Course :Human Pathology

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Overview of cell injury

- Cells actively control the composition of their immediate environment and intracellular milieu within a narrow range of physiological parameters ("homeostasis")
  Under physiological stresses or pathological stimuli ("injury"), cells can undergo adaptation to achieve a new steady state that would be compatible with their viability in the new environment.

- If the injury is too severe ("irreversible injury"), the affected cells die.

Cellular reaction to injury

The cell's reaction to a injury are divided into the following types :

- Adaptation to environmental stress
- Hypoxic cell injury
- Free radical injury
- Necrosis and
- Apoptosis.

Adaptation to environmental Stress

- **Hypertrophy**

1. Hypertrophy is an **increase in the size of an organ or tissue due to an increase in the size of cells.**

2. Other characteristics include an increase in protein synthesis and an increase in the size or number of intracellular organelles.

3. A cellular adaptation to increased workload results in hypertrophy, as exemplified by the increase in skeletal muscle mass associated with exercise.

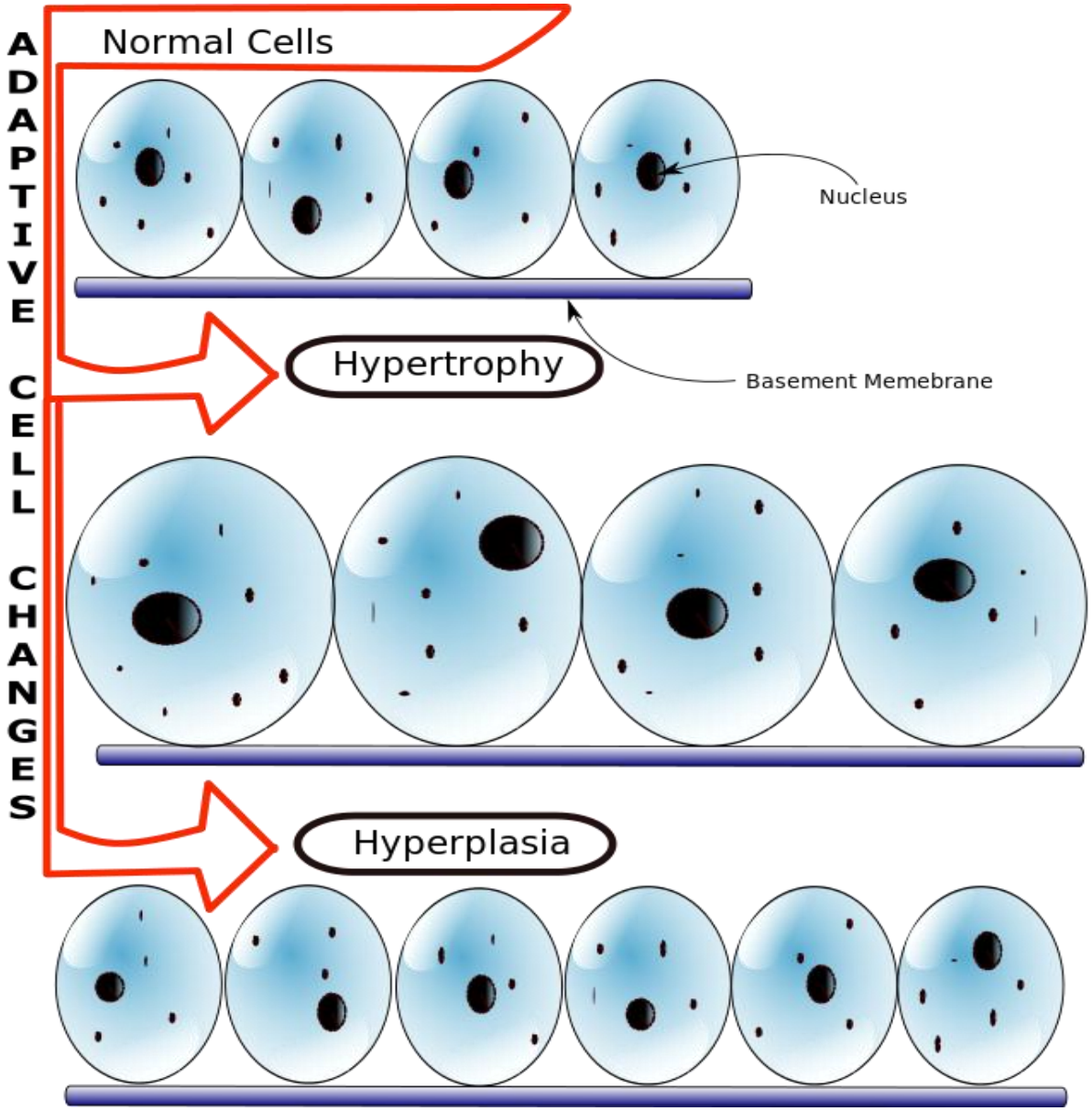
Adaptation to environmental Stress

- **B. Hyperplasia**

1. Hyperplasia is an **increase in the size of an organ or tissue caused by an increase in the number of cells.**

2. It is exemplified by glandular proliferation in the breast during pregnancy.

3. In some cases, hyperplasia occurs together with hypertrophy. During pregnancy, uterine enlargement is caused by both hypertrophy and hyperplasia of the smooth muscle cells in the uterus.


