1 Instructor's Manual
Cell Pathology

TEACHING FOCUS

Cells consist of smaller functional units, cellular organelles, which can be seen with an electron microscope. Organelles consist of molecules that can be further dissected and studied by using the techniques of molecular biology. These research endeavors are laying the groundwork for *molecular pathology,* a science that will encompass all living phenomena and provide explanations for pathologic processes at the level of the basic units of living nature: molecules, atoms, and their elementary particles.

OBJECTIVES	CONTENT	TEACHING RESOURCES
1. Describe the essential components of a typical cell and their functions.	*Text, pp. 2–6* *Table: 1-1* *Figures: 1-1, 1-2, 1-3, 1-4*	PPT Chapter 1, Slide(s) 1–27 Clinicopathologic Review question(s): 1 End of Chapter Review question(s): 1–6 Pretest question(s): 10–12
2. Explain homeostasis and the integrated response of a cell to external stimuli.	*Text, p. 7* *Figure: 1-6*	PPT Chapter 1, Slide(s) 28 End of Chapter Review question(s): 7, 8
3. Define *reversible cell injury*.	*Text, pp. 8–9* *Figure: 1-9*	PPT Chapter 1, Slide(s) 29–30 Clinicopathologic Review question(s): 7 End of Chapter Review question(s): 9
4. Explain the cytoplasmic changes in reversible cell injury and the concept of hydropic change.	*Text, p. 9* *Table: 1-2* *Figures: 1-7, 1-8, 1-9*	PPT Chapter 1, Slide(s) 30 Clinicopathologic Review question(s): 5
5. Compare and contrast reversible and irreversible cell injury.	*Text, pp. 8–10* *Table: 1-2* *Figure: 1-10*	PPT Chapter 1, Slide(s) 28–31 End of Chapter Review question(s): 10 Test Bank question(s): 1
6. List the most important causes of cell injury.	*Text, p. 10* *Table: 1-2* *Figures: 1-11, 1-12, 1-13*	PPT Chapter 1, Slide(s) 29–31 Clinicopathologic Review question(s): 6 End of Chapter Review question(s): 11–13 Test Bank question(s): 3, 13 Pretest question(s): 2
7. Describe three types of cell adaptations.	*Text, pp. 12–15*	PPT Chapter 1, Slide(s) 42–43 End of Chapter Review question(s): 14 Pretest question(s): 1
8. Give three examples of atrophy.	*Text, p. 13* *Figure: 1-14*	PPT Chapter 1, Slide(s) 44–45 End of Chapter Review question(s): 15 Test Bank question(s): 4 Pretest question(s): 3

OBJECTIVES	CONTENT	TEACHING RESOURCES
9. Define and explain *hypertrophy* and *hyperplasia* and give appropriate examples of each.	*Text, pp. 13–14* *Figures: 1-15, 1-16, 1-17*	PPT Chapter 1, Slide(s) 46–50 Clinicopathologic Review question(s): 2, 12 End of Chapter Review question(s): 15 Test Bank question(s): 5 Pretest question(s): 4
10. Compare and contrast metaplasia and dysplasia and give appropriate examples of each.	*Text, p. 14*	End of Chapter Review question(s): 16 Test Bank question(s): 6 Pretest question(s): 5
11. Define various forms of intracellular accumulation.	*Text, p. 15* *Figure: 1-18*	PPT Chapter 1, Slide(s) 51 End of Chapter Review question(s): 17 Test Bank question(s): 7 Pretest question(s): 6
12. Explain the pathogenesis of fatty liver.	*Text, pp. 15–16* *Figure: 1-19*	PPT Chapter 1, Slide(s) 52 End of Chapter Review question(s): 18 Test Bank question(s): 14
13. Explain the significance of cellular aging.	*Text, p. 16* *Figures: 1-19, 1-20*	End of Chapter Review question(s): 19–21, 24–26 Pretest question(s): 7
14. Compare two forms of cell death: necrosis and apoptosis.	*Text, pp. 17–20* *Table: 1-3* *Figures: 1-25, 1-26*	PPT Chapter 1, Slide(s) 53–61 End of Chapter Review question(s): 24–26 Test Bank question(s): 1, 8, 9
15. List examples of coagulative, liquefactive, caseous, and enzymatic necrosis.	*Text, pp. 17–18* *Figures: 1-21, 1-22, 1-23*	PPT Chapter 1, Slide(s) 54–57 Clinicopathologic Review question(s): 8–11 End of Chapter Review question(s): 22 Pretest question(s): 7–9
16. Understand the difference between dystrophic and metastatic calcification.	*Text, p. 18* *Figure: 1-24*	Clinicopathologic Review question(s): 9 End of Chapter Review question(s): 23 Test Bank question(s): 8–10, 15

