WELCOME

TO

This is an Education Platform

We Provide PDF Notes for Pharmacy Students

Web Site http://www.fdspharmacy.in/

You tube https://www.youtube.com/c/FDSpharmacy

Telegram https://t.me/Fdspharmacy

App https://play.google.com/store/apps/details?id=com.FDSPharmacyMedia.FDSPharmacy

E-mail fdspharmacyinfo@gmail.com

PATHOPHYSIOLOGY

UNIT 1

TOPIC :

- **Basic principles of Cell injury and Adaptation:**
  Introduction, definitions, Homeostasis, Components and Types of Feedback systems, Causes of cellular injury, Pathogenesis (Cell membrane damage, Mitochondrial damage, Ribosome damage, Nuclear damage),Morphology of cell injury– Adaptive changes (Atrophy, Hypertrophy, hyperplasia, Metaplasia, Dysplasia),Cell swelling, Intra cellular accumulation, Calcification, & Alkalosis, Electrolyte imbalance

Basic Principles of Cell Injury and Adaptation

→ Cells are the basic units of life, and the proper functioning of tissues and organs depends on the health of individual cells.
When cells are exposed to stresses or harmful agents, they respond in several ways:

- They may adapt to the change
- They may undergo reversible injury (can recover)
- They may suffer irreversible injury, leading to cell death

→ Understanding how cells respond to injury is fundamental in pathology, as most diseases begin with cellular damage.

Cell Injury

→ A condition in which cells are unable to maintain homeostasis due to exposure to harmful stimuli, leading to structural and functional abnormalities.

Types of Cellular Responses to Injury

1. Reversible Cell Injury

- Occurs when the injury is mild or short-lived.
- The cell can return to normal structure and function if the stress is removed.
- Characteristics of reversible injury:
  - Cellular swelling
  - Fatty changes (especially in the liver and heart)
  - Plasma membrane alterations (blebbing)
  - Clumping of nuclear chromatin

Example: *Liver cell swelling due to mild hypoxia.*

2. Irreversible Cell Injury

- Occurs when the stress is severe or prolonged.
- Leads to permanent damage to cell structures, especially mitochondria and membranes.
- The cell undergoes death, either by:
  - Necrosis – uncontrolled death with inflammation
  - Apoptosis – programmed death without inflammation

Example: *Myocardial cell death due to prolonged ischemia (heart attack).*

3. Cellular Adaptations

- Cells may undergo structural or functional changes to survive under stress. This process is called cellular adaptation.
- If the stressor is removed, the cell may return to its normal state.

Adaptation	Definition	Example
Atrophy	↓ Cell size and function	Muscle wasting in immobilization
Hypertrophy	↑ Cell size due to increased workload	Cardiac hypertrophy in hypertension
Hyperplasia	↑ Number of cells	Endometrial hyperplasia
Metaplasia	Change in one type of adult cell to another	Respiratory epithelium in smokers
Dysplasia	Disordered cell growth (pre-cancerous change)	Cervical dysplasia

Homeostasis

→ It is derived from two greek words.

- ***Homeo*** *means* ***Same/Constant***
- ***Stasis*** *Means* ***State***

→ It means staying the same

→ It is a condition when our internal environment is constant with respect to external environment.

→ It is a condition that may vary but remains relatively Constant.

Homeostasis Control Mechanism

- All the body organs coordinate with each other to maintain homeostasis
- This coordination is mainly controlled by Neuroendocrine System (Nervous + Endocrine System]
- It has three components :-

i) Receptors :- It is a type of sensor, which recieve/detect changes or other stimuli

ii) Control Centre :- It recieve the stimuli from receptors and analyse it.

iii) Effectors/feedback system :- If there are any change take place in internal environment, then feedback system is take back into its constant state or in homeostasis

It is of two types:-

1) Positive feedback system (+) :- Used to increase when anything is decrease in our internal environment, then it is try to back into its normal situation by increasing it.

Eg : During childbirth, it stimulate the release of oxytocin which increases the contraction of the uterus to help in childbirth.

2) Negative feedback system (-) :- used to decrease When anything is increase in our internal Environment (body), then this system is try to back into normal condition by decreasing it .

Eg : the regulation of body temperature, where the body sweats to cool down when it's too hot or shivers to warm up when it's too cold.

