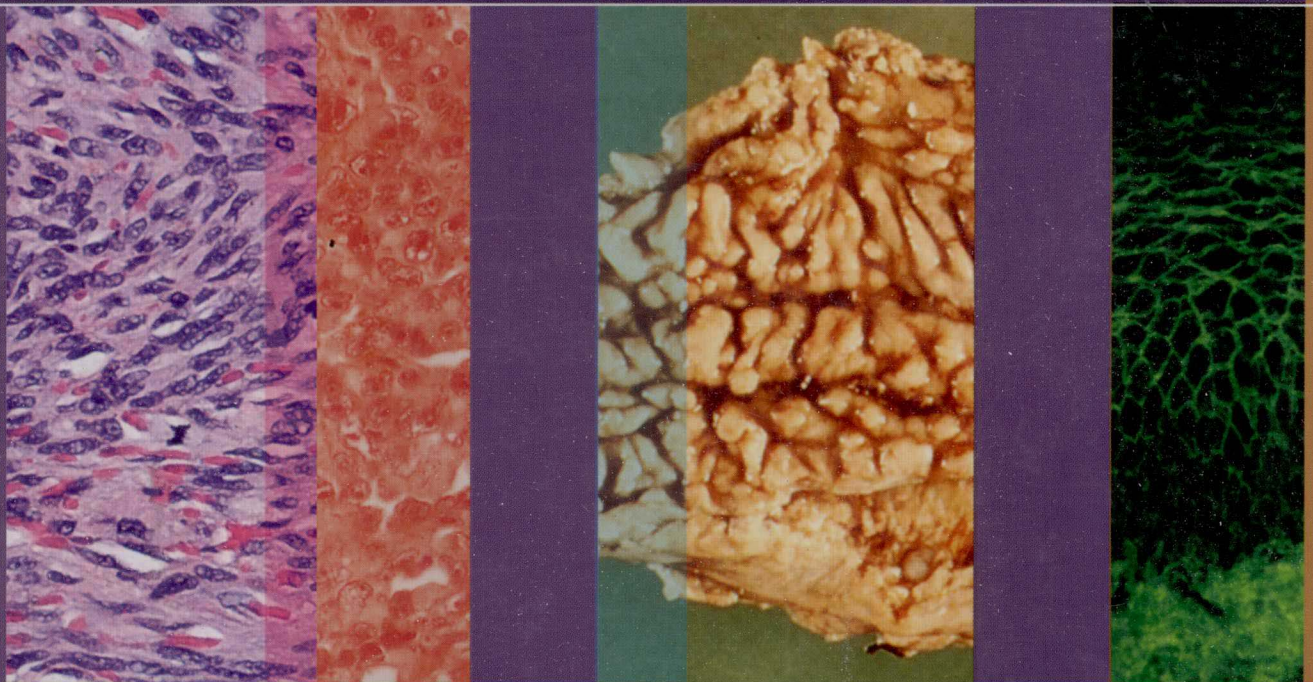


Lippincott's
Illustrated **Q&A** Review of

Rubin's Pathology

SECOND EDITION



Bruce A. Fenderson • David S. Strayer
Raphael Rubin • Emanuel Rubin

Wolters Kluwer
Health

Lippincott
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Dedication

We dedicate this book to our many teachers and colleagues for generously sharing their time and knowledge, and to all students of medicine for their intellectual stimulation and passion for learning.

Preface

Lippincott's Illustrated Q&A Review of Rubin's Pathology presents the key concepts of modern pathology in the form of clinical vignette-style questions. Using the format of the National Board of Medical Examiners (NBME), the questions address the major topics in general and systemic pathology presented in *Rubin's Pathology: Clinicopathologic Foundations of Medicine*. In addition to being a learning companion to this textbook, these questions will serve as a stand-alone resource for self-assessment and board review.

The questions are prepared at a level appropriate for second-year medical students. They provide a roadmap for students completing their courses in pathology and preparing for the United States Medical Licensing Examination (USMLE). Students in the allied health sciences (e.g., nursing and physical therapy) will also find considerable didactic value in clinical vignette-style questions.

Clinical vignette-style questions strengthen problem-solving skills. Students must integrate clinical and laboratory data, thereby simulating the practice of pathology and medicine in general. Case-based questions probe a level of competency that is expected for success on national licensing examinations. Given below are key features of this text:

- Multiple choice questions follow the USMLE template. Case-based questions include (1) patients' demographics, (2) clinical history, (3) physical examination findings, and (4) results of diagnostic tests and procedures. Each clinical vignette is followed by a question stem that addresses a key concept in pathology.
- Questions frequently involve "two-step" logic—a strategy that probes the student's ability to integrate basic knowledge into a clinical setting. The answer choices appear homogeneous and are listed alphabetically to avoid unintended cueing.
- Over 200 full-color images link clinical and pathologic findings.
- Answers are linked to the clinical vignettes and address key concepts. Incorrect answers are explained in context.
- Normal laboratory reference values are included for key laboratory tests.
- As an additional test-taking practice tool, the questions are also presented in an electronic format on our connection Web site (<http://thePoint.lww.com/LIQRpathology2>). Questions can be presented in both "quiz" and "test" modes. In quiz mode, students receive instant feedback regarding the correctness of their answer choice, along with a rationale. The test mode helps familiarize the user with the computer-generated USMLE experience.

We hope that this review of pathology will encourage students to think critically and formulate their own questions concerning mechanisms of disease. We are mindful of the words of e. e. Cummings, who wrote "always the beautiful answer who asks a more beautiful question." We wish our students success in their learning adventure. Most importantly, *have fun with pathology*.

Bruce A. Fenderson
Raphael Rubin
David S. Strayer
Emanuel Rubin

Acknowledgments

The contributions of the editors and authors of *Rubin's Pathology: Clinicopathologic Foundations of Medicine*, 5th and 6th editions were invaluable in the preparation of this text. We are particularly indebted to Dr. Ivan Damjanov and Dr. Hector Lopez for their contributions. Finally, we gratefully acknowledge the staff at Lippincott Williams & Wilkins for their expert help with manuscript preparation.

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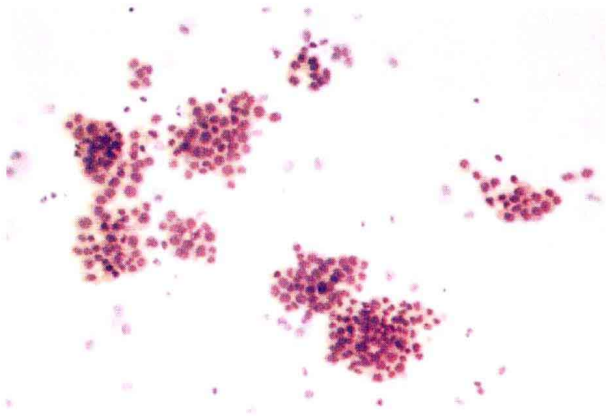
Chapter 1

Cell Injury

QUESTIONS

Select the single best answer.

