

SOLUTION PHARMACOLOGY CELLULAR INJURY AND ADAPTATION

1. Cells age and die like every other living thing. It is a normal, physiologic process distinct from disease. Natural, physiologic, planned cell death is apoptosis.
2. **Apoptosis**—a programmed commitment to die.
3. Cell death caused by disease is **necrosis**.
4. Cellular adaptations may occur in cells pushed to **physiologic extremes** by unusual physiologic demand. Regardless of the cause, cell adaptations return to normal once the stress or injury is relieved.
5. Process of cell damage and repair.

Solution

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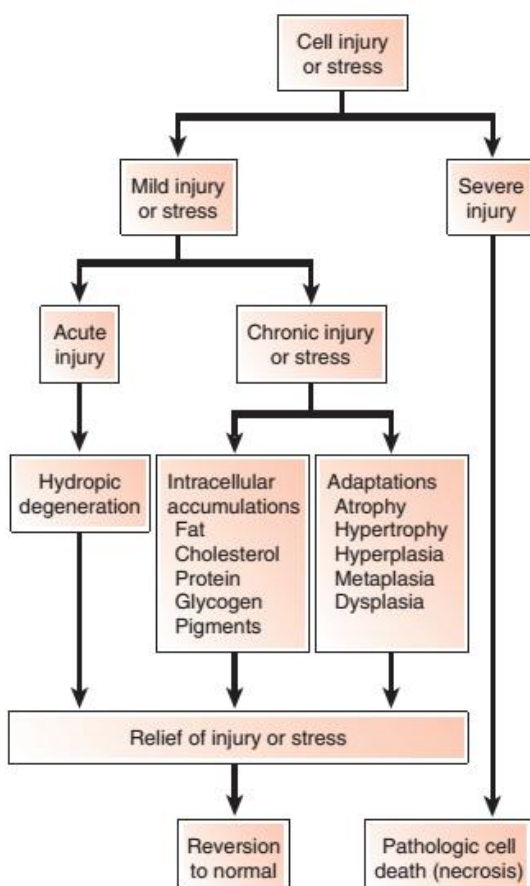
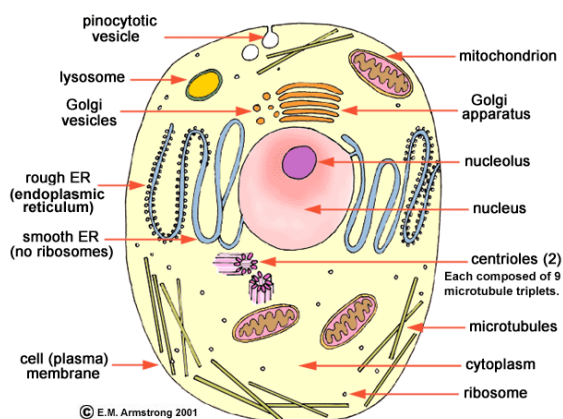


Figure 2-8 Cell reactions to injury or stress. Cells react in similar ways to mild chronic injury or unusual physiologic demand (stress).



6. **Inadequate oxygenation (hypoxia)**: Hypoxia is the most common cause of cell injury and is usually caused by insufficient arterial blood flow (**ischemia**)
7. Hypoxia initiates a series of chemical and acid-base imbalances that may be reversible if blood flow or oxygenation is restored however, prolonged hypoxia produces cell death

8. **Low body temperature (Hypothermia)** may cause cardiac arrest subsequent to slowing of the heart's intrinsic pacemaker.
9. **Ionizing radiation:** Ionizing radiation is radiation strong enough to break (ionize) water (H₂O) into H⁺ (hydrogen ion) and OH⁻ (hydroxyl ion). In acute radiation injury the hydroxyl ion attaches to DNA and prevents cell reproduction.
10. **Toxic molecular injury:** Virtually any natural or synthetic molecule can cause injury. Depending on the chemical, injury may occur in different organs and by different mechanisms.
11. Genetic defects: There are two main types of genetic defects: mutations and cytogenetic abnormalities. A **mutation** is a permanent change in DNA represented by an abnormal sequence of nucleotide bases.
12. **Cytogenetic disease** is large-scale change in chromosomes and is characterized by extra or missing whole chromosomes or parts of chromosomes.
13. **Cholesterol:** The most extensive and most damaging intracellular accumulation is cholesterol, deposited in the cells of arteries in atherosclerosis.
14. **Pigments:** The most widely occurring cell pigment accumulation is **lipofuscin**.
15. Melanin is a dark-brown compound that gives skin its color. It is synthesized by melanocytes in the epidermis and deposited in the cytoplasm of cells in the basal layer of the epidermis.
16. As cells encounter physiologic stresses or pathologic stimuli, they can undergo adaptation, achieving a new steady state and preserving viability and function. The principal adaptive responses are *hypertrophy*, *hyperplasia*, *atrophy*, and *metaplasia*.

