Pathology Exam Revision Notes

MODULE 1 - CONCEPTS

NOMENCLATURE

Aetiology	- cause of the disease
Pathogenesis	- mechanism causing disease
Pathology	- morphology and molecular changes to tissue
Clinical Manifestations	- signs & symptoms
Complications	- secondary, systemic, remote consequences
Prognosis	- anticipated course of disease
Epidemiology	- incidence, prevalence, disturbance

CELLULAR ADAPTATIONS

Physiological - cellular adaptations to normal stimulation (eg/ hormones/endogenous)
Pathological - cellular adaptations to stimuli secondary to underlying disease to avoid injury

Hypertrophy
- Increased cell size
- Results in increased organ size
- Results from increased organelles and structural proteins
- Increased demands on cell/work load
- Physiological and Pathological
- Typically in non-dividing cells (myocytes, skeletal muscle)

Hyperplasia
- Increased cell number
- Results in increased organ size
- Typically in proliferating cell types (capable of dividing)
- Physiological and Pathological

Dysplasia
- Decreased cell size/number
- Decreased organ size
- Decreased number of organelles and structural proteins
- Result of decreased work load, limited nutrients & vascularisation/innervation
- Physiological and pathological

Metaplasia
- Change from one differentiated cell to another
- Cells sensitive to stress replaced by cells better able to withstand stress
- Result from pathological adaptations
- Stem cell reprogrammaing

- Failure to adapt to stress results in injury
- Reversible if stimuli can be removed
- Irreversible if stimuli not removed (death)

INJURY INDUCING STIMULI
- Chemicals Agents
- Physical Agents
- Physical Trauma to Single Gene Defect
- Infectious Agents
- Ageing
- Hypoxia
- Gene Defects
- Nutritional Imbalance
- Immunological Reactions

IRREVERSIBLE INJURY

- Stimuli not removed
- Cell death : apoptosis & necrosis
- Causes: Cell Specific Damage
  - Tissue
  - State
  - Adaptability
  - Genetics

- Causes: Injury Specific Factors
  - Duration
  - Severity
  - Type

- Haematoxylin-Eosin Staining
  - Haematoxylin
    - Basic dye, stain acidic structure purple-blue (nucleic acids)
  - Eosin
    - Acid dye, stain basic structure red-pink (proteins and cytoplasm)
- Morphological Features
  - Loss of membrane integrity - plasma (cell contents leak), lysosomal (degrade cytoplasm), mitochondrial (no ATP)
  - Mitochondrial dysfunction - cannot be recovered

- Non-functional but viable
- Biochemical changes occur and become non-viable (dead) before macroscopic changes are apparent

REVERSIBLE INJURY

- If stimuli removed cell recovered
- Compromise function of cell/organ
- Morphological Features
  - Cell blebbing
  - ER and Mitochondrial Swelling
  - Cellular Swelling
  - Fatty change
  - Nuclear Alterations

MECHANISMS CAUSING DISEASE

- Decreased ATP
  - Result from:
    - Mitochondria dysfunction
    - Decreased Oxygen
    - Toxins
  - Result in:
    - No energy for cellular functions
    - ATP dependent ion channels fail —> Swelling & blebbing
    - Protein Misfolding (decreased synthesis)—> apoptosis
    - Nuclear chromatin clumping

- Damaged Mitochondria
  - Result from:
    - Influx of calcium
    - Increased ROS
    - Lipid peroxidation
  - Result in:
    - Decreased ATP synthesis —> increased ROS —> necrosis
    - Cytochrome C leaves cell —> decreased ATP from ETC —> apoptosis

- Increased ROS
  - Free radial oxygen with unpaired outer electron orbitals - unstable and reactive
  - Attack macromolecules (nucleic acid, proteins, lipids)
  - By-product of respiration, produced by phagocytic leukocytes
  - Removed by scavengers
  - Result in:
    - Oxidative stress
    - Damage to DNA and proteins —> apoptosis

- Increased Calcium
  - Result from:
    - Failure of ATP dependent Calcium channels
    - Damage to intracellular store: ER & mitochondria
  - Result in:
    - Activation of protease/caspase enzymes —> nuclear and membrane damage
    - Increased calcium in mitochondrial —> dysfunction —> apoptosis

- Loss of Membrane Integrity
  - Plasma
    - Cell contents leak
  - Lysosomal
    - Cytosol degraded
  - Mitochondrial
    - Dysfunction

- Protein and DNA Damage
  - Result from:
    - Drugs, radiation, oxidative stress
  - DNA damage/mutation result in apoptosis if cannot be repaired

NECROSIS
- Irreversible cell death
- Loss of membrane integrity
  - Leakage of cellular contents into space
  - Degradation of cellular proteins and organelles
- Mitochondrial dysfunction
- Proteins denatured
- Cell enlargement
  - Swelling of cell, ER and mitochondria
- Breakdown of DNA/nucleus
  - Pyknosis - shrinkage/condensation
  - Karyolysis - nucleus disappear / digested away
  - Karyorrhexis - fragmentation
- Inflammation
- Pathological

Type of Necrosis
- Coagulative
  - Ischemia - Solid Organs
  - Nucleus lost, denatured proteins
  - Tissue architecture preserve

- Liquefactive
  - Enzymatic digestion of molecules
  - No tissue architecture
  - Associated with infection in brain

- Caseous
  - Tissue architecture obliterated
  - Fragmented, lysed cells with amorphous granulation
  - Infection with Mycobacterium tuberculosis