Adaptations
FIG. 1.6 Basic subcellular constituents of cells. The table provides the relative volumes of intracellular organelles (hepatocyte) and their roles in the cell.
**FIG. 1.7** Plasma membrane organization and asymmetry. (A) The plasma membran...
FIG. 1.9  Cytoskeletal elements and cell–cell interactions. Interepithelial adhesion in...
Coagulation
Homeostasis

- Maintenance of a steady state

Diagram:

- NORMAL CELL (homeostasis)
  - Stress
  - Injurious stimulus
- REVERSIBLE INJURY
  - Mild, transient
- ADAPTATION
  - Inability to adapt
- CELL INJURY
  - Severe, progressive
- IRREVERSIBLE INJURY
  - NECROSIS
  - CELL DEATH
  - APOPTOSIS
Adaptations

• Reversible functional and structural responses to physiologic stress and some pathogenic stimuli
• New altered “steady state” is achieved
Adaptive responses

- **Hypertrophy**
  - *hyper* = above, more
  - *trophe* = nourishment, food

- **Hyperplasia**
  - *plastein* = (v.) to form, to shape; (n.) growth, development

- **Dysplasia**
  - *dys* = bad or disordered

- **Metaplasia**
  - *meta* = change or beyond

- **Hypoplasia**
  - *hypo* = below, less

- **Atrophy, Aplasia, Agenesis**
  - *a* = without
  - nourishment, form, beginning

- **Altered demand (muscle activity)**
- **Altered stimulation**
  (growth factors, hormones)
- **Altered nutrition**
  (including gas exchange)
TABLE 1-1  -- Cellular Responses to Injury

<table>
<thead>
<tr>
<th>Nature of Injurious Stimulus</th>
<th>Cellular Response</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALTERED PHYSIOLOGICAL STIMULI; SOME NONLETHAL INJURIOUS STIMULICELLULAR ADAPTATIONS</strong></td>
<td></td>
</tr>
<tr>
<td>• Increased demand, increased stimulation (e.g., by growth factors, hormones)</td>
<td>• Hyperplasia, hypertrophy</td>
</tr>
<tr>
<td>• Decreased nutrients, decreased stimulation</td>
<td>• Atrophy</td>
</tr>
<tr>
<td>• Chronic irritation (physical or chemical)</td>
<td>• Metaplasia</td>
</tr>
<tr>
<td><strong>REDUCED OXYGEN SUPPLY; CHEMICAL INJURY; MICROBIAL INFECTION</strong></td>
<td></td>
</tr>
<tr>
<td>• Acute and transient</td>
<td>• Acute reversible injury</td>
</tr>
<tr>
<td>• Progressive and severe (including DNA damage)</td>
<td>• Cellular swelling fatty change</td>
</tr>
<tr>
<td><strong>METABOLIC ALTERATIONS, GENETIC OR ACQUIRED; CHRONIC INJURY</strong></td>
<td>• Irreversible injury → cell death</td>
</tr>
<tr>
<td><strong>CUMULATIVE SUBLETHAL INJURY OVER LONG LIFE SPAN</strong></td>
<td>• Necrosis</td>
</tr>
<tr>
<td><strong>INTRACELLULAR ACCUMULATIONS; CALCIFICATION</strong></td>
<td>• Apoptosis</td>
</tr>
<tr>
<td><strong>CELLULAR AGING</strong></td>
<td></td>
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</tbody>
</table>
Cell death, the end result of progressive cell injury, is one of the most crucial events in the evolution of disease in any tissue or organ. It results from diverse causes, including ischemia (reduced blood flow), infection, and toxins. Cell death is also a normal and essential process in embryogenesis, the development of organs, and the maintenance of homeostasis.

Two principal pathways of cell death, necrosis and apoptosis.

Nutrient deprivation triggers an adaptive cellular response called autophagy that may also culminate in cell death.
Adaptations

- Hypertrophy
- Hyperplasia
- Atrophy
- Metaplasia
Hypertrophy refers to an increase in the size of cells, resulting in an increase in the size of the organ.

No new cells, just larger cells. The increased size of the cells is due to the synthesis of more structural components of the cells usually proteins.

Cells capable of division may respond to stress by undergoing both hypertrophy and hyperplasia.

Non-dividing cell increased tissue mass is due to hypertrophy.
Physiological hypertrophy—normal?


http://jcsm.info/documents/0311/The%20role%20of%20myostatin%20in%20muscle%20wasting-Dateien/13539_2011_35_Fig2_HTML.gif
Exercise hypertrophy

Microscopic views of muscle hypertrophy. Enlarged type 2 (fast twitch) fibers stain dark with ATPase at pH 9.4. Enlarged fast twitch fibers stain pale with cytochrome c oxidase. Hypertrophied fibers with less sarcoplasmic reticulum relative to fiber proteins stain paler with the trichrome stain.

http://neuromuscular.wustl.edu/pathol/hypertrophy.htm
Hypertrophy resulting from pathological injury (hypertension)
Circulation as a Circuit
Cardiac Muscle Hypertrophy

http://static.wikidoc.org/a/a8/Comparison_of_hypertrophy_and_normal_myocardial_micro_2.JPG
Physiologic adaptation vs. pathology

- Normal myocyte
- Adaptation: response to increased load
- Adapted myocyte (hypertrophy)
- Cell injury
- Reversibly injured myocyte
- Cell death
Scarred necrosis
Physiological hypertrophy—normal

Estrogen acting on smooth muscle during pregnancy
Microscopic physiological hypertrophy
Mechanisms of muscle hypertrophy

- Increased protein synthesis $\rightarrow$ increased cell size $\rightarrow$ increased organ size
- Nondividing cells produce more protein and membrane without division
- Mechanosensors, PI3K /Akt signaling pathway important in exercise-induced growth
- Growth factors, vasoactive agents, hormones mediate stress-induced response
- Unrelieved stress eventually results in irreversible injury
Subcellular organelle may undergo selective hypertrophy

As example, individuals treated with drugs such as barbiturates show hypertrophy of the smooth endoplasmic reticulum (ER) in hepatocytes, which is an adaptive response that increases the amount of enzymes (cytochrome P-450 mixed function oxidases) available to detoxify the drugs.
Hyperplasia is an increase in the number of cells in an organ or tissue, usually resulting in increased mass of the organ or tissue.