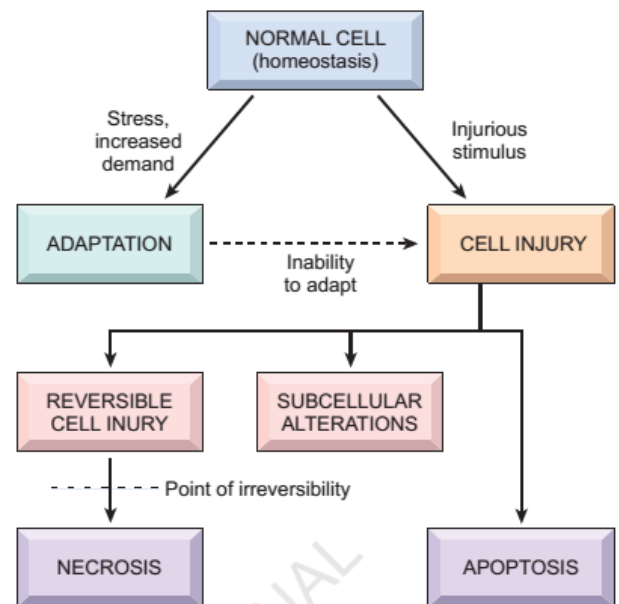
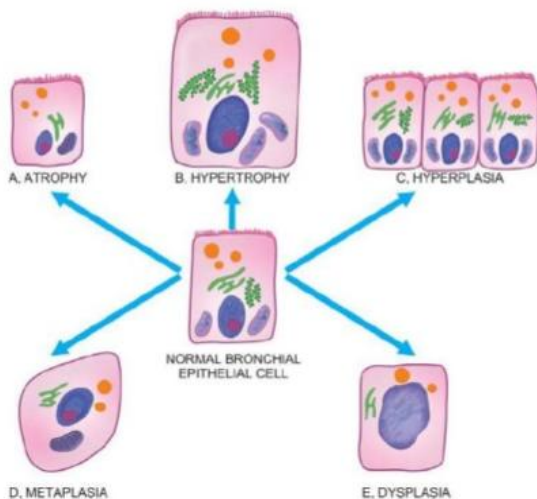


Figure 1-1

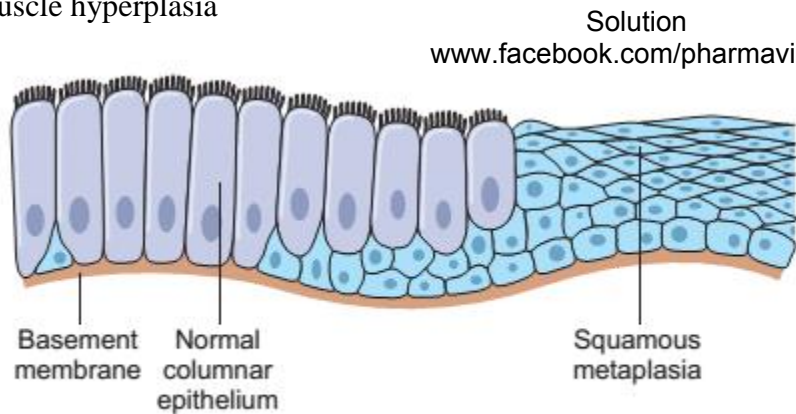
Stages in the cellular response to stress and injurious stimuli.

17. Adaptation is a reversible changes in the number, size, phenotype, metabolic activity or function of cell in response to change in their environments.