Causes of Cellular Injury (Etiological Agents)

→ Cell injury occurs when cells are exposed to harmful agents or experience internal stress. The causes can be classified as follows:

❖ Physical Agents
- Mechanical trauma (e.g., crush injury, fracture)
- Temperature extremes (burns, frostbite)
- Radiation (UV, ionizing radiation)
- Electric shock
- Pressure changes (e.g., barotrauma)

❖ Chemical Agents
- Strong acids or alkalis
- Drugs and poisons (e.g., paracetamol overdose, cyanide)
- Environmental toxins (e.g., lead, mercury)
- Insecticides, pesticides

❖ Biological Agents
- Viruses – damage cell structure (e.g., HIV, hepatitis)
- Bacteria – produce toxins (e.g., diphtheria toxin)
- Fungi and parasites

❖ Oxygen Deficiency (Hypoxia)

- Ischemia: reduced blood flow (e.g., heart attack)
- Anemia: reduced oxygen-carrying capacity
- Carbon monoxide poisoning: prevents oxygen binding to hemoglobin

❖ Nutritional Imbalance

- Protein or vitamin deficiencies
- Obesity and excess lipid accumulation
- Starvation

❖ Immunological Reactions

- Autoimmune diseases (e.g., SLE)
- Allergic reactions (hypersensitivity)

Pathogenesis of Cell Injury

➢ Pathogenesis refers to the mechanisms by which injury develops in a cell after exposure to a harmful agent.
➢ The major intracellular targets of injury include:

A. Cell Membrane Damage

Effects:

- Loss of membrane integrity
- Influx of calcium ions and water
- Leakage of enzymes and proteins
- Loss of ion gradients and cell swelling

Example: Enzymes from lysosomes leak into the cytoplasm → **autodigestion of the cell**

B. Mitochondrial Damage

Mitochondria are essential for ATP production. Injury here leads to:

Consequences:

- ↓ ATP → failure of energy-dependent cellular functions
- ↑ Production of reactive oxygen species (ROS)
- Release of **cytochrome c**, which triggers **apoptosis**

Example: *Hypoxia → no oxidative phosphorylation → ATP depletion → cell death*

C. Ribosome Damage

Ribosomes are responsible for **protein synthesis**. Damage leads to:

Effects:

- Detachment from rough ER
- Inhibition of protein synthesis
- Accumulation of misfolded proteins
- Cell loses ability to maintain essential functions

Example: *In liver cells, toxins like CCl_4 cause ribosomal detachment → ↓ protein synthesis*

D. Nuclear Damage

The nucleus controls cell division and genetic expression. Damage occurs in **irreversible injury.**

Types of Nuclear Changes (Seen in Necrosis):

Change	Description
Pyknosis	Shrinkage and condensation of nucleus
Karyorrhexis	Fragmentation of the nucleus into pieces
Karyolysis	Dissolution of nucleus due to DNA degradation

Example: Seen in cells undergoing necrosis (e.g., infarcted tissues)

Morphology of Cell Injury

→ When cells are exposed to stressful conditions or increased functional demands, they may undergo adaptive changes. These are reversible and help the cell survive. However, if the stress persists or becomes severe, it can lead to irreversible damage and cell death.

→ Cellular adaptation is thus a protective mechanism, allowing tissues to respond to injury, physiological demand, or abnormal stimuli.

1. Atrophy

➢ Atrophy is a decrease in the size of a cell, tissue, or organ due to a reduction in cell size or number. It results in reduced function and metabolic activity.

Types of Atrophy:

- **Physiological:** Normal aging process
  - Example: Thymus atrophy in elderly
- **Pathological:** Due to disease or lack of use
  - Example: Muscle atrophy from immobilization (e.g., fractured limb in cast)

Causes:

- Decreased workload (disuse atrophy)
- Loss of nerve supply (denervation)
- Diminished blood supply (ischemia)
- Inadequate nutrition
- Aging (senile atrophy)
- Hormonal withdrawal (e.g., endometrial atrophy post-menopause)

Morphological Features:

- Decreased cell size and organ weight
- Accumulation of lipofuscin pigment ("wear and tear" pigment)

2. Hypertrophy

➢ Hypertrophy is an increase in the size of individual cells, resulting in an enlargement of the organ or tissue without an increase in cell number.

Types of Hypertrophy:

- **Physiological:** Due to increased functional demand
  - Example: Skeletal muscle hypertrophy in athletes
- **Pathological:** Due to abnormal load
  - Example: Cardiac hypertrophy from hypertension

Causes:

- Increased workload
- Hormonal stimulation (e.g., uterus in pregnancy)

Morphological Features:

- Enlarged cells and nuclei
- Organ size and weight increases
- No new cells formed (only enlargement)

3. Hyperplasia

➢ Hyperplasia is an increase in the number of cells in a tissue or organ, which may result in increased volume.

