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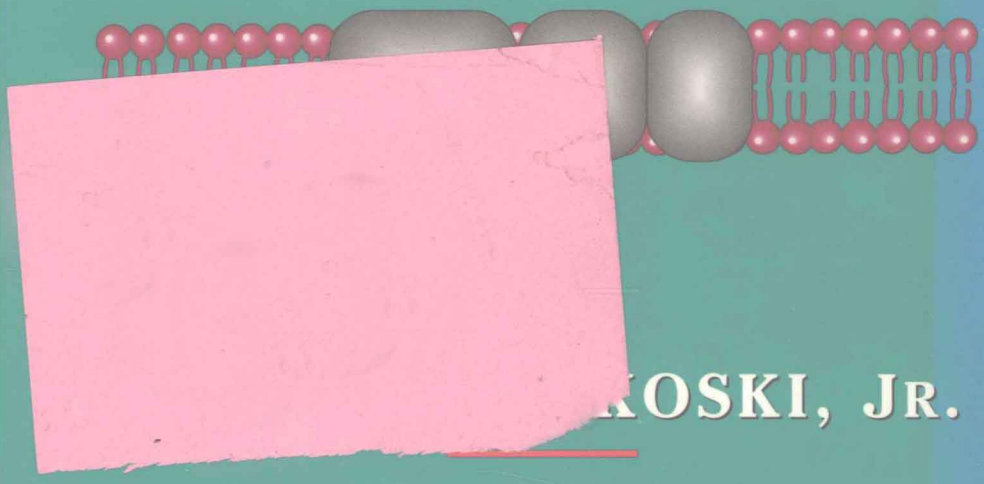
BIOCHEMISTRY REVIEW



ROSKI, JR.

JACK D. HERBERT

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BIOCHEMISTRY REVIEW

To those generations of students who
forced us to reexamine and then, chastened, to clarify
our own cloudy understanding of so much that we thought we knew.

PREFACE

This book provides a succinct outline review of the essentials of biochemistry and molecular biology, and each chapter contains review questions and explanations. Chapters 1 to 6 cover the fundamentals, Chapters 7 to 14 consider intermediary metabolism, Chapters 15 to 18 cover the area of molecular biology, and Chapters 19 to 24 cover specialized topics of cell biology. Chapter 25, on the integration of energy metabolism, considers metabolic regulation, feeding and fasting, and diabetes. Following Chapter 25, the comprehensive examination contains a randomized selection of biochemical items similar to those encountered in standardized examinations. The appendix consists of a glossary of selected biochemical and medical terms for students. We believe that instructors also will find the medical definitions helpful. The appendix additionally contains helpful hints for studying biochemistry and a list of items that students should master. The order of topics in this review parallels that found in *Biochemistry* (1996) by Robert Roskoski, Jr., also published by the W.B. Saunders Company.

On the inside of the front cover are printed lists of some general principles of biochemistry and general principles of bioenergetics. These principles are guidelines for understanding and analyzing reactions and metabolic pathways. Although the principles are numbered for reference, it is the concept and not the arbitrary number that is important. These concepts help make sense out of what is sometimes regarded as a tangled mass of interconnected metabolic reactions. Learning is facilitated by relating new material to the familiar. Once the concept behind each principle is mastered, it is easier for the student to relate the unfamiliar to these principles and to prototypical reactions and processes.

ORGANIZATION

The questions at the end of each chapter and in the comprehensive examination appear in the formats used on the United States Medical Licensing Examination. Some questions are based upon recall, enabling readers to assess the depth and extent of their knowledge. Other questions require the application of the fundamentals of biochemistry to understand clinical situations. Besides common clinical conditions such as diabetes, atherosclerosis, infectious diseases, and cancer, many questions are based upon metabolic abnormalities that accompany both common and rare inborn errors of metabolism. The emphasis, however, is not so much on rare diseases as on understanding and explaining the metabolic aberration that results from the metabolic disease.

CLINICAL CASES

The self-evaluation at the end of each chapter concludes with a narrative concerning a clinical situation and approximately four questions. These case presentations, which

are something extra (*lagniappe*), are designed to illustrate the importance of biochemistry in understanding the pathogenesis of disease. Because biochemistry is generally taught early in the course of study, care was taken not to make the cases too arcane. The specialized medical descriptions are explained where they are used, and the normal values for the clinical studies are noted directly in the text. The standard laboratory values are listed in *Cecil Textbook of Medicine* (1992), published by the W.B. Saunders Company. These narratives are longer and more intricate than are generally used in standard examinations. The approach and potential insight gained from considering these cases are designed to solidify biochemical and medical principles and approaches. These cases can also be used for practice- or problem-based learning.

CONVENTIONS

The tricarboxylic acid cycle, or citric acid cycle, is called the Krebs cycle in honor of its discoverer and because clinicians rarely use the former terms. The nonsystematic name glyceride is used for acylglycerol, again because clinicians prefer the term glyceride. The calorie is used as the nutritional unit of energy owing to its widespread use in the United States. Extensive use is made of the International System of units, however, and the joule is used as the unit of energy for all calculations involving bioenergetics.

ACKNOWLEDGMENTS

We thank Carol Vartanian for editing this book and for providing balanced feedback in a gracious and cordial manner. We are grateful to Dr. Ab Sadeghi-Nejad of Tufts University and the New England Medical Center for his valuable comments on the 25 clinical cases. We thank Martha Gay for editing the questions and answers. Finally, we credit Risa Clow, illustrator at the W.B. Saunders Company, for overseeing the art work, and William R. Schmitt, Editorial Manager at the W.B. Saunders Company, who served as acquisitions editor.

TO THE STUDENT

One principle not listed on the cover, but which is given in all of our classes, is that *biochemistry is fun!*

ROBERT ROSKOSKI, JR., M.D., Ph.D.
JACK D. HERBERT, Ph.D.