- 1 Bone marrow cells from an organ donor are cultured in vitro at 37°C in the presence of recombinant erythropoietin. A photomicrograph of a typical “burst-forming unit” is shown in the image. This colony, committed to the erythrocyte pathway of differentiation, represents an example of which of the following physiologic adaptations to transmembrane signaling?

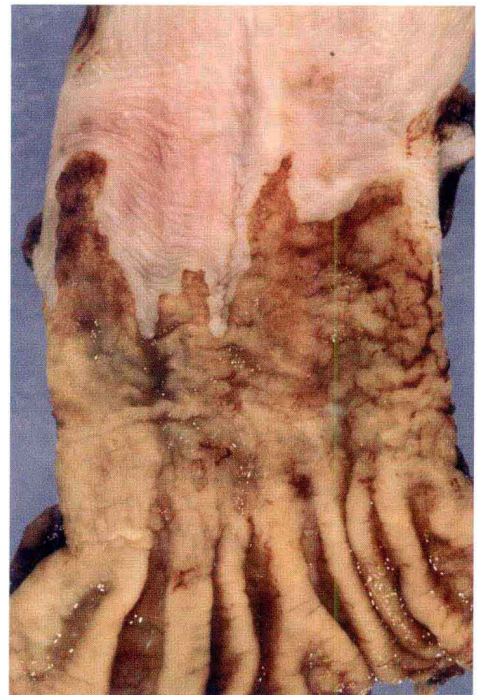


- (A) Atrophy
- (B) Dysplasia
- (C) Hyperplasia
- (D) Hypertrophy
- (E) Metaplasia

- 2 A 50-year-old chronic alcoholic presents to the emergency room with 12 hours of severe abdominal pain. The pain radiates to the back and is associated with an urge to vomit. Physical examination discloses exquisite abdominal tenderness. Laboratory studies show elevated serum amylase. Which of the following morphologic changes would be expected in the peripancreatic tissue of this patient?

- (A) Coagulative necrosis
- (B) Caseous necrosis
- (C) Fat necrosis
- (D) Fibrinoid necrosis
- (E) Liquefactive necrosis

- 3 A 68-year-old man with a history of gastroesophageal reflux disease suffers a massive stroke and expires. The esophagus at autopsy is shown in the image. Histologic examination of the abnormal tissue shows intestine-like epithelium composed of goblet cells and surface cells similar to those of incompletely intestinalized gastric mucosa. There is no evidence of nuclear atypia. Which of the following terms best describes this morphologic response to persistent injury in the esophagus of this patient?



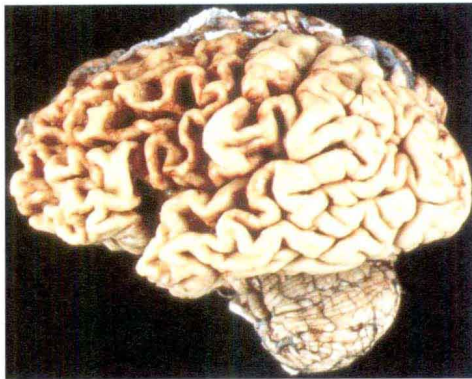
- (A) Atypical hyperplasia
- (B) Complex hyperplasia
- (C) Glandular metaplasia
- (D) Simple hyperplasia
- (E) Squamous metaplasia

- 4 A CT scan of a 43-year-old woman with a parathyroid adenoma and hyperparathyroidism reveals extensive calcium deposits in the lungs and kidney parenchyma. These radiologic findings are best explained by which of the following mechanisms of disease?

2 Chapter 1

- (A) Arteriosclerosis
- (B) Dystrophic calcification
- (C) Granulomatous inflammation
- (D) Metastatic calcification
- (E) Tumor embolism

- 5 A 75-year-old woman with Alzheimer disease dies of congestive heart failure. The brain at autopsy is shown in the image. This patient's brain exemplifies which of the following responses to chronic injury?

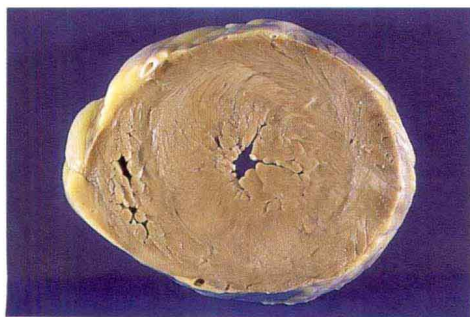


- (A) Anaplasia
- (B) Atrophy
- (C) Dysplasia
- (D) Hyperplasia
- (E) Hypertrophy

- 6 A 68-year-old woman with a history of heavy smoking and repeated bouts of pneumonia presents with a 2-week history of fever and productive cough. A chest X-ray reveals a right lower lobe infiltrate. A transbronchial biopsy confirms pneumonia and further demonstrates preneoplastic changes within the bronchial mucosa. Which of the following best characterizes the morphology of this bronchial mucosal lesion?

- (A) Abnormal pattern of cellular maturation
- (B) Increased numbers of otherwise normal cells
- (C) Invasiveness through the basement membrane
- (D) Transformation of one differentiated cell type to another
- (E) Ulceration and necrosis of epithelial cells

- 7 A 64-year-old man with long-standing angina pectoris and arterial hypertension dies of spontaneous intracerebral hemorrhage. At autopsy, the heart appears globoid. The left ventricle measures 2.8 cm on cross section (shown in the image). This adaptation to chronic injury was mediated primarily by changes in the intracellular concentration of which of the following components?



- (A) DNA
- (B) Glycogen
- (C) Lipid
- (D) mRNA
- (E) Water

- 8 A 24-year-old woman contracts toxoplasmosis during her pregnancy and delivers a neonate at 37 weeks of gestation with a severe malformation of the central nervous system. MRI studies of the neonate reveal porencephaly and hydrocephalus. An X-ray film of the head shows irregular densities in the basal ganglia. These X-ray findings are best explained by which of the following mechanisms of disease?

- (A) Amniotic fluid embolism
- (B) Dystrophic calcification
- (C) Granulomatous inflammation
- (D) Metastatic calcification
- (E) Organ immaturity

- 9 A 30-year-old man with AIDS-dementia complex develops acute pneumonia and dies of respiratory insufficiency. At autopsy, many central nervous system neurons display hydropic degeneration. This manifestation of sublethal neuronal injury was most likely mediated by impairment of which of the following cellular processes?