18. Physiologic adaptation usually represents response of cell to normal stimulation by hormones. Example- Hormone induced enlargement of breast and uterus during pregnancy.
19. **Atrophy** is decreased size and function of a cell. It is an adaptive response to decreased demand or to increased stress; the cell shuts down its metabolic processes to conserve energy. It may be caused by-
- (a) Reduced functional demand. For example, muscle atrophy occurs in a limb encased in a cast.
 - (b) Inadequate blood supply (ischemia). For example, atherosclerosis of the renal artery can impair blood flow enough to cause atrophy of a kidney.
 - (c) Absent or reduced neural or hormonal support. For example, to remain healthy, skeletal muscle cells must be continually stimulated by intact nerves; interruption of nerve supply leads to muscle atrophy.
 - (d) Chronic inflammation associated with chronic injury. For example, chronic inflammation of the stomach lining is associated with a condition known as chronic atrophic gastritis.
20. Atrophy results from decreased protein synthesis and increased protein degradation in the cell.
21. **Hypertrophy** is an increase in the size of cells resulting in an increase in the size of the organ. It can be caused by.
- (a) Hormonal stimulation. Cells depend on hormonal support. Too little and they wither; too much and they enlarge and become overactive. For example, following delivery, women's breasts enlarge and become temporarily hyperfunctional in order to produce milk, a change induced by secretion of prolactin (a hormone) from the pituitary.
 - (b) Increased functional demand. Increased functional demand stresses cells and causes them to enlarge and increase their activity. For example, a heart under the constant strain of high blood pressure increases in size because the individual cardiac muscle cells increase in size.
22. **Hyperplasia** is the enlargement of a tissue or organ owing to an increase in the number of cells, as opposed to an increase in the cell size. It is caused by:
- (a) Hormonal stimulation. For example, the increase of estrogen in female puberty causes an increase in the number of endometrial cells.
 - (b) Increased functional demand. For example, low atmospheric oxygen stimulates bone marrow production of RBC to carry oxygen. It is for this reason that people living at high altitude have increased numbers of circulating red blood cells (RBC)
 - (c) Chronic stress or injury. For example, the stress of exceptionally high blood pressure
 - (d) **Hyperplasia is an important response of connective tissue cells in wound healing, in which proliferating fibroblasts and blood vessels aid in repair.**

23. Hypertrophy and hyperplasia can also occur together, and obviously both result in an enlarged (*hypertrophic*) organ. Thus, the massive physiologic enlargement of the uterus during pregnancy occurs as a consequence of estrogenstimulated smooth muscle hypertrophy and smooth muscle hyperplasia

24. **Metaplasia** is a reversible change in which one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type. In this type of cellular adaptation, cell sensitive to a particular stress are replaced by other cell types better able to withstand the adverse environment.



25. The term *necrosis* was first used by morphologists to refer to a series of changes that accompany cell death, largely resulting from the degradative action of enzymes on lethally injured cells.

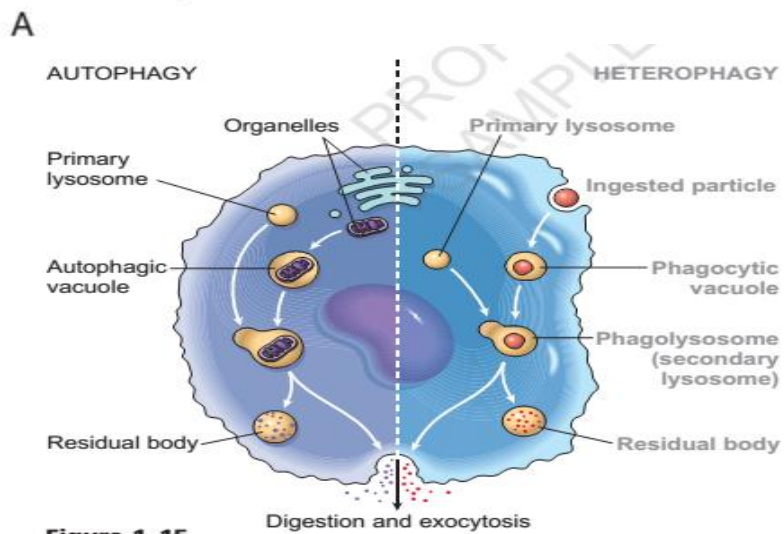


Figure 1-15

Necrotic cells are unable to maintain membrane integrity, and their contents often leak out.

