Cellular Adaptations to Injury

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Cells must constantly adapt, even under normal conditions, to changes in their environment.

How cells adopt certain adaptive mechanisms to survive and carry out the cellular functions against severe physiologic and pathologic stresses.

Adaptations- reversible changes in the number, size, phenotype, metabolic activity, or functions of cells in response to changes in their environment.
Physiologic adaptations represent responses of cells to normal stimulation by hormones or endogenous chemical mediators (e.g., the hormone-induced enlargement of the breast and uterus during pregnancy).

Pathologic adaptations responses to stress that allow cells to modulate their structure and function and thus escape injury. Such adaptations can take several distinct forms.
Cellular adaptation - a state that lies intermediate between the normal, unstressed cell and the injured, overstressed cell.
There are numerous types of cellular adaptations:

1. Associated with up or down regulation of specific cellular receptors involved in metabolism of certain components.
2. Associated with the induction of new protein synthesis by the target cell.
3. Associated with a switch by cells from producing one type of a family of proteins to another or markedly overproducing one protein.
These adaptations then involve all steps of cellular metabolism of proteins—receptor binding, signal transduction, transcription, translation, or regulation of protein packaging and release.
1. Hyperplasia

(1) **Definition:** An increase in the number of cells in an organ or tissue, which may then have increased volume.

- Hyperplasia takes place if the cell population is capable of dividing, and thus increasing the number of cells.

(2) **Types:**

- **Physiologic:** Response to need, e.g. hyperplasia of the female breast epithelium at puberty or in pregnancy.
Left Normal breast   Right Hyperplasia

（From ROBBINS BASIC PATHOLOGY, 2003）
Compensatory: Response to deficiency, e.g. Hyperplasia following surgical removal of part of liver or of one kidney; hyperplasia of the bone marrow in anemia.

Excessive stimulation: Pathologic: as in ovarian tumor producing estrogen and stimulating endometrial hyperplasia; pancreatic islet hyperplasia in infants of a diabetic mother (stimulated by high glucose level).
• Hyperplasia is the result of growth factor–driven proliferation of mature cells and, in some cases, by increased output of new cells from tissue stem cells.

• Types of Physiologic hyperplasia
  (1) hormonal hyperplasia-increases the functional capacity of a tissue when needed
  (2) compensatory hyperplasia, which increases tissue mass after damage or partial resection.
Hormonal influences- important cause of physiologic hyperplasia.

Examples: hyperplasia of endometrial cells and stroma by estrogen stimulation in the early menstrual cycle. This also can be seen when exogenous estrogens are given in menopause.
• **Failure of regulation:** Pathologic, as in hyperthyroidism or as in hyperparathyroidism resulting from renal failure or vitamin D deficiency.

• **Neoplastic:** Total loss of normal control mechanism. Should not be termed hyperplasia.

• **Hyperplasia** is also an important response of connective tissue cells in wound healing, in which proliferating fibroblasts and blood vessels aid in repair.
Mechanisms:

excessive hormonal stimulation or the effects of growth factors on target cells.
2. Hypertrophy:

(1) **Definition:** An increase in the size of cells, and with such change, an increase in the size of the organ accompanied by an increase in functional capacity.

- The organ size is increased due to the synthesis of more structural components of the cells.
- No new cells but only larger cells.
- A normal process
- Occurs as a response to trophic signals (promoting cellular growth, differentiation, and survival) and increase in functional demands.
• Hypertrophy occurs in non dividing cells i.e. myocardial fibers.
• Occurs in permanent cells
• Due to synthesis of more cellular structural components
• Changes in a hypertrophied cell are
  – Increased synthesis of more structural components; basically proteins
  – Higher DNA content of nucleus

• 2 types of hypertrophy can occur
Left Normal heart
Right Hypertrophied heart
Hypertrophied heart

(From ROBBINS BASIC PATHOLOGY, 2003)
(2) **Types:**

- **Physiologic:** occurs due to normal hormone signals
- Ex. the physiologic growth of the uterus during pregnancy involves both hypertrophy and hyperplasia. The cellular hypertrophy is stimulated by estrogenic hormones through smooth muscle estrogen receptors.
Pathologic: causes:
- increased workload, hormonal stimulation and growth factors stimulation.

i.e. hypertrophy of heart the most common stimulus is chronic hemodynamic overload, due either to hypertension or to faulty valves. It eventually reaches a limit beyond which enlargement of muscle mass is no longer able to compensate for the increased burden, and cardiac failure ensues.
The relationship between hyperplasia and hypertrophy:

Although hypertrophy and hyperplasia are two distinct processes, frequently both occur together, and they well be triggered by the same mechanism.
3. Atrophy

(1) **Definition:** Acquired loss of size due to reduction of cell size or number of parenchyma cells in an organ.