- (A) DNA synthesis
- (B) Lipid peroxidation
- (C) Mitotic spindle assembly
- (D) Plasma membrane sodium transport
- (E) Ribosome biosynthesis

- 10 A 62-year-old man is brought to the emergency room in a disoriented state. Physical examination reveals jaundice, splenomegaly, and ascites. Serum levels of ALT, AST, alkaline phosphatase, and bilirubin are all elevated. A liver biopsy demonstrates alcoholic hepatitis with Mallory bodies. These cytoplasmic structures are composed of interwoven bundles of which of the following proteins?

- (A) α_1 -Antitrypsin
- (B) β -Amyloid ($A\beta$)
- (C) Intermediate filaments
- (D) Prion protein (PrP)
- (E) α -Synuclein

- 11 A 65-year-old man suffers a heart attack and expires. Examination of the lungs at autopsy reveals numerous pigmented nodules scattered throughout the parenchyma (shown in the image). What is the appropriate diagnosis?



- (A) Anthracosis
- (B) Asbestosis
- (C) Hemosiderosis
- (D) Sarcoidosis
- (E) Silicosis

12 A 32-year-old woman with poorly controlled diabetes mellitus delivers a healthy boy at 38 weeks of gestation. As a result of maternal hyperglycemia during pregnancy, pancreatic islets in the neonate would be expected to show which of the following morphologic responses to injury?

- (A) Atrophy
- (B) Dysplasia
- (C) Hyperplasia
- (D) Metaplasia
- (E) Necrosis

13 A 59-year-old female alcoholic is brought to the emergency room with a fever (38.7°C/103°F) and foul-smelling breath. The patient subsequently develops acute bronchopneumonia and dies of respiratory insufficiency. A pulmonary abscess is identified at autopsy (shown in the image). Histologic examination of the wall of this lesion would most likely demonstrate which of the following pathologic changes?



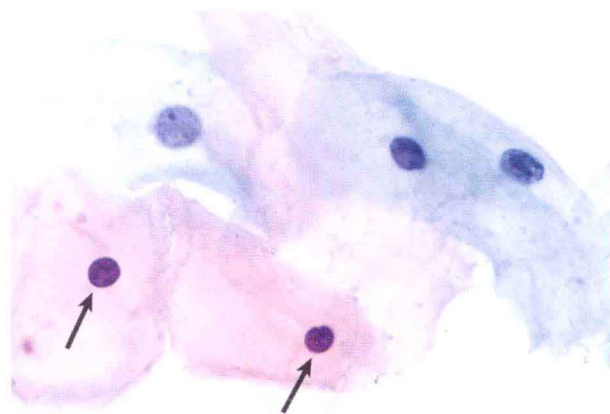
- (A) Caseous necrosis
- (B) Coagulative necrosis
- (C) Fat necrosis
- (D) Fibrinoid necrosis
- (E) Liquefactive necrosis

14 A 20-year-old man from China is evaluated for persistent cough, night sweats, low-grade fever, and general malaise. A chest X-ray reveals findings "consistent with a Ghon complex." Sputum cultures grow acid-fast bacilli. Examination of hilar lymph nodes in this patient would most likely demonstrate which of the following pathologic changes?

- (A) Caseous necrosis
- (B) Coagulative necrosis
- (C) Fat necrosis
- (D) Fibrinoid necrosis
- (E) Liquefactive necrosis

15 A 31-year-old woman complains of increased vaginal discharge of 1-month duration. A cervical Pap smear is shown in the image. Superficial epithelial cells are identified with arrows. When compared to cells from the deeper intermediate

layer (top), the nuclei of these superficial cells exhibit which of the following cytologic features?



- (A) Karyolysis
- (B) Karyorrhexis
- (C) Pyknosis
- (D) Segmentation
- (E) Viral inclusion bodies

16 A 30-year-old woman suffers a tonic-clonic seizure and presents with delirium and hydrophobia. The patient states that she was bitten on the hand by a bat about 1 month ago. The patient subsequently dies of respiratory failure. Viral particles are found throughout the brainstem and cerebellum at autopsy. In addition to direct viral cytotoxicity, the necrosis of virally infected neurons in this patient was mediated primarily by which of the following mechanisms?

- (A) Histamine release from mast cells
- (B) Humoral and cellular immunity
- (C) Neutrophil-mediated phagocytosis
- (D) Release of oxygen radicals from macrophages
- (E) Vasoconstriction and ischemia

17 A 52-year-old woman loses her right kidney following an automobile accident. A CT scan of the abdomen 2 years later shows marked enlargement of the left kidney. The renal enlargement is an example of which of the following adaptations?

- (A) Atrophy
- (B) Dysplasia
- (C) Hyperplasia
- (D) Hypertrophy
- (E) Metaplasia

18 An 82-year-old man has profound bleeding from a peptic ulcer and dies of hypovolemic shock. The liver at autopsy displays centrilobular necrosis. Compared to viable hepatocytes, the necrotic cells contain higher intracellular concentrations of which of the following?

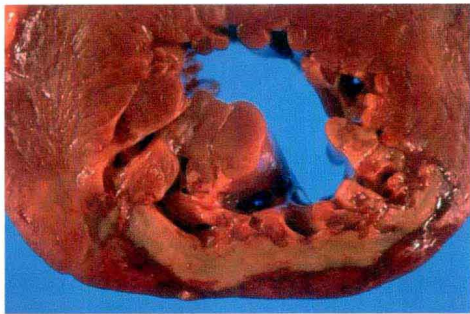
- (A) Calcium
- (B) Cobalt
- (C) Copper
- (D) Iron
- (E) Selenium

19 A 28-year-old woman is pinned by falling debris during a hurricane. An X-ray film of the leg reveals a compound fracture of the right tibia. The leg is immobilized in a cast for 6 weeks.

When the cast is removed, the patient notices that her right leg is weak and visibly smaller in circumference than the left leg. Which of the following terms best describes this change in the patient's leg muscle?

- (A) Atrophy
- (B) Hyperplasia
- (C) Metaplasia
- (D) Ischemic necrosis
- (E) Irreversible cell injury

- 20** A 70-year-old man is hospitalized after suffering a mild stroke. While in the hospital, he suddenly develops crushing substernal chest pain. Analysis of serum proteins and ECG confirm a diagnosis of acute myocardial infarction. The patient subsequently develops an arrhythmia and expires. A cross section of the left ventricle at autopsy is shown in the image. Histologic examination of the affected heart muscle would demonstrate which of the following morphologic changes?

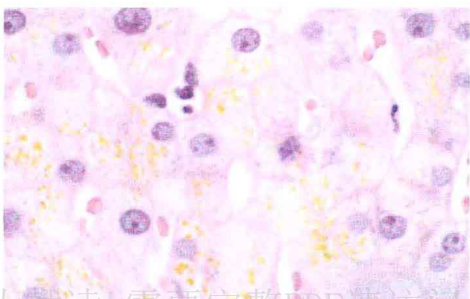


- (A) Caseous necrosis
- (B) Coagulative necrosis
- (C) Fat necrosis
- (D) Fibrinoid necrosis
- (E) Liquefactive necrosis

- 21** Which of the following histologic features would provide definitive evidence of necrosis in the myocardium of the patient described in Question 20?

