Lec. 2

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Cell injury, adaptation and cell death (2)

Causes of cell injury

- Hypoxia (oxygen deprivation)

  Occurs due to

  - Loss of blood supply - Ischaemia
  - Inadequate blood supply
  - Loss of oxygen carrying capacity – anaemia
- Physical agents
  - Mechanical trauma
  - Temperature
  - Radiation

Electric shock

Rapid change in atmospheric pressure

- Chemical agents and drugs

  Sodium, glucose, oxygen – in high concentration

  Alcohol

  Cyanide
- Infectious agents

  virus, bacteria, protozoa

- Immunological reactions
    - Hypersensitivity reactions
    - Autoimmune diseases
    - Anaphylactic shock
- Genetic derangements
- Nutritional
    - Malnutrition
    - Vitamin deficiency
    - Obesity

Mechanisms of cell injury

- Cellular response to injurious stimuli depends on the type of injury, its duration and its severity
- Consequences depend on the type, state and adaptability of the injured cells
- Cell injury results from functional and biochemical abnormalities in one or more of several essential cellular components

- Five targets of injurious stimuli
    1. Cell membrane
    2. Aerobic respiration
    3. Protein synthesis
    4. Cytoskeleton
    5. Genetic apparatus
- Various etiological factors cause cell injury by different mechanisms

Reversible hypoxic injury

Decrease oxygen supply

Decrease oxygen

Anaerobic glycolysis

Lactic acid accumulation and low PH

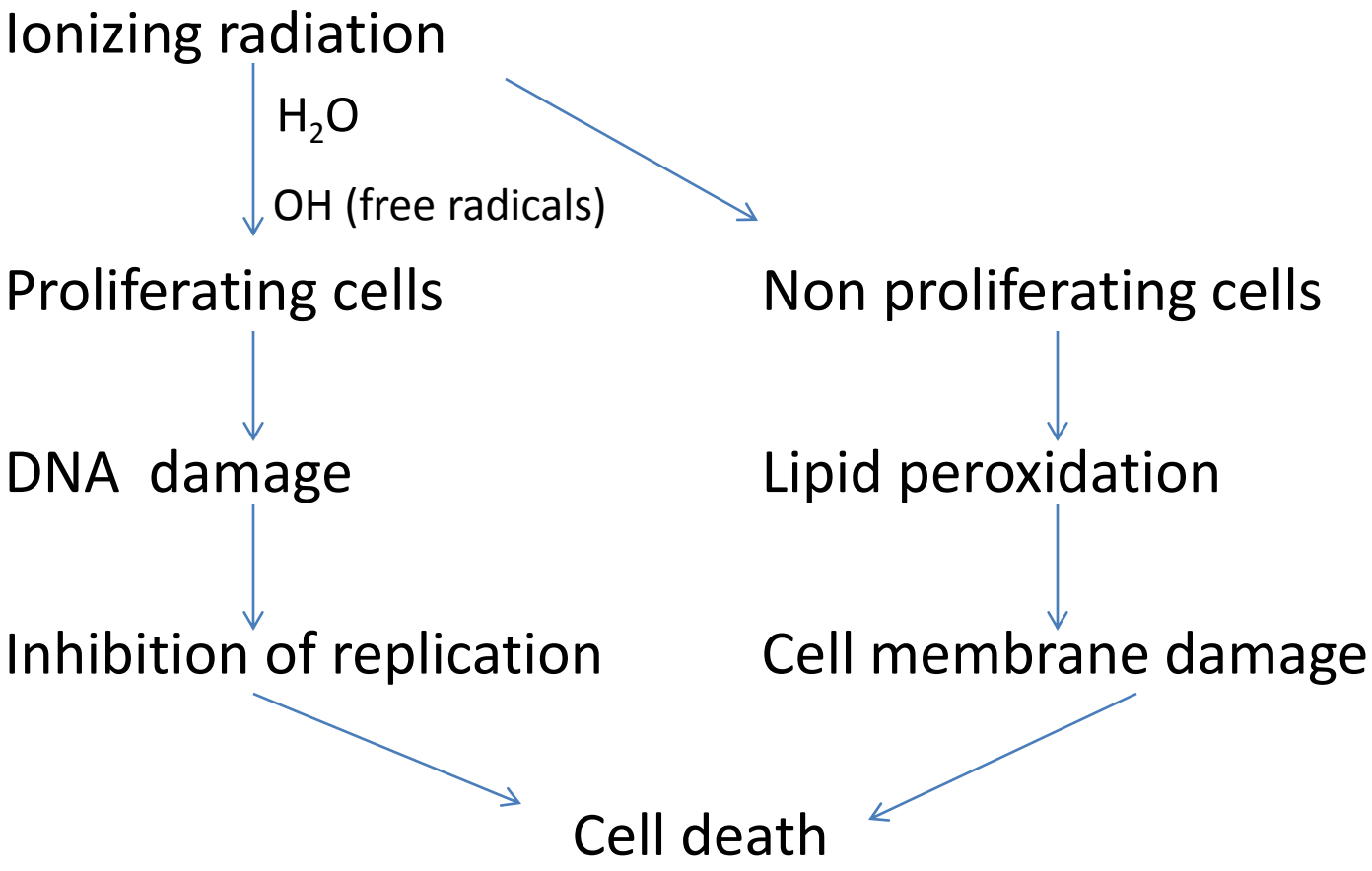
Intracellular protien synthesis decreases