26. **Autophagy.** Autophagy refers to lysosomal digestion of the cell's own components and is contrasted with *heterophagy*, in which a cell (usually a macrophage) ingests substances from the outside for intracellular destruction.

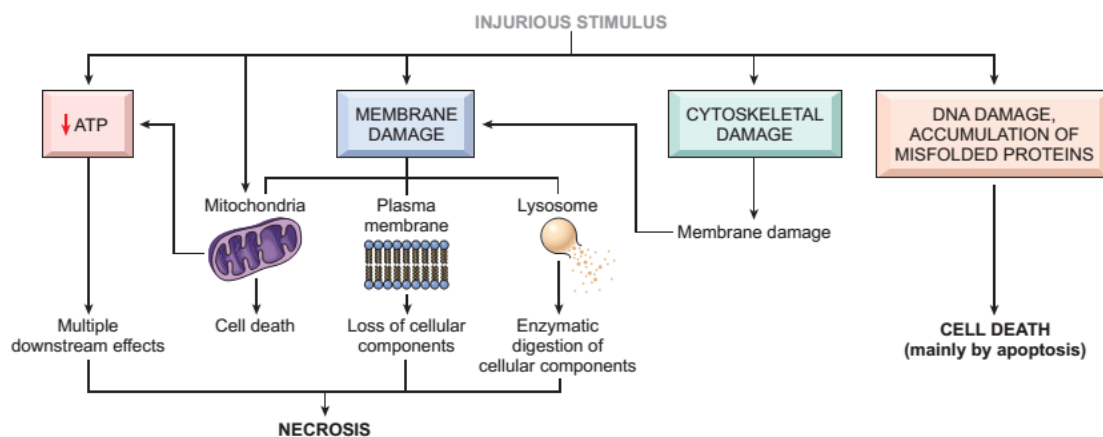


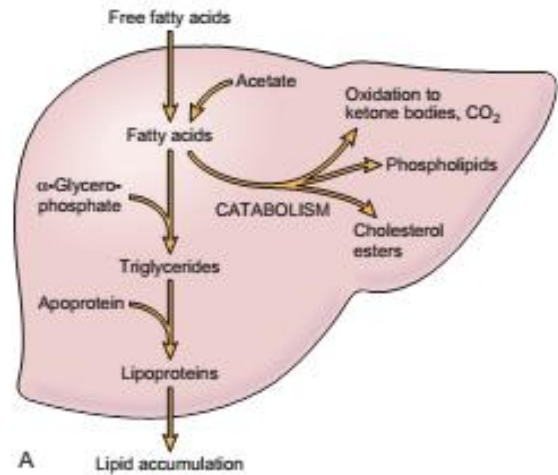
Figure 1-16

The principal cellular and biochemical sites of damage in cell injury. Note that loss of adenosine triphosphate (ATP) results first in reversible injury (not shown) and culminates in necrosis. Mitochondrial damage may lead to reversible injury and death by necrosis or apoptosis.

SUMMARY

Mechanisms of Cell Injury

- **ATP depletion:** failure of energy-dependent functions → reversible injury → necrosis
- **Mitochondrial damage:** ATP depletion → failure of energy-dependent cellular functions → ultimately, necrosis; under some conditions, leakage of proteins that cause apoptosis
- **Influx of calcium:** activation of enzymes that damage cellular components and may also trigger apoptosis
- **Accumulation of reactive oxygen species:** covalent modification of cellular proteins, lipids, nucleic acids
- **Increased permeability of cellular membranes:** may affect plasma membrane, lysosomal membranes, mitochondrial membranes; typically culminates in necrosis
- **Accumulation of damaged DNA and misfolded proteins:** triggers apoptosis



Solution

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27. *Apoptosis* is a pathway of cell death that is induced by a tightly regulated suicide program in which cells destined to die activate enzymes capable of degrading the cells' own nuclear DNA and nuclear and cytoplasmic proteins.

