Pathophysiology

Pathology — the study of disease

Physiology — the normal functions of cells, organs, and organ systems

Pathophysiology — how diseases alter normal physiologic processes.

Chapter 3
Cell Responses to Challenges

Cells respond to challenges:
— Cellular Adaptations —
changes in normal cell division and/or morphology
Increasing infiltrates

Cellular Adaptations

5 types:
- Atrophy
- Hyper trophy
- Hyperplasia
- Atypical hyperplasia (dysplasia)
- Metaplasia

Atrophy—decrease in cell size

5 causes:
- Disuse
- Denervation
- Decreased hormonal stimulation
pituitary tumor -> decreased secretion of TSH -> atrophy of thyroid

- Malnutrition

- Decreased blood flow to the cell (ischemic)

Cells respond to these by:

- Cell decreases overall metabolic process, particularly protein synthesis

  \[ \downarrow \]

- Decreased O2 consumption by the cell

- ↑ in # of autophagic vacuoles (contain hydrolytic enzymes for digesting cell organelles)

- ↓ in # and size of organelles

These factors result in decrease in the size of the cell (atrophy)
Hypertrophy

increase in cell size

results from increased work demand or hormonal stimulation of the cell

most commonly observed in cells that are unable to undergo mitotic cell division.

Ex. Cardiac muscle
Skeletal muscle

Changes that occur:

- ↑ in metabolic processes particularly protein synthesis
- ↑ O2 consumption
- # of autophagic vacuoles
- ↑ # & size of organelles

These factors combine to cause an overall increase in cell size

Hyperplasia

An increase in the # of normal cells resulting from an increase in the rate of cell division.

Results from increased workload and/or increased hormonal stimulation.

Typically observed in tissues composed of cells able to undergo cell division.

Ex. Tissues composed of epithelial cells, like skin.
3 types:

Compensatory hyperplasia - increased cell division in response to tissue damage.

Ex.: Regeneration of the liver
- Callus formation on the skin.

Hormonal hyperplasia - increase in cell division in response to increased hormonal stimulation.

Ex. Hyperplasia of uterine lining due to increased estrogen levels during the menstrual cycle.
Pathologic hyperplasia - result of excessive hormonal stimulation of cells

Ex. Pituitary tumor causing increased synthesis and release of TSH → Hyperplasia of the thyroid gland (goiter)

Dysplasia - aka atypical hyperplasia - a proliferation of mature cells that are abnormal in size, shape, and organization.
occurs in response to chronic injury or irritation of tissues composed of cells able to undergo mitosis.

Thought to be precursor of

Neoplasia - cells that are abnormal in size, shape, and undergoing uncontrolled cell division

\[ \downarrow \]

Tumor formation

Metaplasia - the replacement of one mature cell type with another, less differentiated, cell type
occurs in response to chronic irritation or injury of tissue composed of cells able to undergo mitosis.

Common example seen in bronchi of smokers
Metaplasia
Chronic injury or irritation

Dysplasia
Persistent severe injury or irritation

Figure 3: Reversible changes in cells lining the bronchi.
Cellular Infiltrates

consist of increased amounts of
lipids
Carbohydrates
proteins
pigments (melanin or hemoproteins)
Calcium
Uric acid

Hepatocytes (liver cells) are
important in fat metabolism.

Chronic alcoholism damages hepatocytes
so they can't metabolize lipids, but
they still take up the lipids from
the blood. — "Fatty liver" characteristic
of chronic alcoholism is precursor of cirrhosis.
Cell injury can be result of:

- Mechanical damage: crushing, etc.

Radiation: exposure to excessive heat or ionizing radiation

- Chemical agents: ex. alcohol, acids etc.

- Hypoxia - lack of O2

- Free radicals - highly reactive molecules that can cause cell damage

Infectious agents - microbial infections

Immunologic reactions - Ex. Allergic reactions
Hypoxic injury of cells

A lack of sufficient O$_2$ for the cell to carry out normal metabolic functions.

Usually results from ischemic
Main events in hypoxic injury:

Within 1-3 min of hypoxia the cell shifts from aerobic metabolism to anaerobic metabolism.

- Build up of lactic acid in the cell

- Drastic reduction in ATP production

  - $\text{Na}^+/\text{K}^+$ and $\text{Na}^+/\text{Ca}^{2+}$ ATPase pumps in cell membrane begin to shut down

  - Disruption of normal concentration gradients for these ions is disrupted ($\text{Na}^+$ and $\text{Ca}^{2+}$ conc. inside cell increase)

    - Creates osmotic gradient that draws water into the cell
Cell death due to prolonged low pH of intracellular fluids:

- Denaturation of cell proteins
- Chromatin clumping
- Injury to lysosomal membranes
- Release of hydrolytic enzymes
- Cell death

ER swells causing ribosomes to drop off, disrupting protein synthesis.

- Cell membrane becomes permeable to enzymes and other proteins
- Loss of enzymes and proteins from the cell
- Water enters mitochondria, causing them to swell and damaging mitochondrial membranes, preventing return to aerobic metabolism.
Free Radicals

molecules that have an unpaired electron, making them highly reactive.

React with biomolecules in cells disrupting normal functions.

Three common types:
- superoxide (\(O_2^-\))
- hydroxyl radical (\(OH^*\))
- Nitric oxide (\(NO^*\))

Free radicals are created in two ways:
- absorption of high energy radiation or UV light
- Result of normal endogenous cell reactions

Some cells use free radicals to destroy invading microbes

Ex. Macrophages use superoxide + NO to kill engulfed bacteria

Oxidative stress results from build-up of free radicals in cells.

Cells usually protect themselves from oxidative stress by synthesizing antioxidants—enzymes that convert free radicals into less reactive molecules.
ex. superoxide dismutase (SOD)

\[ \text{O}_2 \xrightarrow{\text{SOD}} \text{H}_2 \text{O}_2 + \text{O}_2 \]

catalase converts \( \text{H}_2 \text{O}_2 \rightarrow \text{H}_2 \text{O} + \text{O}_2 \)

Vitamin C + Vitamin E are believed to have antioxidant properties.

**Cell Death**

Two types:

- **Necrosis** — death of a cell due to injury
- **Apoptosis** — programmed cell death, activation of a “suicide program” in the cell
resulting in release of enzymes within the cell.

Cell breaks up into small membrane bound packages. These packages are then phagocytosed by phagocytes and digested.

In necrosis enzymes are released into the extracellular fluids when the cell ruptures. These enzymes will damage surrounding cells and can potentially cause the death of these cells.
Four types of necrosis:

- Coagulative necrosis - results from hypoxia and is most common in tissues with cells that have an abundance of hydrolytic enzymes. Ex muscle cells rupture releasing these enzymes + lactic acid

This denatures proteins that are also released as the cell ruptures. The proteins coagulate giving the tissue a whitish color