(2) **Types:**

- Physiologic: i. e. Aging; shrinking mammary gland after lactation; the uterus after delivery or in old age.
Atrophy

- Adaptive response of the cell to certain situations where the cell shuts down its differentiated functions, reduces its size and minimizing its energy needs.
- Results from decreased protein synthesis and increased protein degradation in cells.
- Protein synthesis decreases because of reduced metabolic activity.
- Physiologic atrophy is common during normal development.
- Example the uterus decreases in size shortly after parturition, and this is a form of physiologic atrophy.
- Pathologic atrophy depends on the underlying cause and can be local or generalized. The common causes of atrophy are the following.
The fundamental cellular change is identical in all, representing a retreat by the cell to a smaller size at which survival is still possible.

Although atrophic cells may have diminished function, they are not dead.

Atrophy represents a reduction in the structural components of the cell.

The cell contains fewer mitochondria, myofilaments, a lesser amount of endoplasmic reticulum, and increasing in the number of autophagy vacuoles.
Some of the cell debris within the autophagosome vacuole may resist digestion and persist as membrane bound residual bodies that may remain as a sarcophagus in the cytoplasm.

When present in sufficient amounts, they impart a brown discoloration to the tissue (brown atrophy).
Causes of atrophy

1. Due to reduced functional demand
   • This is the most common cause of atrophy.
   • After a long time of disuse of muscles ie in prolonged bed rest, or a limb in a plaster cast after fracture the muscles can atrophy- disuse atrophy.

2. Inadequate supply of oxygen
   • Ischemia - reduction of oxygen to tissues.
   • Total ischemia- the oxygen supply is totally cut off the cells undergo reversible cell injury and death
   • However if there is prolonged ischemia over a long period of time the cell may be still viable but undergo atrophy. Examples are ischemic injury to brain and kidney.
3. Lack of nutrition
   - In chronic illness or situations of chronic starvation the body and muscle mass may reduce in a drastic manner.
   - This is because in contrast to vital organs the muscle mass is expendable and not vital for survival.

4. Interruption of trophic signals
   - Trophic signals - chemical transmitters and hormones that control cell function.
   - Short supply of trophic signals reduce signals to the cells or stopped
• Results in a loss of function primarily leading to loss of cell size or atrophy.
• Examples are deficiency of ACTH, TSH and FSH results in atrophy of the adrenal glands, thyroid and the ovary. Atrophy of the endometrium in response to estrogen lack in menopause is an example of physiologic atrophy.

5. Persistence of cell injury
• Commonly caused by chronic inflammation by bacteria or viral infections, immunologic and granulomatous disorders. Examples are atrophy of the thyroid gland in autoimmune thyroiditis.
Left Normal
Right Atrophy
4. Metaplasia

(1) **Definition:** Metaplasia is a reversible change in which one adult cell type is replaced by another adult cell type. Metaplasia is replacement of one specialized cell type by another. Usually occurs in epithelial tissue.

(2) **Causes:**

- Changes in environment: i.e. stones in excretory ducts of salivary gland, pancreas, or bile duct lead to change from columnar epithelium to stratified squamous epithelium.
Squamous metaplasia in bronchitis

(offerred by Prof. Orr)
Schematic diagram of columnar to squamous metaplasia

(From ROBBINS BASIC PATHOLOGY, 2003)
• **Irritation or inflammation:** i.e. In the habitual cigarettes smoker, the normal columnar ciliated epithelial cells of the trachea and bronchi are often replaced focally or widely by stratified squamous epithelial cells.

• **Nutritional:** vitamin A deficiency causing squamous metaplasia.
Thank you!!!