PRETEST

Instruction: *Choose the one best answer.*

1. Inhibition of ATP production by hypoxia causes which of the following?
a. Decreased production of lactic acid in the cytoplasm
b. Granulation of the rough endoplasmic reticulum
c. Constriction of rough endoplasmic reticulum
d. Swelling of the mitochondria
e. Alkalinization of the hyaloplasm

ANS: D

2. Which of the following is an oxygen radical?
a. Hydrogen peroxide
b. Acid hydrolase
c. ATP
d. Carbon tetrachloride
e. Lipofuscin

ANS: A

3. Which of the following organs undergoes atrophy during childhood and adolescence?
a. Uterus
b. Breasts
c. Thymus
d. Thyroid
e. Adrenals

ANS: C

4. Enlargement of the heart caused by hypertension is a result of
a. hyperplasia.
b. hypertrophy.
c. atrophy.
d. metaplasia.
e. dysplasia.

ANS: B

5. Columnar bronchial epithelium irritated by chronic exposure to cigarette smoke changes into stratified squamous epithelium. This change is an example of
a. hypertrophy.
b. hyperplasia.
c. atrophy.
d. metaplasia.
e. degeneration.

ANS: D

6. Chronic hemolysis is characterized by accumulation of an iron-containing brown pigment in the cytoplasm of liver cells. This brown pigment is called
a. melanin.
b. tyrosine.
c. hemosiderin.
d. ceruloplasmin.
e. bilirubin.

ANS: C

7. Which type of necrosis is found in granulomas of tuberculosis?
a. Coagulation necrosis
b. Liquefactive necrosis
c. Caseous necrosis
d. Fat necrosis
e. Fibrinoid necrosis

ANS: C

8. Myocardial infarct represents a form of
a. dystrophic calcification.
b. metastatic calcification.
c. fibrinoid necrosis.
d. coagulation necrosis.
e. wet gangrene.

ANS: D

9. Liquefactive necrosis typically occurs within an infarct of the
a. heart.
b. brain.
c. liver.
d. kidney.
e. pancreas.

ANS: B

10. Which of the following is the site of protein synthesis?
a. Mitochondria
b. Lysosomes
c. Endoplasmic reticulum
d. Intermediate filaments
e. Plasma membrane

ANS: C

11. Which of the following is the site of hormone synthesis?
a. Mitochondria
b. Lysosomes
c. Endoplasmic reticulum
d. Intermediate filaments
e. Plasma membrane

ANS: C

12. The major site of energy production in the cytoplasm is known as
a. mitochondria.
b. lysosomes.
c. endoplasmic reticulum.
d. intermediate filaments.
e. plasma membrane.

ANS: A

CLINICOPATHOLOGIC REVIEW

SYMPTOMS/FINDINGS	QUESTION	ANSWER
1. A liver biopsy was performed, and the tissue was examined histologically. No chromosomes were seen in 100 liver cells.	Is this normal?	Yes. Chromosomes cannot be seen in interphase nuclei; they can be seen only during mitosis. In resting, nondividing cells, DNA, and RNA are distributed in the nucleus in the form of chromatin.
2. The liver cells of an epileptic patient who received a daily dose of phenobarbital showed increased amounts of SER.	What is the explanation for this finding?	Phenobarbital is a drug metabolized in SER. This organelle will undergo hyperplasia if stimulated. Increased amounts of SER in liver cells are found following chronic drug intake.
3. Increased amounts of SER were found by electron microscopy in testicular Leydig cells.	Is this normal?	Yes. Leydig cells synthesize sex hormones. Steroids are produced in the SER; therefore, all steroid-producing cells normally have a well-developed SER.
4. Plasma cells were found to contain increased amounts of RER.	Is this normal?	Yes. Plasma cells secrete immunoglobulins, which, like all other proteins for export, are synthesized on the RER.
5. A mercurial diuretic caused hydropic changes in the kidney cells.	How could this be explained?	Mercury is a heavy metal that inhibits enzymes in proximal kidney cells. Mercury salts, used in small amounts for therapeutic purposes, produce reversible cell injury in the form of hydropic change. In large amounts, mercury causes cell necrosis.
6. The pH in the liver cells of a patient was determined to be 5.2.	Is this normal?	No. Normally, the pH in liver cells is neutral to slightly alkaline (7.0–7.3). Acidification of the cytoplasm is evidence of cell injury, as in