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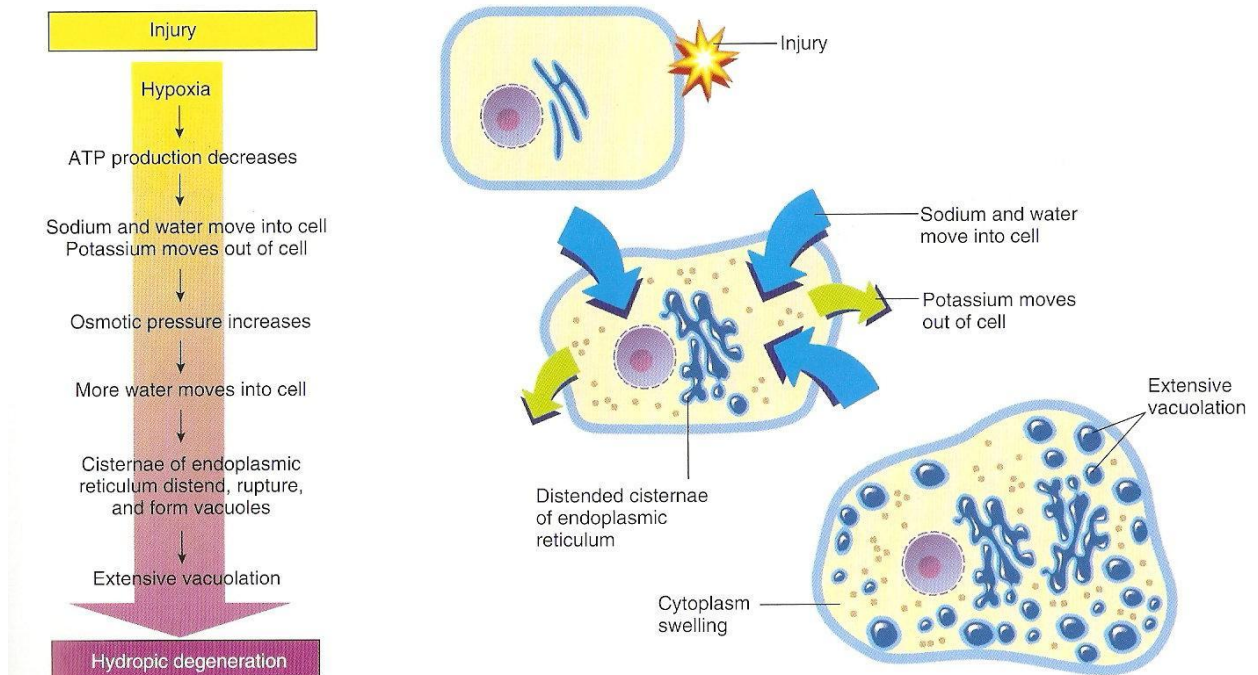


Fig. 1-9 The process of acute cell swelling (hydropic degeneration). ATP, Adenosine triphosphate. (From Huether S, McCance K: Understanding pathophysiology, ed 3, St Louis, 2004, Mosby.)

29. Causes of cell injury-

- (a) Oxygen Deprivation- hypoxia or oxygen deficiency, interfere with aerobic oxidative respiration and is an extremely important and common cause of cell injury. Example- ischemia, inadequate oxygenation of blood, pneumonia or reduction in the oxygen carrying capacity of blood, anemia, carbon monoxide poisoning.
- (b) Chemical Agents- sufficient conc of glucose and salt can create a hyper osmotic environment that leaked the cellular content from the cell. Example- air pollutants, insecticide, CO, Asbestos, ethanol.
- (c) Infectious Agents-
- (d) Immunological reaction-autoimmune reaction against own tissue and allergic reaction against environmental substance.
- (e) Genetic Defects-
- (f) Nutritional Imbalance
- (g) Physically agents- Trauma, temperature, radiation, Electric Shock, Atmospheric pressure.
- (h) Aging

Solution

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Note- References has been taken from various sources including online and offline books. I am thankful to unknown source for information from internet.

Books-

1. KDT
2. Ross & Wilson
3. Tortota
4. FSK Barar
5. Lippincott
6. Sparsh and Gupta.
7. Many More