Cellular Adaptation

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Introduction to Pathology

- Pathos means suffering and logos means study. Literally, Pathology is the study of suffering.
- Pathology is the bridging discipline between basic science and clinical practice.
- Pathology deals with the structural and functional changes in the cells, tissues and organs that underlie diseases.
- Pathology attempts to explain the "whys" and "wherefore" of the signs and symptoms manifested by the patients by the use of molecular, microbiologic, immunologic and morphologic techniques.

Branches of Pathology

Traditionally, the study of pathology is divided into

- General pathology and
- Systemic pathology

General Pathology

General pathology is concerned with basic reactions of cells and tissue to abnormal stimuli that underlie all diseases.

Systemic Pathology

Systemic pathology or special pathology deals with the specific responses of specialised organs and tissue to more or less well defined stimuli.

Aspects of disease process that forms the core of Pathology

- Etiology (cause)
- Pathogenesis (mechanisms of development of disease)
- Morphologic changes (the structural alteration)
- Clinical significance (functional consequences of the morphologic changes)

Normal homeostasis

- Normal cell is confined to a fairly narrow range of function and structure by its genetic programs of metabolism, differentiation and specialisation, by constraints of neighbouring cells, and by the availability of metabolic substrates. It is able to handle normal physiologic demands which is called normal homeostasis.

Cellular Adaptation

- Cellular adaptation is a state that lies intermediate between the normal, unstressed cell and the injured, over-stressed cells.
- Cells must constantly adapt, even under normal conditions, to changes in their environment. Somewhat more excessive physiologic stress or some pathologic stimuli can bring about a number of physiologic and morphologic changes in which a new but altered steady state is achieved, preserving the viability of the cells is called cellular adaptation.

Cell Injury

- If the limit of adaptive response to a stimulus is exceeded, or in certain instances when adaptation is not possible, a sequence of events follows, termed as cell injury
- Cell injury is reversible up to a certain point but if the stimulus persists or severe enough from the beginning, the cell reaches the point of no return and suffers irreversible cell injury and cell death. Cell death is the ultimate result of cell injury.
- Reversible cell injury, irreversible cell injury, necrosis and apoptosis are morphologic patterns of acute cell injury. There are other patterns of morphologic alteration, such as subcellular alteration, which occur largely as a response to more chronic or persistent injurious stimuli; intracellular accumulation, which occur as a result of derangement in the metabolism or excessive storage; pathologic calcification, a common consequences of cell and tissue injury.

Cellular responses to injurious stimuli

- Cellular Adaptation
  - Atrophy
  - Hypertrophy
  - Hyperplasia
  - Metaplasia
- Acute cell injury
  - Reversible cell injury
    - Cellular swelling
    - Fatty change
  - Cell death
    - Necrosis
    - Apoptosis

- Intracellular accumulation
- Pathologic calcification.
- Sub-cellular Alteration and cell inclusions

Types of Cellular Adaptation

- **Physiologic Adaptation**
  - Usually represents responses of the cells to normal stimulation by hormones or endogenous chemical substances, e.g. enlargement of breast and induction of lactation by pregnancy.
- **Pathologic Adaptation**
  - May share the same underlying mechanism, but they provide the cells with ability to survive in their environment and perhaps escape injury.

General Mechanism of Cellular Adaptation

- Up- or down-regulation of specific cellular receptors involved in metabolism of certain components, e.g. in the regulation of cell surface receptors involved in the uptake and degradation of low-density lipoproteins (LDL).
- Induction of new protein synthesis by the target cells, e.g. heat-shock response.
- Production of one type a family of proteins to another or markedly overproducing one protein e.g. cells producing various types of collagens and ECM proteins in chronic inflammation and fibrosis.

Adaptation involves all steps of cellular metabolism of proteins – receptor binding, signal transduction, transcription or regulation of protein packaging and release.

Morphological Types of Cellular Adaptation

There are numerous types of cellular adaptation but 4 are common:

- Atrophy
- Hypertrophy
- Hyperplasia
- Metaplasia

Hyperplasia

- Hyperplasia is one type of cellular adaptation in which there is an increase in number of cells in an organ or tissue, which may cause increased volume.
- Hyperplasia takes place if the cellular population is capable of synthesising DNA, permitting mitotic division.

Types of Hyperplasia

- Physiologic Hyperplasia
  - Hormonal Hyperplasia
  - Compensatory Hyperplasia
- Pathologic Hyperplasia

Hormonal Physiologic Hyperplasia

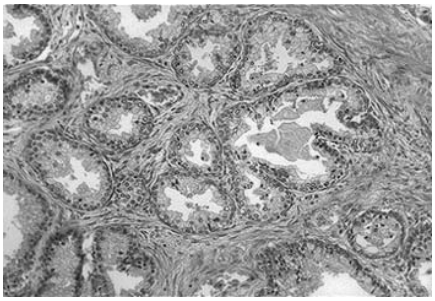
- It occurs due to hormonal stimulation in response to physiologic demands,
  - e.g. proliferation of glandular epithelium of the female breast at puberty and during pregnancy, and hyperplasia of pregnant uterus.