SYMPTOMS/FINDINGS	QUESTION	ANSWER
		anoxia. Anoxia leads to overproduction of lactic acid through anaerobic glycolysis. This occurs after aerobic phosphorylation has been inhibited owing to lack of oxygen. Phosphorylation has been inhibited owing to lack of oxygen.
7. Myelin figures were found in liver cells exposed to carbon tetrachloride.	What is the significance of these myelin figures?	Myelin figures represent concentrically layered membranes resembling the myelin of peripheral nerves. These are structures formed from damaged cell membranes and are commonly found in injured cells. However, they are also found within lysosomes in individuals with lipid storage diseases, such as Tay-Sachs disease.
8. A small heart in a 90-year-old woman was found to be full of lipofuscin.	What is the diagnosis?	A small heart and accumulation of lipofuscin (the so-called brown pigment of aging) are signs of senile atrophy. However, similar changes may be seen in debilitated and emaciated younger patients as well.
9. The left ventricle of the heart was 2.5 cm thick (normal, 1.5 cm).	What is the significance of this finding?	This thickening of the wall of the left ventricle indicates hypertrophy. If the aortic outflow tract and the valves are normal, the myocardial hypertrophy is most likely secondary to arterial hypertension.
10. Large amounts of brown pigment were noted in a liver biopsy specimen obtained from a man who had hemolytic anemia.	What is the brown pigment?	The brown pigment in the liver is hemosiderin. Hemosiderin, an iron-containing pigment, is derived from hemoglobin of hemolyzed red blood cells.
11. A patient with myocardial infarction had no heartbeat for 5 minutes but was resuscitated. He remained unconscious and had to be maintained on a respirator.	Is this man alive?	The argument whether this man is alive or dead could be entertained forever. However, he is most likely "brain dead." If respiratory support was discontinued, he would not be able to breathe and would die shortly thereafter.
12. The wall of the urinary bladder in a patient with prostatic enlargement was found to be thick and	What is the diagnosis of the bladder and the prostatic lesion?	The thickening of the bladder wall is secondary to smooth muscle cell hypertrophy, required to overcome the obstruction of the urinary

SYMPTOMS/FINDINGS	QUESTION	ANSWER
trabeculated.		outflow tract. The prostate is most likely enlarged as a result of hormonally induced hyperplasia.

ANSWERS TO TEXT REVIEW QUESTIONS

1. What are the main components of the nucleus and the cytoplasm?
The main components of the cytoplasm are the mitochondria (ATP biosynthesis), ribosomes (protein synthesis), endoplasmic reticulum (ribosome attachment), Golgi apparatus (glycosylation), and lysosomes (protein degradation). The main components of the nucleus are the nuclear membrane, nucleoplasm, and nucleolus. The nucleoplasm contains chromatin, which undergoes periodic condensation to form chromosomes during mitosis and meiosis. The nucleolus is the site of rRNA synthesis.

2. Which components of the cell contain RNA?
Multiple classes of RNAs (e.g., mRNA, tRNA, and rRNA) are found in the nucleus and the nucleolus and are associated with the ribosomes. RNA is also found in the cytosol and mitochondria.

3. Compare mitochondria with endoplasmic reticulum and Golgi apparatus.
Mitochondria are double-membrane organelles with their own circular DNA. They are involved in ATP biosynthesis. The endoplasmic reticulum (ER) is a meshwork of intracellular membranes, which provides locking sites for ribosomes (rough ER) and pathways for protein secretion. The luminal surface of the ER is continuous with the plasma membrane. The Golgi apparatus is a specialized region of the ER devoted to adding sugar chains to lipids and proteins. These post-translational modifications facilitate intracellular protein sorting and extracellular protein transport.

4. What is the difference between primary and secondary lysosomes, autophagosomes, and heterophagosomes?
Lysosomes are membrane-bound digestive organelles that originate from the Golgi. When "primary lysosomes" fuse with cytoplasmic vesicles, they form "secondary lysosomes," also referred to as *heterophagosomes.* Autophagosomes are secondary lysosomes involved in autodigestion of damaged intracellular organelles.