Types of Hyperplasia:

- **Physiological:**

- **Hormonal:** Breast tissue during puberty/pregnancy
- **Compensatory:** Liver regeneration after partial hepatectomy

- **Pathological:**
  - Due to excessive hormonal stimulation or growth factors
    - Example: Endometrial hyperplasia due to excess estrogen

Causes:

- Hormonal imbalance
- Chronic irritation or injury
- Viral infections (e.g., HPV)

Morphological Features:

- Increased number of cells
- Normal cellular architecture (in early stages)
- May progress to dysplasia or neoplasia if uncontrolled

4. Metaplasia

➢ Metaplasia is a reversible change in which one adult cell type is replaced by another adult cell type better suited to withstand the stress.

Most common example:

- Columnar to squamous epithelial metaplasia in the respiratory tract of smokers

Types:

- Epithelial metaplasia (most common)
- Mesenchymal metaplasia (e.g., cartilage in areas of injury)

Causes:

- Chronic irritation (e.g., smoking, acid reflux)
- Vitamin A deficiency
- Infections or inflammation

Morphological Features:

- Replacement of one differentiated cell type by another
- Change in tissue architecture
- May progress to dysplasia or carcinoma if stimulus persists

Example : Barrett's esophagus – squamous to columnar metaplasia due to acid reflux

5. Dysplasia

➢ Dysplasia is disordered growth and maturation of cells, characterized by changes in size, shape, and organization of mature cells.
It is often a precancerous condition.

Causes:

- Chronic irritation (e.g., cervical dysplasia from HPV infection)
- Prolonged metaplasia
- Genetic mutations

Features of Dysplastic Cells:

- Enlarged, irregular nuclei (hyperchromatic)
- Loss of uniformity (pleomorphism)
- Disordered arrangement
- Increased mitotic activity

Outcome:

- Mild dysplasia may be reversible if stimulus is removed
- Severe dysplasia may progress to carcinoma in situ

Example: Cervical dysplasia detected in Pap smear test

Cell Swelling

→ Cell swelling is simply defined as the accumulation of water inside the cell, leading to enlargement of the cell.

→ Cell swelling occurs mainly due to a disturbance in the function of the Na^+/K^+ pump in the cell membrane.

→ This pump normally removes sodium (Na^+) from the cell and brings in potassium (K^+), using ATP energy.

→ If this pump fails (due to lack of ATP), sodium accumulates inside, and water enters the cell, causing swelling.

Mechanism (Pathogenesis)

➢ Cell swelling results from ATP depletion, especially due to hypoxia or toxic injury, which leads to:

- Failure of Na^+/K^+ ATPase pump on the plasma membrane
- Sodium (Na^+) accumulates inside the cell
- Water follows sodium into the cell via osmosis
- Cell becomes swollen due to water overload
- Organelle swelling, especially mitochondria and endoplasmic reticulum

Causes of Cell Swelling

- High fever
- Burns
- Ischemia (reduced blood supply)
- Chemical agents (toxins, drugs)
- Bacterial or viral infection

Effects of Cell Swelling

- Cells become pale, swollen, and enlarged
- Cytoplasm appears vacuolated
- Affected organs (like liver, kidney) increase in weight and size
- Function of the organ may be mildly impaired

Intracellular Accumulations

- Intracellular accumulation refers to the build-up of abnormal amounts of various substances within cells, which may be harmless or harmful. These substances can accumulate transiently or permanently and may be produced inside the cell or come from outside (exogenous sources).

Sites of Accumulation

- Cytoplasm (e.g., lysosomes, endoplasmic reticulum)
- Nucleus

Types of Accumulated Substances

1. *Normal Cellular Substances (in excess)*

- **Lipids, proteins, carbohydrates, water**

2. *Abnormal Endogenous Substances*

- Misfolded proteins
- Products of abnormal metabolism

3. *Exogenous Substances*

- Pigments (e.g., carbon, tattoo ink)
- Minerals, infectious agents

Mechanisms Leading to Accumulation

- ❖ Abnormal metabolism – e.g., fatty liver due to defective lipid metabolism
- ❖ Defect in protein folding/transport – e.g., Alzheimer's
- ❖ Lack of enzyme – e.g., lysosomal storage diseases
- ❖ Ingestion of indigestible substances – e.g., carbon in lungs

Calcification

→ Calcification refers to the abnormal deposition of calcium salts in tissues. These deposits are mostly composed of calcium phosphate crystals and may be associated with cell injury, aging, or systemic disturbances in calcium metabolism.

Types of Pathologic Calcification

- There are two main types:

1. Dystrophic Calcification

- Dystrophic calcification is the deposition of calcium salts in dead or dying tissues, despite normal serum calcium levels.

Seen in:

- Areas of necrosis
- Damaged heart valves
- Atherosclerotic plaques
- Tuberculous lymph nodes
- Old scars

Mechanism:

- Tissue injury → cell membrane damage → influx of calcium
- Phosphate released from dead cells binds with calcium
- **Calcium phosphate crystals** form and accumulate

Significance:

- Indicates **prior cell injury**
- May lead to **organ dysfunction**, e.g., calcified heart valves

2. Metastatic Calcification

- Metastatic calcification is the deposition of calcium salts in normal, healthy tissues, due to elevated serum calcium levels (hypercalcemia).

