cellular injery, necrosis and gangrene

- **Cell injury**
- **Cell injury defined as morphological or functional changes or both as a result of stresses to the cell encountered.**
- **Causes of cell injury**
- **1-Hypoxia (Decreased oxygen supply)**
- **2 - Infectious agents**
- **Bacteria, viruses, fungi and parasites**
- **3-Physical agents**
- **Trauma, extremes of temperature, radiation and electric shock**
- **4-Chemical agents and drugs**
- **Strong acids and alkalis, poisons, some therapeutic drugs**
- **5-Immunological reactions**
- **Allergy and autoimmunity**
- **6- Nutritional imbalances**
- **Protein deficiency and lack of specific vitamins.**
- **7- Genetic derangements**
- **Chromosomal alterations, gene mutations.**

- Mechanisms of cell injury
- 1-Impaired energy production (ATP depletion)
- -Mainly caused by hypoxia and toxins
- Effects
- 1-Failure of sodium pump---- sodium to enter the cell and potassium to exit-------
- Followed by water entry ------accumulation of water inside cell

- 2-Increased intracellular calcium
- -Calcium is maintained at extremely low levels
- -Ischemia and toxins can cause calcium influx across plasma membrane or Release from mitochondria and endoplasmic reticulum.
- -Effects
- Activates the following enzymes
- a- phospholipase -----degrade membrane phospholipids
- b- proteases---- breakdown protein
- c- ATPase------ increase ATP depletion
- d- Endonucleases-------chromatin fragmentation.

- 3- Production of oxygen free radicals
- Oxygen free radicals are highly reactive unstable oxygen molecules that can react with organic and inorganic materials e.g. superoxide and hydrogen peroxides.
- Effects
- -Damage of lipids
- -Damage of proteins
- -Fragmentation of cellular DNA
- -Mitochondrial damage

- Effects of cell injury
- 1-Reversible cell injury (Degeneration)
- Caused by mild injury of short duration
- Affects active parenchymatous cells
- The morphological changes affect only the cytoplasm
- Includes:
- -Cloudy swelling
- -Hydropic swelling
- -Fatty change
- 2- Irreversible cell injury (cell death)
- Caused by severe injury or injury of long duration
- Damage to nucleus
- Includes:
- -Necrosis
- -Apoptosis

- **Definition**: Local death of cells or tissues within the living body.
  Macroscopic Picture: Necrotic tissue appears opaque and whitish or yellowish in color.
  Microscopic Picture: The changes are nuclear and cytoplasmic.
  (1) Nuclear Changes:
  (a) ***Pyknosis:*** The nucleus Shrinks, its chromatin becomes dense stains darkly.
  (b) ***Karyorrhxis:*** The nucleus breaks up into multiple small fragment.
  (c) ***Karyolysis:*** The nucleus appears to dissolve and fails to take stain due to chromatin hydrolysis.
  (2) Cytoplasmic Changes:
  (a) the cells appear swollen (cytomegaly).
  (b) In haematoxyline and eosin stained sections there is cytoplasmic eosinophilia.
  (c) The cells loose the cell membrane.

- **Types of Necrosis:**
  (1) Coagulative Necrosis: Commonly caused by sudden cut of the blood supply. Example are myocardial, renal infarction.
  (2) Liquefactive Necrosis: The necrotic tissue is rapidly liquefied and change into fluid. Example are suppurative inflammation with the formation of pus, it is due to infection. And in the necrosis of brain and spinal cord, it is due to cut of blood supply.
  (3) Caseating Necrosis: The necrotic tissues looks like the casein of cheese. Example are tuberculosis, it is due to antigen antibody reaction.
  (4) Fat necrosis; Necrosis of fatty tissues occurs in two condition,
  - trauma of subcutaneous fat (traumatic fat necrosis)
  - the release of pancreatic enzymes in acute hemorrhagic pancreatitis (enzymatic fat necrosis)

- **GANGRENE**
  Definition: Gangrene is massive tissue necrosis followed by putrefaction**.**
  Causes:
  (1) ***Necrosis***
  (2) ***Putrefaction:*** Is caused by saprophytic bacteria which breaks down protein of the necrotic tissue liberating hydrogen sulphide that gives the tissue a foul odour. Hydrogen sulphide unites with the iron of haemoglobjn forming iron sulphide that stains the gangrenous tissue black.

- **1. DRY GANGRENE**
  Dry gangrene of a limb results from **gradual occlusion of its arterial supply**:
  The commonest example is dry gangrene of the lower limb, tissues **poor in blood supply** and **evaporation can occur**.
  Pathology:.
  The gangrenous process follows the following steps:
  (1) Arterial occlusion.
  (2) Distal to the occlusion massive necrosis occurs. The affected part is pale and cold. Sensations are lost. Later on it stains red by the blood escaped from the necrotic vessels. Evaporation of tissue fluids causes dryness and affected part becomes **shrunken and mummified**.
  (3) Saprophytic bacteria invade necrotic tissue and cause putrefaction,and the color become **black**.
  When gangrene reaches a level with good blood supply it stops. The toxic products of putrefaction act as an irritant and cause a zone of acute inflammation in the neighbouring healthy part. It appears as a narrow red line between the healthy and gangrenous part called ***line of demarcation.***
  From the healthy side granulation tissue grows towards the gangrenous part with the formation of a groove on the surface called ***line of separation.*** This groove may slowly deepens until it separates the gangrenous part leaving a ***conical stump.*** The stump is conical as the gangrene spreads higher up in the skin and subcutaneous tissue than in muscles and bone as the blood supply of the skin and subcutaneous tissue is less abundant.

- **II. MOIST GANGRENE**
  Moist or wet gangrene is caused by **sudden arterial and venous occlusion**. It occurs mainly in internal organs as the intestine, tissues **rich in blood supply** and from which **no evaporation of fluids** can occur. Gangrene spreads rapidly. The line of demarcation is poor and the line of separation is absent. The toxaemia is severe.
- **III. INFECTIVE GANGRENE**
  A subtype of moist gangrene in which bacteria cause both tissue necrosis and putrefaction. it is highly fatal due to the severe toxaemia. **example; gas gangrene.**