1. **Cellular aging**

There are two theories behind this:-

1. Wear and tear theory
2. Genome based theories

**Wear and tear theory:**

According to this cellular aging is due to life long exposure to the same exogenous substance that diminishes cell survive ability e.g

Free radical mediated cellular aging is an example.

**Free-radical mediated cellular aging:** In this mechanism, cellular aging is due to persistent exposure to the free radicals that results in cell death. These free radicals continuous exposure results in decreased level of anti-oxidants and cause cell death. These free radicals also cause post-translational changes in extracellular and intracellular proteins. e.g

Non-enzymatic glycosylation results in the formation of some end products that interact with adjacent protein as in diabetes mellitus sugar attach with the protein.

**Genome based theory:**

According to this theory, DNA repair process become slow down with age that results in loss of intrinsic property of cell. It is the cellular mediated cell death. Every cell has some specific sequences of cell death. With the advanced age, this sequence of events goes to final step and results in cell death.

**Necrosis**

“It is a spectrum of morphological changes that follow cell death due to progressive degradation action of enzymes due to lethally injured cell”.

**Types of necrosis:**

**Autolysis**: When the cells of necrotic area release enzymes, such degradation action is called autolysis.

**Heterolysis**: When cells of inflamed area reach to the site of infection to defend against the foreign particles, such type of degradation is called heterolysis.

**Changes in necrosis:**

Two types of changes are:

1. Cytoplasmic changes

2. Nuclear changes

1. **Cytoplasmic changes:**

During histology, we perform staining with hematoxylin and eosin stain. Hematoxylin gives bluish colour and eosin gives pinkish colour.

**Eosinophilia**: In necrosis, there is denaturation of protein by lysosomal enzyme. The eosin part binds with the denatured protein and gives pinkish colour that results in “eosinophilia”.

**Basophilia**: Cytoplasmic RNA binds with hematoxylin part producing blue appearance called “basophilia”

In the later stages, nucleus no longer exists that results in the absence of basophilia.

After some time there is formation of some vacuoles inside the cell. These vacuoles fuse with each other that has a shape of mouth-eaten insect.

**2.Nuclear changes:**

**Pyknosis:** Nuclear material is condensed and shrinked that binds with the hematoxylin part. Such process is called pyknosis.

**Karyorhexis:** In karyorhexis, fragmentation of nuclear material occurs.

**Karyolysis:** In karyolysis, nuclear material fade off and ultimately cells have no nucleus.

**Morphological types of necrosis:**

There are two types of necrosis

1. Coagulative necrosis

2. Liquefactive necrosis

**Coagulative necrosis:** In coagulative necrosis, cells are injured but outline of cell is preserved for some time. In such type of necrosis there is denaturation of protein not only the structural but also the functional protein and ultimately no enzymes are available to digest the cell. Such type of pattern is called coagulative necrosis.

**e.g.** ischemia of all tissues except brain.

**Liquefactive necrosis:** In liquefactive necrosis, there is denaturation of protein and also degrative action of enzymes like autolysis and heterolysis. This type of necrosis is liquefactive necrosis.

**e.g.** ischemia of brain. In brain, microglial cells contain a lots of enzymes.

**Other types of necrosis**

1. **Gangrenous necrosis:** It occurs in limbs. e.g ischemia of lower limbs that results in gangrenous necrosis or coagulative necrosis. Such type of gangrene is called ‘’dry gangrene’’.

If in such conditions of gangrenous necrosis bacterial infection it results in liquefactive necrosis and gangrene is known as ‘’wet gangrene’’.

1. **Caseous necrosis:** This type of necrosis occurs in tuberculosis. Caseous means white cheesy material. In such type of necrosis, there is granuloma formation that contains central necrotic reigon.
2. **Fibrinoid necrosis:** This occurs in the immunological disorders when antigen binds with anti-body. This antigen-antibody complex circulates into the blood vessels and cause damage to the blood vessels.

Fibrin leakage will result and binding of fibrin to blood vessels will cause fibrin like thread. Surrounding of fibrin to blood vessels is known as fibrinoid necrosis.

1. **Fat necrosis:** Pancreas contain lipase that is released into intestine through pancreatic duct and cause breakdown of triglycerides.

In this case of acute pancreatitis, lipase is released from the pancreas and cause breakdown of fats into triglycerides and fatty acids. This fatty acid binds with calcium and produce soap-like appearance or “saponification”. This pattern is known as fat necrosis.