- (A) Disaggregation of polyribosomes
- (B) Increased intracellular volume
- (C) Influx of lymphocytes
- (D) Mitochondrial swelling and calcification
- (E) Nuclear fragmentation

- 22** A 90-year-old woman with mild diabetes and Alzheimer disease dies in her sleep. At autopsy, hepatocytes are noted to contain golden cytoplasmic granules that do not stain with Prussian blue. Which of the following best accounts for pigment accumulation in the liver of this patient?

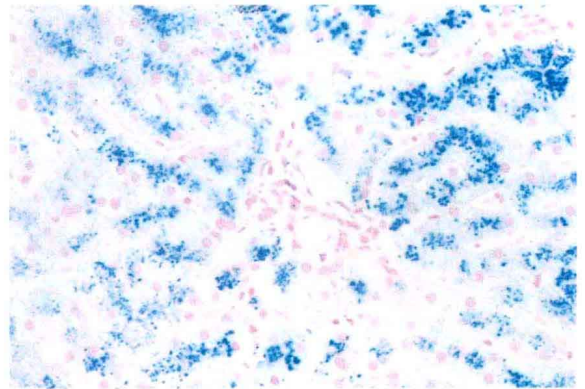


- (A) Advanced age
- (B) Alzheimer disease
- (C) Congestive heart failure
- (D) Diabetic ketoacidosis
- (E) Hereditary hemochromatosis

- 23** Which of the following mechanisms of disease best describes the pathogenesis of pigment accumulation in hepatocytes in the patient described in Question 22?

- (A) Degradation of melanin pigments
- (B) Inhibition of glycogen biosynthesis
- (C) Malabsorption and enhanced deposition of iron
- (D) Peroxidation of membrane lipids
- (E) Progressive oxidation of bilirubin

- 24** A 45-year-old man presents with increasing abdominal girth and yellow discoloration of his skin and sclera. Physical examination reveals hepatomegaly and jaundice. A Prussian blue stain of a liver biopsy is shown in the image. What is the major intracellular iron storage protein in this patient's hepatocytes?



- (A) Bilirubin
- (B) Haptoglobin
- (C) Hemoglobin
- (D) Hemosiderin
- (E) Transferrin

- 25** A 60-year-old man with chronic cystitis complains of urinary frequency and pelvic discomfort. Digital rectal examination is unremarkable. Biopsy of the bladder mucosa reveals foci of glandular epithelium and chronic inflammatory cells. No cytologic signs of atypia or malignancy are observed. Which of the following terms best describes the morphologic response to chronic injury in this patient?

- (A) Atrophy
- (B) Dysplasia
- (C) Hyperplasia
- (D) Hypertrophy
- (E) Metaplasia

- 26** A 60-year-old man is rushed to the hospital with acute liver failure. He undergoes successful orthotopic liver transplantation; however, the transplanted liver does not produce much bile for the first 3 days. Poor graft function in this patient is thought to be the result of "reperfusion injury." Which of the following substances was the most likely cause of reperfusion injury in this patient's transplanted liver?

- (A) Cationic proteins
- (B) Free ferric iron
- (C) Hydrochlorous acid
- (D) Lysosomal acid hydrolases
- (E) Reactive oxygen species

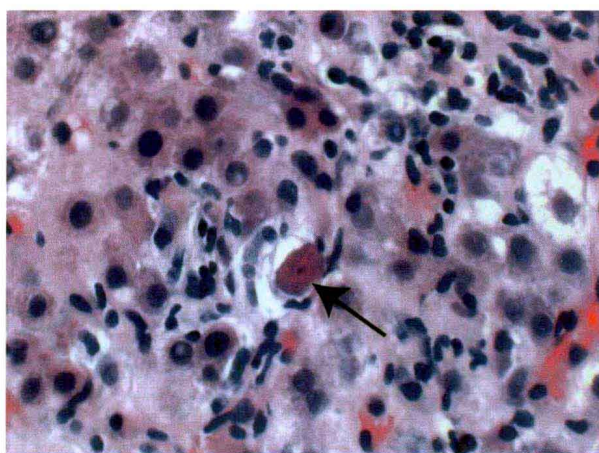
27 A 68-year-old woman with a history of hyperlipidemia dies of cardiac arrhythmia following a massive heart attack. Peroxidation of which of the following molecules was primarily responsible for causing the loss of membrane integrity in cardiac myocytes in this patient?

- (A) Cholesterol
- (B) Glucose transport proteins
- (C) Glycosphingolipids
- (D) Phospholipids
- (E) Sodium-potassium ATPase

28 A 22-year-old construction worker sticks himself with a sharp, rusty nail. Within 24 hours, the wound has enlarged to become a 1-cm sore that drains thick, purulent material. This skin wound illustrates which of the following morphologic types of necrosis?

- (A) Caseous necrosis
- (B) Coagulative necrosis
- (C) Fat necrosis
- (D) Fibrinoid necrosis
- (E) Liquefactive necrosis

29 A 42-year-old man undergoes liver biopsy for evaluation of the grade and stage of his hepatitis C virus infection. The biopsy reveals swollen (ballooned) hepatocytes and moderate lobular inflammatory activity (shown in the image). The arrow identifies an acidophilic (Councilman) body. Which of the following cellular processes best accounts for the presence of scattered acidophilic bodies in this liver biopsy?



- (A) Aggregation of intermediate filament proteins
- (B) Apoptotic cell death
- (C) Coagulative necrosis
- (D) Collagen deposition
- (E) Intracellular viral inclusions

30 Which of the following biochemical changes characterizes the formation of acidophilic bodies in the patient described in Question 29?

- (A) Fragmentation of DNA
- (B) Loss of tumor suppressor protein p53
- (C) Mitochondrial swelling
- (D) Synthesis of arachidonic acid
- (E) Triglyceride accumulation

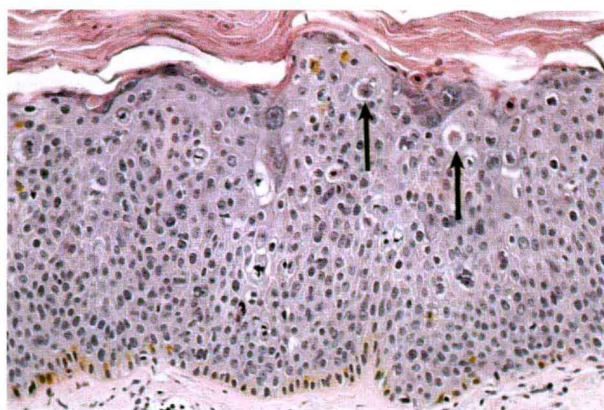
31 A 56-year-old woman with a history of hyperlipidemia and hypertension develops progressive, right renal artery stenosis. Over time, this patient's right kidney is likely to demonstrate which of the following morphologic adaptations to partial ischemia?