5. Compare intermediate filaments with microfilaments and microtubules.
The cytoskeleton helps maintain cell shape and orchestrate cell motility. Intermediate filaments (e.g., keratin and vimentin) are cell-type–specific cytoskeletal proteins. Microfilaments contain actin and myosin. Microtubules contain tubulin.

6. Explain autocrine, paracrine, and endocrine cell stimulation.
Endocrine stimulation occurs when a hormone (peptide or steroid) enters the blood and binds to receptors on target cells at a distant location. Autocrine stimulation is self-stimulation. Paracrine stimulation occurs when a chemical signal is delivered over a short distance from one cell type to another.

7. What is homeostasis?
Homeostasis refers to the remarkable ability of all living cells and organisms to maintain an internal chemical composition that does not vary significantly, despite often dramatic shifts in the external environment.

8. How is cellular steady state maintained, and what does it mean when a cell reaches the point of no return?
Mechanisms of homeostasis include selective metabolism and catabolism, as well as controlled intracellular and extracellular transport across the plasma membrane. When a cell is unable to maintain homeostasis, it is said to have reached the "point of no return" and will die (undergo coagulative necrosis).

9. Explain the pathogenesis of hydropic change and the role of Na^+, K^+-adenosine triphosphatase in cellular swelling.
Water volume in a cell is regulated primarily by a membrane pump, the Na^+/K^+-ATPase. When this pump fails because of insufficient ATP, water, and Na^+ ions are retained within the cell. This leads to hydropic swelling—a form of acute, reversible cell injury.

10. What are the microscopic signs of irreversible cell injury?
Microscopic signs of irreversible cell injury include plasma membrane blebbing, cytoskeletal diseases, mitochondrial swelling, and changes in nuclear morphology (pyknosis, karyorrhexis, and karyolysis).

11. Explain the pathogenesis of hypoxia or anoxia and give clinical examples of these conditions.
Hypoxia refers to partial lack of oxygen, and *anoxia* refers to complete lack of oxygen delivery to cells and tissues. Lack of oxygen is a major cause of morbidity and mortality. Examples include suffocation, near-drowning, pneumonia, anemia, myocardial infarction, and cyanide poisoning.

12. What are oxygen radicals, and how do they damage cells?
Toxic oxygen radicals are formed in small amounts in cells, but they are rapidly catabolized. Progressive accumulation of hydrogen peroxide (H_2O_2) and hydroxyl radicals (OH) accompanies reversible cell injury. These toxic oxygen species can cause direct DNA, protein, and membrane damage.

13. How do toxins, microbes, and chemical mediators of inflammation kill cells?
Toxins kill cells through direct and indirect effects on cell structure and function. Microbes kill cells by mediating direct cell lysis (some viruses) by activating host immune effector cells (viruses and bacteria), and through the release of cytotoxic chemicals. Mediators of inflammation and immunity can also kill cells through activation of programmed cell death (apoptosis) and through the assembly of membrane channels (membrane attack complex).

14. Compare acute cell injury with cellular adaptations.
Cellular adaptations develop over an extended period of time and are fully reversible when the stress is removed. Acute cell injury may be either manifested as reversible cell swelling or as irreversible necrosis.

15. Compare atrophy with hypertrophy and hyperplasia and give clinical examples of each condition.
Atrophy denotes a decrease in cell/tissue size or formation (e.g., disuse of skeletal muscle). *Hypertrophy* denotes an increase in cell/tissue size or function (e.g., effect of anabolic steroids on skeletal muscle). *Hyperplasia* denotes an increase in cell number (e.g., estrogen-stimulated growth of uterine endometrium). These conditions are reversible cellular adaptations to chronic persistent stress.

16. Explain the significance of smoking-induced metaplasia of the bronchial epithelium in the pathogenesis of bronchial neoplasia.
In response to cigarette smoke, columnar epithelial cells of the bronchial epithelium undergo squamous metaplasia. Although reversible, squamous metaplasia represents a necessary step in a sequence of cellular and genetic changes leading to bronchial squamous cell neoplasia (new uncontrolled cell growth).