Hyperplasia and hypertrophy are distinct processes but frequently occur together.

Both can be triggered by the same external stimulus.

Hyperplasia takes place if the cell population is capable of dividing, resulting in increased cell numbers.
HYPERPLASIA

Physiologic vs Pathologic

Physiologic
hormonal vs compensatory
Physiological, hormonal hyperplasia
Pathological hormomal hyperplasias

- Hyperplasia reversible with appropriate treatment

- Benign Prostate Hyperplasia
  - BPH from accumulation of stable DHT-AR complexes
  - Androgen-driven up-regulation of fibroblast growth factor (FGF) and TGF-beta
  - FGF stimulates proliferation of stroma
Prostate normal vs. hyperplasia

Benign prostatic hyperplasia and androgens

Hyperplasia regresses if the hormonal stimulation is eliminated

Hyperplasia is distinct from cancer, but cancerous proliferation may arise
Atrophy is reduced size of an organ or tissue resulting from a decrease in cell size and number

Physiologic or Pathologic.

*Physiologic atrophy* is common during normal development.

Some embryonic structures, such as the notochord and thyroglossal duct, undergo atrophy during fetal development.

The uterus decreases in size shortly after parturition.
When a fractured bone is immobilized in a plaster cast or when a patient is restricted to complete bedrest, skeletal muscle atrophy ensues.

The initial decrease in cell size is reversible once activity is resumed, leading to osteoporosis of disuse.

Some of these skeletal muscle fibers here show atrophy, compared to normal fibers. The number of cells is the same as before the atrophy occurred, but the size of some fibers is reduced. This is a response to injury by "downsizing" to conserve the cell. In this case, innervation to the small, atrophic fibers was lost. (This is a trichrome stain.)
The normal metabolism and function of skeletal muscle are dependent on its nerve supply. Damage to the nerves leads to atrophy of the muscle fibers supplied by those nerves.

Loss of Innervation (denervation atrophy)
Loss of Innervation (denervation atrophy)
Normal Lung

http://www.meddean.luc.edu/lumen/bbs/p/pulpathi/pulpath3.jpeg

http://www.microscopy-uk.org.uk/mag/imgsep08/Apocap4.jpg
Microscopic examination of the lung reveals no alveolar development, only tubular bronchioles incapable of significant gas exchange, in this premature baby with pulmonary hypoplasia from oligohydramnios. This results in insufficient gas exchange from respiration following birth.
A decrease in blood supply such as ischemia

The brain may undergo progressive atrophy, mainly because of reduced blood supply as a result of atherosclerosis

This is called senile atrophy; it also affects the heart
Tissue compression for any length of time can cause atrophy.

Atrophy in the setting below is likely the result of ischemic changes caused by compromise of the blood supply by the pressure exerted by the mass.

Fig 1. CT scans showing large parietal left extradural hematoma (A and D). B and E, immediate post op CT scan: complete evacuation of the lesion by craniectomy. C and F, delayed cerebral atrophy in the exam performed about four months after surgery.

http://www.scielo.br/img/revistas/anp/v65n4b/a29fig1d.gif
Profound protein-calorie malnutrition (marasmus) is associated with the use of skeletal muscle as a source of energy after other reserves such as adipose stores have been depleted.

Cachexia is also seen in patients with chronic inflammatory diseases and cancer. In the former, chronic overproduction of the inflammatory cytokine tumor necrosis factor (TNF) is thought to be responsible for appetite suppression and lipid depletion, culminating in muscle atrophy.
Many hormone-responsive tissues, such as the breast and reproductive organs, are dependent on endocrine stimulation for normal metabolism and function.

**Testicular atrophy**
Decreased protein synthesis and increased protein degradation in cells because of reduced metabolic activity.

The degradation of cellular proteins occurs mainly by the ubiquitin-proteasome pathway.
Atrophy can be accompanied by increased autophagy

Autophagy ("self eating") is the process in which the starved cell eats its own components

Autophagic vacuoles are membrane-bound vacuoles that contain fragments of cell components

The vacuoles ultimately fuse with lysosomes, and their contents are digested by lysosomal enzymes
METAPLASIA

*Reversible change in which one differentiated cell type is replaced by another cell type.*

It may represent an adaptive substitution of cells that are sensitive to stress by cell types better able to withstand the adverse environment.
Metaplasia of esophageal epithelium

Glandular, or Barrett’s, metaplasia of the normal esophageal squamous mucosa has occurred here, with the appearance of gastric type columnar mucosa, secondary to gastric reflux.
Mechanisms of Metaplasia

Result of a reprogramming of stem cells that are known to exist in normal tissues, or of undifferentiated mesenchymal cells present in connective tissue

Precursor cells differentiate along a new pathway

The differentiation of stem cells to a particular lineage is brought about by signals generated by cytokines, growth factors, and extracellular matrix components in the cells' environment