ADAPTIVE CELL CHANGES
Normal Cells
Nucleus
Basement Memebrane
Hypertrophy
Hyperplasia

Adaptation to environmental Stress

- **C. Aplasia**

1. Aplasia is a **failure of cell production**.

2. During fetal development, aplasia results in **agenesis**, or absence of an organ due to failure of production.

Adaptation to environmental Stress

- **E. Atrophy**

1. Atrophy is a **decrease in the size of an organ or tissue and results from a decrease in the mass of pre-existing cells** .

2. Most often, causal factors are disuse, nutritional or oxygen deprivation, diminished endocrine stimulation, aging, and denervation (lack of nerve stimulation in peripheral muscles caused by injury to motor nerves).

Hypoxic cell injury

- **A. Causes.** Hypoxic cell injury results from cellular **anoxia** or **hypoxia**, which in turn results from various mechanisms, including:

1. Ischemia (obstruction of arterial blood flow), which is the most common cause

2. Anaemia, which is a reduction in the number of oxygen-carrying red blood cells

3. Carbon monoxide poisoning, which results in diminution in the oxygen-carrying capacity of red blood cells by chemical alteration of haemoglobin

4. Decreased perfusion of tissues by oxygen-carrying blood, which occurs in cardiac failure, hypotension, and shock.

Stages of hypoxic cell injury

Early stage

Hypoxic cell injury first affects the mitochondria, with resultant decreased oxidative phosphorylation and adenosine triphosphate (ATP) synthesis

Late stage

Hypoxic cell injury eventually results in **membrane damage** to plasma and to lysosomal and other organelle membranes, with loss of membrane phospholipids

Cell death

- Finally, **cell death** is caused by severe or prolonged injury.

1. The **point of no return** is marked by **irreversible damage to cell membranes**, leading to **massive calcium influx, extensive calcification of the mitochondria**, and cell death.

2. Intracellular enzymes and various other proteins are released from necrotic cells into the circulation as a consequence of the loss of integrity of cell membranes.

Free radical injury

- **A. Free radicals**

1. These molecules have a single unpaired electron in the outer orbital.

2. Examples include the activated products of oxygen reduction, such as the superoxide($O_2^{-\bullet}$) and the hydroxyl ($OH^{\bullet}$) radicals.

Mechanisms causing free radicals

1. Normal metabolism

2. Oxygen toxicity, such as in the alveolar damage that can cause adult respiratory distress syndrome .

3. Ionizing radiation

4. Ultraviolet light

5. Drugs and chemicals

Mechanisms that degrade free radicals

1. Intracellular enzymes, such as glutathione peroxidase, catalase, and superoxide dismutase

2. Exogenous and endogenous antioxidants, such as vitamin A, vitamin C, vitamin E, cysteine,glutathione, selenium, ceruloplasmin, and transferrin

3. Spontaneous decay.

Necrosis

- Necrosis is a form of cell injury that results in the premature death of cells in living tissue.
- Necrosis is caused by factors external to the cell or tissue, such as infection, toxins, or trauma that result in the unregulated digestion of cell components.
- **Necrosis** is the sum of the degradative and inflammatory reactions occurring after tissue death caused by injury (e.g., hypoxia and exposure to toxic chemicals); it **occurs within living organisms**.

Apoptosis

- Apoptosis is an important mechanism for the removal of cells. An example is apoptotic removal of cells with irreparable DNA damage (from free radicals, viruses, and cytotoxic immune mechanisms), protecting against neoplastic transformation.
- In addition, apoptosis is an important mechanism for physiologic cell removal during development and in programmed cell cycling (e.g., the formation of digits during embryogenesis and the loss of endometrial cells during menstruation).

Comparison of Necrosis and Apoptosis- morphology

Necrosis

- Involves many contiguous cells
- Increased cytoplasmic eosinophilia due to denaturation of proteins
- Progressive nuclear condensation and fragmentation with eventual disappearance of nuclei

Apoptosis

- Involves single cells or small clusters of cells
- Cytoplasmic shrinking and increased eosinophilic staining
- Chromatin condensation and fragmentation

Comparison of Necrosis and Apoptosis-biochemical changes

Necrosis

- Passive form of cell death not requiring gene involvement or new protein synthesis
- DNA fragmentation is haphazard rather than regular, resulting in an electrophoretic smudge pattern

Apoptosis

- Active form of cell death requiring gene expression, protein synthesis, and energy consumption
- DNA fragmentation is regular at nucleosomal boundaries, resulting in an electrophoretic “laddered” pattern