- (A) Atrophy
- (B) Dysplasia
- (C) Hyperplasia
- (D) Hypertrophy
- (E) Neoplasia

32 A 5-year-old boy suffers blunt trauma to the leg in an automobile accident. Six months later, bone trabeculae have formed within the striated skeletal muscle at the site of tissue injury. This pathologic condition is an example of which of the following morphologic adaptations to injury?

- (A) Atrophy
- (B) Dysplasia
- (C) Metaplasia
- (D) Metastatic calcification
- (E) Dystrophic calcification

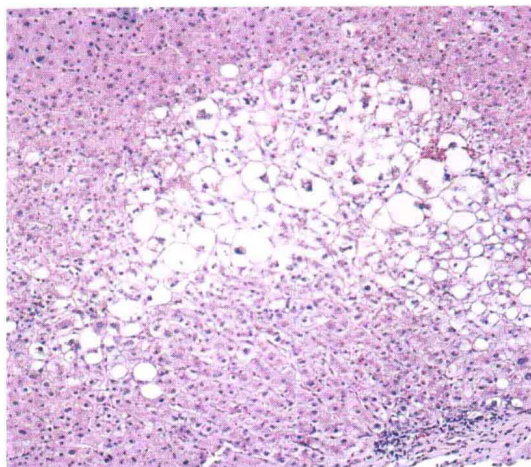
33 A 43-year-old man presents with a scaly, erythematous lesion on the dorsal surface of his left hand. A skin biopsy reveals atypical keratinocytes filling the entire thickness of the epidermis (shown in the image). The arrows point to apoptotic bodies. Which of the following proteins plays the most important role in mediating programmed cell death in this patient's skin cancer?



- (A) Catalase
- (B) Cytochrome c
- (C) Cytokeratins
- (D) Myeloperoxidase
- (E) Superoxide dismutase

34 A 16-year-old girl with a history of suicidal depression swallows a commercial solvent. A liver biopsy is performed to assess the degree of damage to the hepatic parenchyma. Histologic examination demonstrates severe swelling of the centrilobular hepatocytes (shown in the image). Which of

the following mechanisms of disease best accounts for the reversible changes noted in this liver biopsy?

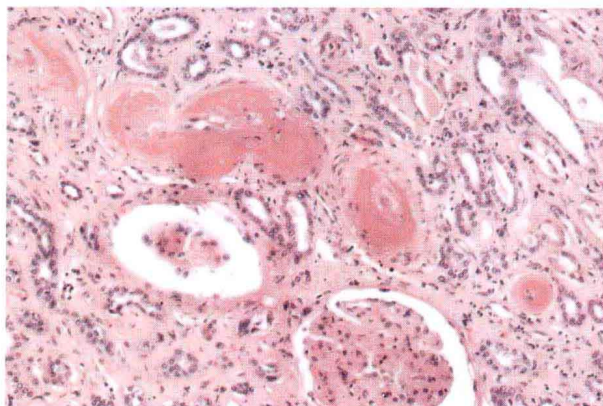


- (A) Decreased stores of intracellular ATP
- (B) Increased storage of triglycerides and free fatty acids
- (C) Intracytoplasmic rupture of lysosomes
- (D) Mitochondrial membrane permeability transition
- (E) Protein aggregation due to increased cytosolic pH

35 A 40-year-old man is pulled from the ocean after a boating accident and resuscitated. Six hours later, the patient develops acute renal failure. Kidney biopsy reveals evidence of karyorrhexis and karyolysis in renal tubular epithelial cells. Which of the following biochemical events preceded these pathologic changes?

- (A) Activation of Na^+/K^+ ATPase
- (B) Decrease in intracellular calcium
- (C) Decrease in intracellular pH
- (D) Increase in ATP production
- (E) Increase in intracellular pH

36 A 58-year-old man presents with symptoms of acute renal failure. His blood pressure is 220/130 mm Hg (malignant hypertension). While in the emergency room, the patient suffers a stroke and expires. Microscopic examination of the kidney at autopsy is shown in the image. Which of the following morphologic changes accounts for the red material in the wall of the artery?



- (A) Apoptosis
- (B) Caseous necrosis
- (C) Fat necrosis
- (D) Fibrinoid necrosis
- (E) Liquefactive necrosis

37 A 10-year-old girl presents with advanced features of progeria (patient shown in the image). This child has inherited mutations in the gene that encodes which of the following types of intracellular proteins?



- (A) Helicase
- (B) Lamin
- (C) Oxidase
- (D) Polymerase
- (E) Topoisomerase

38 A 32-year-old woman develops an Addisonian crisis (acute adrenal insufficiency) 3 months after suffering massive hemorrhage during the delivery of her baby. A CT scan of the abdomen shows small adrenal glands. Which of the following mechanisms of disease best accounts for adrenal atrophy in this patient?

- (A) Chronic inflammation
- (B) Chronic ischemia
- (C) Hemorrhagic necrosis
- (D) Lack of trophic signals
- (E) Tuberculosis

39 A 47-year-old man with a history of heavy smoking complains of chronic cough. A "coin lesion" is discovered in his right upper lobe on chest X-ray. Bronchoscopy and biopsy fail to identify a mass, but the bronchial mucosa displays squamous metaplasia. What is the most likely outcome of this morphologic adaptation if the patient stops smoking?

- (A) Atrophy
- (B) Malignant transformation
- (C) Necrosis and scarring
- (D) Persistence throughout life
- (E) Reversion to normal

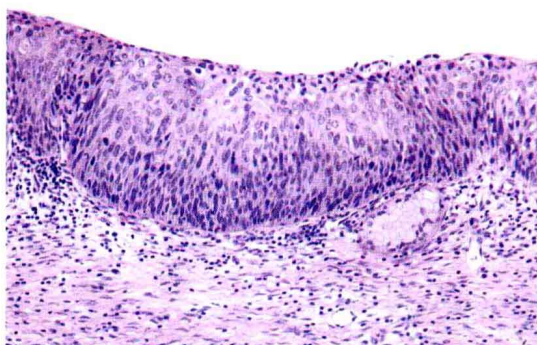
40 A 60-year-old farmer presents with multiple patches of discoloration on his face. Biopsy of lesional skin reveals actinic keratosis. Which of the following terms best describes this response of the skin to chronic sunlight exposure?