17. Compare anthracosis and hemosiderosis.
Anthracosis and hemosiderosis are two examples of intracellular storage diseases. *Anthracosis* is a type of pneumoconiosis, in which carbon (coal dust) is deposited in the lungs. *Hemosiderosis* refers to the deposition of iron in various organs of the body. Hemosiderin is an aggregated form of the iron carrier protein, ferritin, which may be visible by light microscopy.

18. Explain the pathogenesis of fatty liver induced by alcohol.
Fatty liver in alcoholic patients is caused by multiple mechanisms, including (1) increased delivery of free fatty acids, (2) increased lipid biosynthesis, (3) decreased utilization of liver triglycerides, and (4) decreased export of lipids from the liver.

19. Discuss the merits of the wear-and-tear and the genetic hypotheses of aging.
The wear-and-tear hypothesis attributes the aging-related decline in physiologic function to a failure of cells to undergo repair and regeneration. The genetic hypothesis attributes the aging-related decline in physiologic function to fundamental (predetermined) genetic limits. The fact that individuals age at different rates argues in favor of the genetic hypothesis.

20. What is meant by the term *brain death*?
Brain death is a legal term that indicates that the vital centers in the brain that control heart rate and respiration are dead. A person who is brain-dead cannot live any longer without artificial mechanical assistance.

21. Compare the gross appearances of various forms of necrosis.
Morphologic types of necrosis include coagulative, liquefactive, caseous, fibrinoid, and fat necrosis. In coagulative necrosis, the most common form, tissues retain their original form and consistency. Liquefactive necrosis is characterized by rapid dissolution of tissue by release of hydrolytic enzymes. This often results in the formation of a fluid-filled cavity. Caseous necrosis is seen in tuberculosis. The tuberculosis granuloma has the appearance of waxy cheese, owing to the buildup of mycobacterial peptidoglycans. Fibrinoid necrosis accompanies injury to the wall of an artery. It is observed microscopically as a homogeneous, red-stained material in the wall of the vessel. Fat necrosis accompanies the release of lipolytic enzymes from an acutely injured pancreas. These enzymes convert surrounding (peripancreatic) fat tissue to liquified fats and calcium soaps.

22. What is the difference between dry and wet gangrene?
Necrosis of the extremities can dry out under sterile conditions to form dark (mummified) tissue referred to as *dry gangrene.* Bacterial contamination of the necrotic tissue lends to secondary liquefaction and is referred to as *wet gangrene.*

23. Compare metastatic calcification and dystrophic calcification.
Metastatic calcification occurs as a consequence of hypercalcemia. Excess of calcium in the blood leads to deposition of calcium salts in various normal tissues, most often in the lungs, kidneys, and stomach. Dystrophic calcification is characterized by deposition of calcium salts in previously damaged tissues. Such calcification may be found in atherosclerotic arteries, damaged cardiac valves, or tumors. Dystrophic calcification of breast tumors may be detected by mammography.

24. What is apoptosis?
Apoptosis is programmed cell death. It is energy dependent and requires activation of cell suicide genes encoding the enzymes that mediate this form of cell death.

25. Provide two examples of physiologic apoptosis and two examples of pathologic apoptosis.
Physiologic apoptosis may occur during prenatal life in the developing fetus or at any stage of postnatal life. Physiologic apoptosis during fetal life is essential for the formation of fingers and lumen in the gastrointestinal tract. Lack of apoptosis results in syndactyly and atresia of the esophagus or the intestines. Pathologic apoptosis can be induced in liver cells by hepatitis viruses. Striated muscle cells of patients who have genetic muscular dystrophy undergo apoptosis.

26. Compare apoptosis with necrosis.
The main differences between necrosis and apoptosis are listed in the following table.

Feature	Necrosis	Apoptosis
Cause	Exogenous injury	May be exogenous or endogenous
Mechanisms	Vital processes inhibited	Energy dependent, vital processes active
Cells affected	Multiple	Single

Cell morphology	Swollen, ruptured (apoptotic bodies)	Rounded up, fragmented
Cell membrane	Ruptured	Functionally intact
Outcome	Phagocytosis by neutrophils	Phagocytosis by macrophages and "nonprofessional macrophages"

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Chapter 01: Cell Pathology

Answer Key for End of Chapter Review Questions

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Cell membrane	Ruptured	Functionally intact

Outcome	Phagocytosis by neutrophils	Phagocytosis by macrophages and "nonprofessional macrophages"