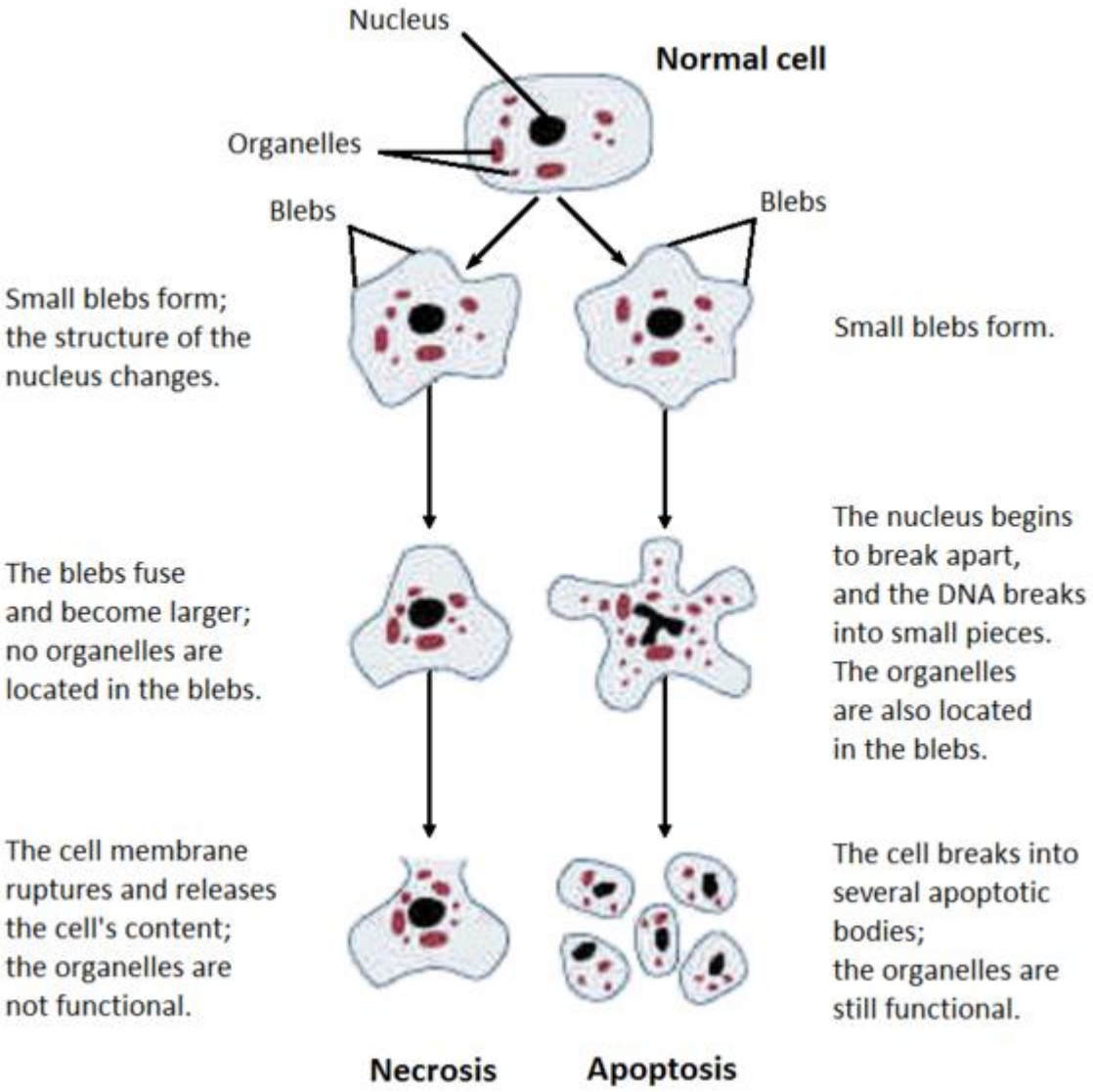
Comparison of Necrosis and Apoptosis- Inflammation.

Necrosis

- Marked inflammatory reaction, liberation of lysosomal enzymes, digestion of cell membranes, and disruption of cells
- Influx of macrophages due to release of chemotactic factors
- Removal of debris by phagocytic macrophages

Apoptosis

- No inflammatory reaction
- Apoptotic bodies engulfed by neighbouring macrophages and epithelial cells


Nucleus
Normal cell
Organelles
Blebs
Blebs
Small blebs form;
the structure of the
nucleus changes.
Small blebs form.
The blebs fuse
and become larger;
no organelles are
located in the blebs.
The nucleus begins
to break apart,
and the DNA breaks
into small pieces.
The organelles
are also located
in the blebs.
The cell membrane
ruptures and releases
the cell's content;
the organelles are
not functional.
The cell breaks into
several apoptotic
bodies;
the organelles are
still functional.
Necrosis
Apoptosis