Compensatory Physiologic Hyperplasia

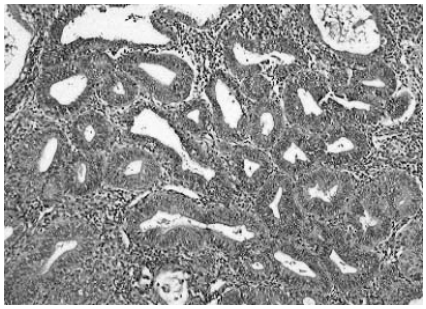
- It occurs when a part of an organ is removed,
  - e.g. hyperplasia that occurs when a portion of liver is removed.

Pathologic Hyperplasia

- Most forms of pathologic hyperplasia are instances of excessive hormonal stimulation or are effects of growth factors on target cells,
  - e.g. hyperplasia of endometrium, hyperplasia of prostate, hyperplasia of connective tissue cells in wound healing, skin warts.



Hyperplasia of Prostate



Hyperplasia of Endometrium

Hypertrophy

- Hypertrophy is one type of adaptive response in which there is increase in size of cells resulting from synthesis of more structural components in response to increased functional demand or by specific hormonal stimulation.

Types of hypertrophy

- Physiologic hypertrophy
- Pathologic hypertrophy

Examples

- **Physiologic hypertrophy**
  - Hypertrophy of myometrium during pregnancy stimulated by oestrogen
  - Hypertrophy of skeletal muscle of muscle-builders induced by workload.
- **Pathologic hypertrophy**
  - Hypertrophy of cardiac muscle induced by increased workload in hypertension or chronic haemodynamic overload

Atrophy

- Atrophy is an adaptive response in which there is shrinkage in the size of the cells by loss of cell substances.
- When a sufficient number of cells are involved, the entire tissue or organ diminishes in size or become atrophic

Causes of Atrophy

- Decreased work load
- Loss of innervations
- Diminished blood supply
- Inadequate nutrition
- Loss of endocrine stimulation
- Aging

Examples of Atrophy

- When a limb is immobilised in plaster cast or when muscle become paralysed from loss of innervations, as in poliomyelitis, atrophy of the muscle occur.
- In late adult life, the brain undergoes progressive atrophy, presumably due to atherosclerosis narrows its blood supply and the sex glands shrink with depletion of endocrine stimulation.

Types of Atrophy

- **Physiologic atrophy**
  - loss of endocrine stimulation following menopause.
- **Pathologic atrophy**
  - Loss of nerve.

Mechanism of Atrophy

- Atrophy represents a reduction in structural components of cells.
- The cell contains fewer mitochondria and microfilaments and lesser amount of endoplasmic reticulum.
- There is finely regulated balance between protein synthesis and degradation in normal cells. Either decreased synthesis or increased catabolism or both may cause atrophy.

- Slight increase of degradation over a long period of time may result in atrophy.
- Intracellular non-lysosomal proteinases play a role in such protein degradation.
- Atrophy also accompanied by marked increases in number of autophagic vacuoles within the cells that contain fragments of cell components (e.g. mitochondria, endoplasmic reticulum), which are destined for destruction, into which the lysosome discharge their hydrolytic contents. The cellular components are then digested.

Metaplasia

- Metaplasia is one type of adaptive response in which one adult cell type (epithelial or mesenchymal) is replaced by another cell type. It represents an adaptive substitution of cells more sensitive to stress by cell types better able to withstand the adverse environment.

Examples of Metaplasia

Epithelial Metaplasia

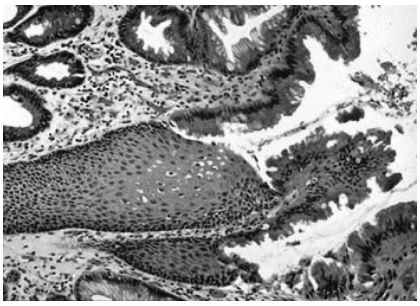
- **Columnar to Squamous Metaplasia:**
  - **Occurs in respiratory tract in response to irritation. In habitual cigarette smoker, the normal columnar ciliated epithelial cells of the trachea and bronchi are often replaced focally or widely by stratified squamous epithelial cells.**

- Stone in the excretory duct of the salivary glands, pancreas or bile ducts may cause replacement of normal columnar epithelium by non-functioning stratified squamous epithelial cells.
- Deficiency of vitamin A induces squamous metaplasia in the respiratory epithelium.
- Squamous metaplasia of endocervical epithelium in response to chronic inflammation.

- *In all instances, the more rugged stratified squamous epithelium is able to survive under circumstances in which more fragile specialised epithelium most likely would have succumbed.*
- *The influences that predispose to such metaplasia, if present, may induce cancer transformation in metaplastic epithelium. Thus common form of cancer in respiratory tract is composed of squamous cells.*

Squamous to columnar cell metaplasia:

- **Barrett's oesophagus**, in which the squamous oesophageal epithelium is replaced by gastric columnar cells. The resulting cancers that may arise are glandular (adeno) carcinoma.



Barrett's esophagus

Mesenchymal Metaplasia

- Fibrous connective tissue cells may become transformed to osteoblasts or chondroblasts to produce bone or cartilage where it is normally not encountered. This occurs particularly in foci of injury but occasionally with no cause.

Pathogenesis of Metaplasia

- Metaplasia is thought to arise from genetic reprogramming of stem cells that are known to exist in most epithelium or of undifferentiated mesenchymal cells, present in connective tissue. Chemical, vitamins or growth factors most likely play a role in such metaplasia.