Common Sites:

- Gastric mucosa
- Kidneys
- Lungs
- Arteries
- Pulmonary veins

Mechanism:

- High blood calcium levels → excess calcium diffuses into normal tissues
- Precipitates with phosphate ions → forms calcium salts

Significance:

- May impair normal function of vital organs (e.g., kidney → nephrocalcinosis)

Enzyme Leakage and Cell Death

→ Enzyme leakage refers to the release of intracellular enzymes into extracellular fluids (especially blood) due to cell membrane damage, particularly during cell injury or death.
→ Cell death is the irreversible loss of cell structure and function, leading to permanent cessation of life at the cellular level.
→ The lysosomes inside the cell are filled with highly destructive hydrolytic enzymes.
→ These enzymes are so powerful that they can instantly destroy the entire cell if released.
→ That's why they are safely enclosed within the lysosomal membranes under normal conditions.
→ A disturbance in the body's normal function, such as acid-base imbalance,
can damage the lysosomal membranes.
→ This causes the leakage of enzymes into the cytoplasm.
→ Once leaked, these enzymes begin to digest the cell from the inside.
→ This autodigestion eventually leads to cell death.

Acidosis and Alkalosis

Acidosis

→ Acidosis is a condition where blood pH drops below 7.35 due to excess acid or loss of base (bicarbonate).

Types of Acidosis:

Type	Cause	Examples
Respiratory Acidosis	CO_2 retention due to ↓ breathing (hypoventilation)	COPD, asthma, chest injury, drug overdose
Metabolic Acidosis	↑ Acid production or ↓ HCO_3^- (bicarbonate)	Diabetic ketoacidosis, renal failure, diarrhea

Symptoms of Acidosis:

- Headache, Confusion or drowsiness
- Shortness of breath (in metabolic)
- Fatigue, Irregular heartbeat
- Coma (in severe cases)

Alkalosis

→ Alkalosis is a condition where blood pH rises above 7.45 due to loss of acid or excess base (bicarbonate).

Types of Alkalosis:

Type	Cause	Examples
Respiratory Alkalosis	CO_2 loss due to ↑ breathing (hyperventilation)	Anxiety, high altitude, fever
Metabolic Alkalosis	↑ HCO_3^- or excessive loss of H^+	Vomiting, antacid overuse, diuretic use

Symptoms of Alkalosis:

- Dizziness, Muscle cramps or twitching
- Numbness or tingling (especially in hands and face)
- Confusion or agitation, Convulsions (in severe cases)

Electrolyte Imbalance

→ Electrolyte imbalance occurs when the levels of one or more electrolytes become too high (hyper-) or too low (hypo-), disrupting normal physiological functions.
→ The bloodstream contains many chemicals that are very essential for normal body functions.
→ Electrolytes are one of these important substances.
→ Examples of electrolytes include Calcium, Magnesium, Sodium, and Potassium.
→ A disturbance or imbalance in these electrolytes can cause a variety of health problems.

Common Types of Electrolyte Imbalances

✓ **Hyponatremia (↓ Sodium)**

- **Causes**: Diuretics, vomiting, diarrhea, excessive water intake
- **Symptoms**: Headache, confusion, muscle cramps, seizures

✓ **Hypernatremia (↑ Sodium)**

- **Causes**: Dehydration, diabetes insipidus
- **Symptoms**: Thirst, weakness, confusion, coma

✓ **Hypokalemia (↓ Potassium)**

- **Causes**: Diuretics, vomiting, diarrhea
- **Symptoms**: Muscle weakness, cramps, arrhythmia

✓ **Hyperkalemia (↑ Potassium)**

- **Causes**: Renal failure, cell lysis, potassium-sparing diuretics
- **Symptoms**: Palpitations, paralysis, cardiac arrest

✓ **Hypocalcemia (↓ Calcium)**

- **Causes**: Vitamin D deficiency, hypoparathyroidism
- **Symptoms**: Muscle spasms, tingling, seizures, tetany

✓ **Hypercalcemia (↑ Calcium)**

- **Causes**: Hyperparathyroidism, bone metastasis
- **Symptoms**: Nausea, vomiting, confusion, kidney stones

✓ **Hypomagnesemia (↓ Magnesium)**

- **Causes**: Malnutrition, alcoholism, diuretics
- **Symptoms**: Tremors, muscle spasms, arrhythmias

✓ **Hypermagnesemia (↑ Magnesium)**

- **Causes**: Renal failure, magnesium-containing medications
- **Symptoms**: Hypotension, weakness, respiratory depression