- (A) Atrophy
- (B) Dysplasia
- (C) Hyperplasia
- (D) Hypertrophy
- (E) Metaplasia

41 A 59-year-old woman smoker complains of intermittent blood in her urine. Urinalysis confirms 4+ hematuria. A CBC reveals increased red cell mass (hematocrit). A CT scan demonstrates a 3-cm renal mass, and a CT-guided biopsy displays renal cell carcinoma. Which of the following cellular adaptations in the bone marrow best explains the increased hematocrit in this patient?

- (A) Atrophy
- (B) Dysplasia
- (C) Hyperplasia
- (D) Hypertrophy
- (E) Metaplasia

42 A 33-year-old woman has an abnormal cervical Pap smear. A cervical biopsy reveals that the epithelium lacks normal polarity (shown in the image). Individual cells display hyperchromatic nuclei, a larger nucleus-to-cytoplasm ratio, and disorderly tissue arrangement. Which of the following adaptations to chronic injury best describes these changes in the patient's cervical epithelium?



- (A) Atrophy
- (B) Dysplasia
- (C) Hyperplasia
- (D) Hypertrophy
- (E) Metaplasia

43 A 24-year-old woman accidentally ingests carbon tetrachloride (CCl_4) in the laboratory and develops acute liver failure. Which of the following cellular proteins was directly involved in the development of hepatotoxicity in this patient?

- (A) Acetaldehyde dehydrogenase
- (B) Alcohol dehydrogenase
- (C) Glucose-6-phosphate dehydrogenase
- (D) Mixed function oxygenase
- (E) Superoxide dismutase

44 A 30-year-old woman presents with a 2-month history of fatigue, mild fever, and an erythematous scaling rash. She also notes joint pain and swelling, primarily involving the small bones of her fingers. Physical examination reveals erythematous plaques with adherent silvery scales that induce punctate bleeding points when removed. Biopsy of lesional skin reveals markedly increased thickness of the epidermis (shown in the image). Which of the following terms best describes this adaptation to chronic injury in this patient with psoriasis?



- (A) Atrophy
- (B) Dysplasia
- (C) Hyperplasia
- (D) Hypertrophy
- (E) Metaplasia

45 A 24-year-old woman with chronic depression ingests a bottle of acetaminophen tablets. Two days later, she is jaundiced (elevated serum bilirubin) and displays symptoms of encephalopathy, including impairment in spatial perception. In the liver, toxic metabolites of acetaminophen are generated by which of the following organelles?

- (A) Golgi apparatus
- (B) Mitochondria
- (C) Nucleus
- (D) Peroxisomes
- (E) Smooth endoplasmic reticulum

46 A 45-year-old woman presents with a 2-month history of fatigue and recurrent fever. She also complains of tenderness below the right costal margin and dark urine. Physical examination reveals jaundice and mild hepatomegaly. The serum is positive for hepatitis B virus antigen. Which of the following best describes the mechanism of indirect virus-mediated hepatocyte cell death in this patient?

- (A) Accumulation of abnormal cytoplasmic proteins
- (B) Immune recognition of viral antigens on the cell surface
- (C) Generation of cytoplasmic free radicals
- (D) Impaired plasma membrane Na^+/K^+ ATPase activity
- (E) Interference with cellular energy generation

- 47** You are asked to present a grand rounds seminar on the role of abnormal proteins in disease. In this connection, intracellular accumulation of an abnormally folded protein plays a role in the pathogenesis of which of the following diseases?
- (A) AA amyloidosis
 - (B) AL amyloidosis
 - (C) α_1 -Antitrypsin deficiency
 - (D) Gaucher disease
 - (E) Tay-Sachs disease
- 48** A 38-year-old woman shows evidence of early cataracts, hair loss, atrophy of skin, osteoporosis, and accelerated atherosclerosis. This patient has most likely inherited mutations in both alleles of a gene that encodes which of the following types of intracellular proteins?
- (A) Deaminase
 - (B) Helicase
 - (C) Oxidase
 - (D) Polymerase
 - (E) Topoisomerase
- 49** A 28-year-old man with a history of radiation/bone marrow transplantation for leukemia presents with severe diarrhea. He subsequently develops septic shock and expires. Microscopic examination of the colon epithelium at autopsy reveals numerous acidophilic bodies and small cells with pyknotic nuclei. Which of the following proteins most likely played a key role in triggering radiation-induced cell death in this patient's colonic mucosa?
- (A) Cytochrome P450
 - (B) β -Catenin
 - (C) E-Cadherin
 - (D) P-Selectin
 - (E) p53

ANSWERS

- 1 The answer is C: Hyperplasia.** Hyperplasia is defined as an increase in the number of cells in an organ or tissue. Like hypertrophy (choice D), it is often a response to trophic signals or increased functional demand and is commonly a normal process. Erythroid hyperplasia is typically seen in people living at high altitude. Low oxygen tension evokes the production of erythropoietin, which promotes the survival and proliferation of erythroid precursors in the bone marrow. The cellular and molecular mechanisms that are responsible for hyperplasia clearly relate to the control of cell proliferation (i.e., cell cycle). None of the other choices describe increased numbers of cells.

Diagnosis: Erythropoiesis, hyperplasia

- 2 The answer is C: Fat necrosis.** Saponification of fat derived from peripancreatic fat cells exposed to pancreatic enzymes is a typical feature of fat necrosis. Lipase, released from pancreatic acinar cells during an attack of acute pancreatitis, hydrolyzes fat into fatty acids and glycerol. Free fatty acids bind with calcium to form soaps, which is a process known as saponification. Entry of calcium ions into the injured tissue reduces the level of calcium in blood. Hypocalcemia is, therefore, a typical finding in patients who had a recent bout of

acute pancreatitis. Patients with acute pancreatitis experience sudden-onset abdominal pain, distention, and vomiting. The other choices are not typically seen in peripancreatic tissue following acute pancreatitis, although liquefactive necrosis (choice E) may be observed.

Diagnosis: Acute pancreatitis

- 3 The answer is C: Glandular metaplasia.** The major adaptive responses of cells to sublethal injury are atrophy, hypertrophy, hyperplasia, metaplasia, dysplasia, and intracellular storage. Metaplasia is defined as the conversion of one differentiated cell pathway to another. In this case, the esophageal squamous epithelium is replaced by columnar epithelium as a result of chronic gastroesophageal reflux. The lesion is characterized histologically by intestine-like epithelium composed of goblet cells and cells similar to those of incompletely intestinalized gastric mucosa. Squamous metaplasia (choice E) occurs in the bronchial epithelium of smokers, among other examples. Choices A, B, and D are preneoplastic changes that are most often described in the uterine endometrium of postmenopausal women.

