalling pathways.
2. Control & Integration: It is performed by specific proteins.

3. Death (Execution): It occurs by following pathways →

- (i) Protein cleavage
- (ii) Protein cross-linking
- (iii) DNA break down

4. Removal of Dead cells

Diffr b/w necrosis & Apoptosis :-

- 1) In Apoptosis, no inflammatory respn seen.
- 2) Apoptosis is a consequence of an active process whereas necrosis is the consequence of a passive and degenerative process.