Cellular Adaptations and Accumulations

- Adaptations: Reversible changes in cells responding to environmental changes
  - Can be physiologic (normal stimulation) or pathologic (stress response)

Types of Adaptations

Hypertrophy | Hyperplasia | Atrophy | Metaplasia

- Occurs in cells with limited division capacity
- Can be physiologic (e.g., uterus during pregnancy/ hypertrophy. Adult muscle cells) or pathologic (e.g., cardiac hypertrophy)

Cardiac Hypertrophy Mechanisms

- Two types of signals drive cardiac hypertrophy [1]:
  1. Mechanical triggers (e.g., stretch)
  2. Soluble mediators (growth factors & adrenergic hormones)

- Signal Transduction Process [1]:
  - Stimuli → Signal transduction pathways → Gene induction → Protein synthesis

- Cellular Changes [2]:
  - Increased protein and myofilament synthesis
  - Enhanced force generation per contraction
  - Adaptation to increased work demands

- Protein Modifications [2]:
  - Switch from adult to fetal/neonatal contractile proteins
  - Replacement of α-myosin heavy chain with β-myosin heavy chain
  - Results in slower, more energy-efficient contractions

An adaptation to stress such as hypertrophy can progress to functionally significant cell injury if the stress is not relieved

Increase in cell number
- Occurs in cells capable of replication
- Types: Hormonal (e.g., breast tissue growth) and Compensatory (e.g., liver regeneration)

Pathologic hyperplasia

• Caused by excessive hormonal or growth factor stimulation.
Normally, after a normal menstrual period.
disturbance in this balance
increased estrogenic stimulation
→ endometrial hyperplasia, (a common cause of abnormal menstrual bleeding).
→ Benign prostatic hyperplasia is by androgens
→ Certain viral infections

The hyperplastic process remains controlled

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Types of Adaptations

Hypertrophy | Hyperplasia | Atrophy | Metaplasia

Shrinkage of cell size
- Causes: decreased workload, loss of innervation, diminished blood supply, etc.
- Results from decreased protein synthesis and increased degradation

→ In many situations, atrophy also is associated with autophagy

Replacement of one adult cell type with another
- Occurs as a protective mechanism against stress
- Examples: Respiratory epithelium changes in smokers, esophageal changes in chronic reflux

→ The influences that induce metaplastic change in an epithelium, if persistent, may predispose to malignant transformation.

Intracellular Accumulations

- Cells may accumulate abnormal amounts of substances, which can be harmless or cause injury
- Main pathways of abnormal intracellular accumulations:
  - Inadequate removal and degradation
  - Excessive production of endogenous substances
  - Deposition of abnormal exogenous materials

Types of Accumulations

Fatty Change (Steatosis)

- Accumulation of triglycerides in parenchymal cells
- Common in liver, also occurs in heart, skeletal muscle, and kidney
- Caused by toxins, protein malnutrition, diabetes, obesity, or anoxia

Glycogen

- Excessive accumulation associated with abnormal glucose or glycogen metabolism
- Occurs in poorly controlled diabetes and glycogen storage diseases

Lipofuscin

- Insoluble brownish-yellow granular material
- Accumulates with aging or atrophy in various tissues
- Marker of past free radical injury

Cholesterol and Cholesteryl Esters

- Tightly regulated in cellular metabolism
- Can accumulate in phagocytic cells due to increased intake or decreased catabolism
- Important in atherosclerosis

Carbon

- Exogenous pigment common in urban environments
- Inhaled and phagocytosed by alveolar macrophages
- Causes anthracosis in lungs and lymph nodes

Melanin

- Endogenous brown-black pigment synthesized by melanocytes
- Protects against UV radiation

Hemosiderin

- Hemoglobin-derived golden yellow to brown pigment
- Accumulates with excess iron
- the iron can be unambiguously identified by the Prussian blue histochemical reaction
- Can lead to hemosiderosis or hemochromatosis