Diagnosis: Barrett esophagus, metaplasia

- 4 The answer is D: Metastatic calcification.** Metastatic calcification is associated with an increased serum calcium concentration (hypercalcemia). Almost any disorder that increases serum calcium levels can lead to calcification in the alveolar septa of the lung, renal tubules, and blood vessels. The patient in this case had a parathyroid adenoma that produced large quantities of parathyroid hormone. Other examples of metastatic calcification include multiple opacities in the cornea of a child given large amounts of vitamin D and partially calcified alveolar septa in the lungs of a patient with breast cancer metastatic to bone. Breast cancer metastases to bone are often osteolytic and, therefore, accompanied by hypercalcemia. Dystrophic calcification (choice B) has its origin in direct cell injury. Arteriosclerosis (choice A) is an example of dystrophic calcification.

Diagnosis: Hyperparathyroidism, metastatic calcification

- 5 The answer is B: Atrophy.** Clinically, atrophy is recognized as diminution in the size or function of an organ. It is often seen in areas of vascular insufficiency or chronic inflammation and may result from disuse. Atrophy may be thought of as an adaptive response to stress, in which the cell shuts down its differentiated functions. Reduction in the size of an organ may reflect reversible cell atrophy or may be caused by irreversible loss of cells. For example, atrophy of the brain in this patient with Alzheimer disease is secondary to extensive cell death, and the size of the organ cannot be restored. This patient's brain shows marked atrophy of the frontal lobe. The gyri are thinned, and sulci are widened. Anaplasia (choice A) represents lack of differentiated features in a neoplasm.

Diagnosis: Alzheimer disease, atrophy

- 6 The answer is A: Abnormal pattern of cellular maturation.** Cells that compose an epithelium exhibit uniformity of size and shape, and they undergo maturation in an orderly fashion (e.g., from plump basal cells to flat superficial cells in a squamous epithelium). When we speak of dysplasia, we mean

that this regular appearance is disturbed by (1) variations in the size and shape of the cells; (2) enlargement, irregularity, and hyperchromatism of the nuclei; and (3) disorderly arrangement of the cells within the epithelium. Dysplasia of the bronchial epithelium is a reaction of respiratory epithelium to carcinogens in tobacco smoke. It is potentially reversible if the patient stops smoking but is considered preneoplastic and may progress to carcinoma. Choices B, D, and E are not preneoplastic changes. Invasiveness (choice C) connotes malignant behavior.

Diagnosis: Pneumonia, dysplasia

- 7 The answer is D: mRNA.** Hypertrophic cardiac myocytes have more cytoplasm and larger nuclei than normal cells. Although the elucidation of the cellular and molecular mechanisms underlying the hypertrophic response is still actively pursued, it is clear that the final steps include increases in mRNA, rRNA, and protein. Hypertrophy results from transcriptional regulation. Aneuploidy (choice A) is not a feature of myofiber hypertrophy. Water influx (choice E), which is typical of hydropic swelling in acute injury, is not a common feature of hypertrophy.

Diagnosis: Hypertrophic heart disease, hypertrophy

- 8 The answer is B: Dystrophic calcification.** Dystrophic calcification reflects underlying cell injury. Serum levels of calcium are normal, and the calcium deposits are located in previously damaged tissue. Intrauterine *Toxoplasma* infection affects approximately 0.1% of all pregnancies. Acute encephalitis in the fetus afflicted with TORCH syndrome may be associated with foci of necrosis that become calcified. Microcephaly, hydrocephalus, and microgyria are frequent complications of these intrauterine infections. Metastatic calcification (choice D) reflects an underlying disorder in calcium metabolism.

Diagnosis: Dystrophic calcification

- 9 The answer is D: Plasma membrane sodium transport.** Hydropic swelling reflects acute, reversible (sublethal) cell injury. It results from impairment of cellular volume regulation, a process that controls ionic concentrations in the cytoplasm. This regulation, particularly for sodium, involves (1) the plasma membrane, (2) the plasma membrane sodium pump, and (3) the supply of ATP. Injurious agents may interfere with these membrane-regulated processes. Accumulation of sodium in the cell leads to an increase in water content to maintain isosmotic conditions, and the cell then swells. Lipid peroxidation (choice B) is often a feature of irreversible cell injury. The other choices are unrelated to volume control.

Diagnosis: Acute reversible injury

- 10 The answer is C: Intermediate filaments.** Hyaline is a term that refers to any material that exhibits a reddish, homogeneous appearance when stained with hematoxylin and eosin (H&E). Standard terminology includes hyaline arteriosclerosis, alcoholic hyaline in the liver, hyaline membranes in the lung, and hyaline droplets in various cells. Alcoholic (Mallory) hyaline is composed of cytoskeletal intermediate filaments (cytokeratins), whereas pulmonary hyaline membranes consist of plasma proteins deposited in alveoli. Structurally abnormal α_1 -antitrypsin molecules (choice A) accumulate in

the liver of patients with α_1 -antitrypsin deficiency. α -Synuclein (choice E) accumulates in neurons in the substantia nigra of patients with Parkinson disease.

Diagnosis: Alcoholic liver disease

- 11 The answer is A: Anthracosis.** Anthracosis refers to the storage of carbon particles in the lung and regional lymph nodes. These particles accumulate in alveolar macrophages and are also transported to hilar and mediastinal lymph nodes, where the indigestible material is stored indefinitely within tissue macrophages. Although the gross appearance of the lungs of persons with anthracosis may be alarming, the condition is innocuous. Workers who mine hard coal (anthracite) develop pulmonary fibrosis, owing to the presence of toxic/fibrogenic dusts such as silica. This type of pneumoconiosis is more properly classified as anthracosilicosis. Hemosiderosis (choice C) represents intracellular storage of iron (hemosiderin). The other choices are not associated with dark pigmentation in the lung.

Diagnosis: Pneumoconiosis, anthracosis

- 12 The answer is C: Hyperplasia.** Infants of diabetic mothers show a 5% to 10% incidence of major developmental abnormalities, including anomalies of the heart and great vessels and neural tube defects. The frequency of these lesions relates to the control of maternal diabetes during early gestation. During fetal development, the islet cells of the pancreas have proliferative capacity and respond to increased demand for insulin by undergoing physiologic hyperplasia. Fetuses exposed to hyperglycemia in utero may develop hyperplasia of the pancreatic β cells, which may secrete insulin autonomously and cause hypoglycemia at birth. Metaplasia (choice D) is defined as the conversion of one differentiated cell pathway to another.