Cytoskeleton changes, loss of microvilli, formation of blebs, cellular and mitochondrial swelling

Pathogenesis of chemical injury

- Direct cytotoxic effect
- Conversion to reactive toxic metabolites

Pathogenesis of physical injury



Morphology of cell injury and necrosis

- Reversible injury

Two patterns –

1. Cellular swelling (hydropic change, vacuolar degeneration)
2. Fatty change – Fat droplets in cytoplasm

- Cellular swelling (hydropic change)

  Difficult to appreciate with light microscopy

  Cytoplasm appear swollen due to increased intracellular water

  Pale → Cloudy swelling

  More water → small clear vacuoles

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  Vacuolar degeneration

*This is a reversible cell injury

- E/M changes
  - Blebs
  - ER swelling
  - Dispersed ribosomes
  - Clumped nuclear chromatin
  - Mitochondrial swelling
- Macroscopy
  - Pallor, increased weight of the organ
  - Cut surface bulges out

Irreversible injury

- Types

  1. Necrosis

  2. Apoptosis

- Necrosis - A spectrum of morphological changes that follow cell death in living tissue

- Morphologic changes are due to
  - Protein denaturation
  - Enzymatic digestion of the cell
    - -Autolysis
    - -Heterolysis

- Five patterns of necrosis are identified
  1. Coagulative necrosis
  2. Liquifactive necrosis
  3. Caseous necrosis
  4. Fat necrosis
  5. Fibrinoid necrosis

- Coagulative necrosis

  -Most common type of necrosis

  -Characteristic of hypoxic death of all tissues except brain

  -Results from denaturation of structural and enzymatic protiens due to intracellular acidosis

  -Dead tissue appear swollen and firm

  -L/M – Ghost outlines of cells

- Colliquative (liquefactive) necrosis
  - Results from enzymatic digestion (autolysis and heterolysis)
  - Characteristic in pus forming bacterial infection(suppurative inflammation)
  - seen in brain due to hypoxia
  - Complete loss of architecture

- Caseous necrosis
  - Distinctive type of coagulative necrosis
  - Seen in tuberculosis
  - Macroscopically – cheese like
  - Micrscopically – pink granular appearence

- Fat necrosis

  - Enzymatic fat necrosis

  eg. Acute pancreatitis

  Lipases are released → Act on fat

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  FFA + calcium → Ca soaps

  - Non enzymatic – eg. trauma to breast

- Fibrinoid necrosis

  -Seen in connective tissue particulary in autoimmune diseases

  - Characterised by loss of normal structure and replacement by homogenous bright pink necrotic material similar to fibrin

Effects of necrosis

- Depends on

  Tissue / organ involved

  Amount / extent of necrosis

  Amount of remaining functioning tissue

  Capacity of cells to proliferate

- Effects

  1. Abnormal function eg. Heart failure

  2. Bacterial infection leading to gangrene

  3. Release of contents within necrotic cells eg serum enzymes

  4. Systemic effects – fever

  5. Local effects, depending on the site eg. Skin –ulcer

- Sequele of necrosis
    - Resolution
    - Organization
    - Calcification
    - Gangrene

Gangrene

- A clinical condition
- Extensive tissue necrosis with secondary bacterial infection
- Two types 1. Primary
  2. Secondary

- Primary gangrene

  Infection with pathogenic bacteria

  Tissue destruction is by exotoxins

  Invades and digest tissue

  eg. Gas gangrene

  Clostridium perfringens – open contaminated wounds, crepitus and foul smelling

- Secondary gangrene

  Necrosis is due to some other causes

  eg. Loss of blood supply

  Saprophytic bacteria then digest the tissue

  eg. Dry gangrene, wet gangrene

- Dry gangrene
  - Occurs in extremities
  - Arterial obstruction
  - eg. Toes and feet of an elderly (Atheresclrosis)
  - Coagulative necrosis
  - Macroscopically – Black dry sharply demarcated area

- Wet gangrene

  Severe bacterial infection with necrosis

  Occurs in naturally moist tissue

  eg. Mouth, bowel, lung, diabetic foot

  Macroscopy – Poorly demarcated reddish black swollen area