CELL INJURY

→ Reversible & irreversible.

reversible cell injury

causes: hypoxia, ischemia.
↑
genetic and aquired causes

~~genetic causes~~

Ischemia due to obstruction to blood flow or diseases of RBCs, lungs, heart

physical ailments → radiation, trauma, UV.

chemical ailments → cyanide, poisons, alcohol.

Microbial agents → bacteria, virus, fungus.

Nutritional causes → vitamin deficiencies, PEM, starvation

Age of cell, immunological causes.

Pathogens.

type, duration & severity of contact with pathogens determine the severity of injury

type of cell (eg: cardiac cells are more prone to hypoxia in comparison to skeletal cells)

Intracellular damages → Mt. damage
ultrastructural changes in the cell visualized by microscope.

Energy often by aerobic & anaerobic pathways.

anaerobic ↑, lactic acid ↑, pH ↓, chromatin form clumps - damaged

ischemia → both aerobic & anaerobic pathways blocked

hypoxia → only aerobic is blocked. hence damage is less.

→ when ATP is reduced.
damage to plasma membrane, nuclear membrane (hydraulic swelling)

FA will not convert to phospholipids & phospholipids degrade & lysis are produced

↓

pumps open.
increased conc. of Ca^{2+} in cytoplasm, get deposited on mitochondria.

protein synthesis

prokinase enzyme activated, ribosomes detach from ER. and form monosomes which cannot form protein hence membranes degraded

CELL INJURY

→ When the cell is exposed to an injurious agent or stress, a sequence of events follows - cell injury.

→ Cell death is the ultimate result of cell injury.

Normal cell
↓
stress.

- Mild stress & prolonged (ADAPTATION)
- Moderate (Reversible cell injury)
- Severe. (Irreversible cell injury)
  ↓
  cell death.
  - Necrosis
  - Apoptosis.

Adaptations (Question)

→ Reversible changes in the no, size, phenotype, metabolic activity or functions of cells in response to changes in their environment.

→ Hypertrophy, hyperplasia, Atrophy & metaplasia.

Hypertrophy

is an increase in the size of parenchymal cells resulting in enlargement of the organ or tissue without any change in the no. of cells

① physiological : Uterus in pregnancy
② Pathological : ventricular hypertrophy in hypertension.

Mechanism

- Growth factors : TGF beta, (transforming) IGF, EGF, (fibroblast like.)
- Hypertrophy agonists - NO, Endothelin - 1, Angiotensin - II.
- Mechanical stretch.

Mechanical stretch (↑ work load) | Agonists (eg adrenergic hormone, angiotensin) | GF

↓
Signal transduction pathways
↓
Transcription factors.

- Induction of embryonic fetal genes.
  ↓
  ↑ Mechanical performance
  ↓ Work load.
- ↑ synthesis of contractile proteins.
  ↓
  ↑ Mechanical performance
- ↑ pathway of growth factors

Hyperplasia

is an increase in the number of parenchymal cells resulting in enlargement of the organs

... tissue.

Hyperplasia. Quite often, both are seen and hypertrophy together.

Physiological Hyperplasia

① Hormonal hyperplasia i.e hyperplasia occurring under the influence of hormonal stimulation.

eg: Hyperplasia of female breast at puberty, during pregnancy and lactation.

② Compensatory hyperplasia i.e hyperplasia occurring following removal of part of an organ or a contralateral organ in paired organs

egs (i) Regeneration of liver following partial hepatectomy.

Pathological Hyperplasia -

- Excessive hormonal stimulation - BPH, Endometrial hyperplasia.
- Cell proliferation - Growth factors & hormones.

Atrophy

Reduction of no. & size of parenchymal cells of an organ or its parts which were once normal is called atrophy

May be physiological and pathological cause

physiologic → atrophy of bones with aging.
→ Atrophy of gonads after menopause

pathological atrophy

→ Starvation atrophy : in starvation there is 1st depletion of carbohydrate & fat stores followed by protein catabolism.

→ Ischaemic atrophy : eg: Atrophy of brain in cerebral atherosclerosis.

→ Disuse atrophy eg: Atrophy of the pancreas in obstruction of pancreatic duct.

→ Neuropathic atrophy eg: Poliomyelitis.

Mechanism

- ↓ protein synthesis reduced metabolic activity
- ↑ protein degradation in cells ubiquitin - proteasome pathway

Metaplasia.

Reversible change in which one adult cell type (epithelial

of mesenchymal) is replaced by another adult cell type.
→ Adaptive response to chronic injury.
→ Reprogramming of precursor cells

Epithelial metaplasia

① Squamous metaplasia: squamous metaplastic change due to chronic irritation that may be mechanical, chemical or infective in origin.
eg: In bronchus (normally lined by pseudostratified columnar ciliated ep) in chronic smokers.

② Columnar metaplasia: There are some conditions in which there is transformation to columnar epithelium.
eg: intestinal metaplasia in healed chronic gastric ulcer.
Barrett's oesophagus.

B. Mesenchymal Metaplasia

Less often, there is transformation of one adult type of mesenchymal tissue to another.

① Osseous metaplasia
eg: Cartilage of larynx & bronchi in elderly people

② Cartilaginous metaplasia.
In healing fractures, cartilaginous metaplasia may occur where there is undue mobility.

The morphology of cell & tissue injury

① Reversible: cellular derangements of reversible injury can be corrected and if the injurious stimulus abates, the cell can return to normal.

② Irreversible: Persistent or excessive injury - cells to pass the nebulous "point of no return" into irreversible injury and cell death.

Reversible cell injury

Two main morphologic changes:
→ Cellular swelling and fatty change.

Intracellular changes:
membrane blebbing
ribosomal detachment
ER swelling.
Nuclear chromatin clumping
cellular swelling
Mitochondrial swelling

cellular swelling

→ 1st manifestation

→ result of failure of energy dependent ion pumps in the plasma membrane.... inability to maintain ionic and fluid homeostasis

→ Organ - pallor & increase in weight of the organ.

- ~~Microsco~~ Microscopic Examination

hydropic change or vacuolar degeneration

Fatty change (steatosis)

→ Abnormal accumulation of triglycerides within the parenchymal cells.

→ Organs affected : liver (most common) heart, muscle, kidney

Morphology:

Gross: liver enlarged, yellow, soft, greasy.