Diagnosis: Diabetes mellitus

- 13 The answer is E: Liquefactive necrosis.** When the rate of dissolution of the necrotic cells is faster than the rate of repair, the resulting morphologic appearance is termed liquefactive necrosis. The polymorphonuclear leukocytes of the acute inflammatory reaction are endowed with potent hydrolases that are capable of digesting dead cells. A sharply localized collection of these acute inflammatory cells in response to a bacterial infection produces rapid death and dissolution of tissue. The result is often an abscess defined as a cavity formed by liquefactive necrosis in a solid tissue. Caseous necrosis (choice A) is seen in necrotizing granulomas. In coagulative necrosis (choice B), the outline of the cell is retained. Fat (choice C) is not present in the lung parenchyma. Fibrinoid necrosis (choice D) is seen in patients with necrotizing vasculitis.

Diagnosis: Pulmonary abscess, liquefactive necrosis

- 14 The answer is A: Caseous necrosis.** Caseous necrosis is a characteristic of primary tuberculosis, in which the necrotic cells fail to retain their cellular outlines. They do not disappear by lysis, as in liquefactive necrosis (choice E), but persist indefinitely as amorphous, coarsely granular, eosinophilic debris. Grossly, this debris resembles clumpy cheese, hence the name caseous necrosis. Primary tuberculosis is often asymptomatic or presents with nonspecific symptoms, such as low-grade fever, loss of appetite, and occasional spells of coughing. The

Ghon complex includes parenchymal consolidation and ipsilateral enlargement of hilar lymph nodes and is often accompanied by a pleural effusion. Fibrinoid necrosis (choice D) is seen in patients with necrotizing vasculitis.

Diagnosis: Tuberculosis, *Mycobacterium tuberculosis*

- 15 The answer is C: Pyknosis.** Coagulative necrosis refers to light microscopic alterations in dying cells. When stained with the usual combination of hematoxylin and eosin, the cytoplasm of a necrotic cell is eosinophilic. The nucleus displays an initial clumping of chromatin followed by its redistribution along the nuclear membrane. In pyknosis, the nucleus becomes smaller and stains deeply basophilic as chromatin clumping continues. Karyorrhexis (choice B) and karyolysis (choice A) represent further steps in the fragmentation and dissolution of the nucleus. These steps are not evident in the necrotic cells shown in this Pap smear.

Diagnosis: Cervical intraepithelial neoplasia, pyknosis

- 16 The answer is B: Humoral and cellular immunity.** Both humoral and cellular arms of the immune system protect against the harmful effects of viral infections. Thus, the presentation of viral proteins to the immune system immunizes the body against the invader and elicits both killer cells and the production of antiviral antibodies. These arms of the immune system eliminate virus-infected cells by either inducing apoptosis or directing complement-mediated cytolysis. In this patient, the rabies virus entered a peripheral nerve and was transported by retrograde axoplasmic flow to the spinal cord and brain. The inflammation is centered in the brainstem and spills into the cerebellum and hypothalamus. The other choices are seen in acute inflammation, but they do not represent antigen-specific responses to viral infections.

Diagnosis: Rabies

- 17 The answer is D: Hypertrophy.** Hypertrophy is a response to trophic signals or increased functional demand and is commonly a normal process. For example, if one kidney is rendered inoperative because of vascular occlusion, the contralateral kidney hypertrophies to accommodate increased demand. The molecular basis of hypertrophy reflects increased expression of growth-promoting genes (protooncogenes) such as *myc*, *fos*, and *ras*. Hyperplasia (choice C) of renal tubular cells may occur, but enlargement of the kidney in this patient is best referred to as hypertrophy (i.e., increased organ size and function).

Diagnosis: Hypertrophy

- 18 The answer is A: Calcium.** Coagulative necrosis is characterized by a massive influx of calcium into the cell. Under normal circumstances, the plasma membrane maintains a steep gradient of calcium ions, whose concentration in interstitial fluids is 10,000 times higher than that inside the cell. Irreversible cell injury damages the plasma membrane, which then fails to maintain this gradient, allowing the influx of calcium into the cell. The other choices would most likely be released upon cell death.

Diagnosis: Coagulative necrosis

- 19 The answer is A: Atrophy.** The most common form of atrophy follows reduced functional demand. For example, after

immobilization of a limb in a cast as treatment for a bone fracture, muscle cells atrophy, and muscular strength is reduced. The expression of differentiation genes is repressed. On restoration of normal conditions, atrophic cells are fully capable of resuming their differentiated functions; size increases to normal, and specialized functions, such as protein synthesis or contractile force, return to their original levels. Ischemic necrosis (choice D) is typically a complication of vascular insufficiency. Irreversible injury to skeletal muscle (choice E) would be an unlikely complication of bone fracture.

Diagnosis: Atrophy, bone fracture

- 20 The answer is B: Coagulative necrosis.** Ischemic necrosis of cardiac myocytes is the leading cause of death in the Western world. In brief, the interruption of blood supply to the heart decreases the delivery of O_2 and glucose. Lack of O_2 impairs mitochondrial electron transport, thereby decreasing ATP synthesis and facilitating the production of reactive oxygen species. Mitochondrial damage promotes the release of cytochrome *c* to the cytosol, and the cell dies. The morphologic appearance of the necrotic cell has traditionally been termed coagulative necrosis because of its similarity to the coagulation of proteins that occurs upon heating.

Diagnosis: Myocardial infarction, coagulative necrosis

- 21 The answer is E: Nuclear fragmentation.** Nuclear fragmentation (karyorrhexis and karyolysis) is a hallmark of coagulative necrosis. Choices A, B, and D are incorrect because they are features of both reversibly and irreversibly injured cells. Lymphocytes (choice C) are a hallmark of chronic inflammation.

Diagnosis: Myocardial infarction

- 22 The answer is A: Advanced age.** Substances that cannot be metabolized accumulate in cells. Examples include (1) endogenous substrates that are not processed because a key enzyme is missing (lysosomal storage diseases), (2) insoluble endogenous pigments (lipofuscin and melanin), and (3) exogenous particulates (silica and carbon). Lipofuscin is a "wear and tear" pigment of aging that accumulates in organs such as the brain, heart, and liver. None of the other choices are associated with lipofuscin accumulation.

Diagnosis: Aging, lipofuscin

- 23 The answer is D: Peroxidation of membrane lipids.** Lipofuscin is found in lysosomes and contains peroxidation products of unsaturated fatty acids. The presence of this pigment is thought to reflect continuing lipid peroxidation of cellular membranes as a result of inadequate defenses against activated oxygen radicals. None of the other mechanisms of disease leads to the formation and accumulation of lipofuscin granules.

Diagnosis: Lipofuscin, intracellular storage disorder

- 24 The answer is D: Hemosiderin.** Hemosiderin is a partially denatured form of ferritin that aggregates easily and is recognized microscopically as yellow-brown granules in the cytoplasm, which turn blue with the Prussian blue reaction. In hereditary hemochromatosis, a genetic abnormality of iron absorption in the small intestine, excess iron is stored mostly in the form of hemosiderin, primarily in the liver. Hemoglobin