COMPANION TEXT

The material in this book complements that in *Biochemistry* (1996) by Robert Roskoski, Jr., published by the W.B. Saunders Company. The 25 chapters in this review parallel those of *Biochemistry.* The illustrations, explanations, and topics in the companion text are more comprehensive than those in this review. The companion text, however, lacks questions and answers, case studies, a comprehensive examination, study hints, and a biochemistry and medical glossary.

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CHAPTER TWENTY-TWO

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CHAPTER TWENTY-FIVE

CHAPTER ONE

CELLS: THE UNITS OF LIFE

SYNOPSIS

OBJECTIVES

1. To define biochemistry and describe the chemical composition of humans.
2. To define the salient features of metabolism.
3. To compare eukaryotic and prokaryotic cells.
4. To classify bacteria as gram positive and gram negative.
5. To compare DNA- and RNA-containing viruses.

Objective 1: To define biochemistry and describe the chemical composition of humans.

I. Definition of biochemistry
  A. Biochemistry includes the study of the molecular composition of living cells
    1. *All forms of life are constructed from fundamental units called cells* (PRINCIPLE 2 OF BIOCHEMISTRY)
      a. The molecules that make up cells and tissues of the body perform specific functions
        (1) **DNA** serves as the genetic repository
        (2) **RNA** transfers genetic information from DNA into protein
        (3) **Proteins** serve structural, catalytic, regulatory, and defensive roles
        (4) **Carbohydrates** play a structural role in cells and tissues and serve as a storage form of energy
        (5) **Lipids** play structural and regulatory roles in cells and serve as the main storage form of energy
      b. *Cells obey the laws of chemistry and physics* (PRINCIPLE 3 OF BIOCHEMISTRY)
    2. Membranes occur in all cells
      a. Biological membranes are made up of lipid bilayers and associated proteins
        (1) Proteins that are embedded in the lipid are called **integral** membrane proteins
        (2) Proteins bound at the surface of a membrane are called **peripheral** proteins
      b. Lipids and proteins can readily diffuse laterally in membranes, but they cannot easily go from one leaflet of the bilayer to the other (i.e., flip-flop is disallowed)
  B. Biochemistry also includes the study of the chemical reactions that biological compounds undergo and the regulation of these reactions
II. Composition of average human adults
  A. 55% Water
  B. 19% Protein
  C. 19% Fat
  D. 7% Mineral
  E. < 1% carbohydrate
  F. < 1% nucleic acid

Objective 2: To define the salient features of metabolism.

III. Metabolism
  A. Definitions
    1. **Metabolism** refers to all of the chemical reactions of an organism
    2. **Catabolism** refers to the degradation of large, complex molecules into smaller simple metabolites
    3. **Anabolism** refers to the biosynthetic conversion of smaller into larger molecules
    4. A **chemical reaction** is the process that converts one or more chemical compounds to other chemical compounds
    5. **Enzymes** are proteins that catalyze nearly all biochemical reactions (PRINCIPLE 5 OF BIOCHEMISTRY)
    6. **Ribozymes** are RNA molecules that catalyze a few reactions in non-humans
  B. Three stages of catabolism (Krebs's classification)
    1. Stage I is the hydrolytic breakdown of complex molecules into their building blocks
    2. Stage II is the conversion of the building blocks to acetyl coenzyme A
    3. Stage III is the oxidation of acetyl coenzyme A to carbon dioxide by the Krebs cycle and the synthesis of ATP by oxidative phosphorylation

C. Bioenergetics
1. Each step of metabolism is accompanied by an energy change
2. *Lipmann's law states that ATP serves as the common currency of energy exchange in all living systems* (PRINCIPLE 10 OF BIOCHEMISTRY)

Objective 3: To compare eukaryotic and prokaryotic cells.

IV. Eukaryotes
A. General properties
1. Structure
a. Eukaryotes have a well-defined **nucleus** surrounded by a nuclear membrane, and the cells are divided into several membrane-bounded compartments (Fig. 1–1)
(1) The nuclei of human somatic cells contain 23 pairs (46 total) of chromosomes
(2) Of these, 22 pairs are alike in males and females and are called autosomes
(3) The remaining pair are the sex chromosomes, denoted XX in females and XY in males
b. Human cells consist of a variety of subcellular components (Table 1–1)
(1) **Lysosomes,** which participate in the hydrolytic degradation of cellular macromolecules, contain **hexosaminidase A** (which is deficient in Tay-Sachs disease), **β-glucosidase** (which is deficient in Gaucher disease), and many other hydrolases
(2) The **endoplasmic reticulum** consists of rough and smooth components based on the presence or absence of ribosomes, respectively
(3) The **cytoskeleton,** which is responsible for the structural framework of the cell, is composed of microfilaments, intermediate filaments, and microtubules
(a) **Microfilaments** are made of actin and myosin
(b) Major classes of **intermediate filaments** include keratins, desmin, vimentin, neurofilaments, and glial filaments
(c) Tubulin makes up **microtubules,** flagella, and centrioles (centrioles function as organizing centers for the mitotic spindle during cell division)
2. Size
a. Most human cells are about $(20\ \mu m)^3$, although there is a considerable range in size
b. The mature red blood cell has a diameter of 7 μm (this value can be used to measure relative sizes by microscopy)
B. Cell division
1. Mitosis
a. Mitosis, which occurs in somatic cells, involves the production of daughter cells containing the diploid genome
b. Mitosis (M), which lasts for 1–2 hours, is the shortest phase of the cell cycle; the other phases are G_1, S, and G_2
(1) G_1 and G_2 are gaps, and S refers to the DNA synthesis phase; these three stages make up interphase

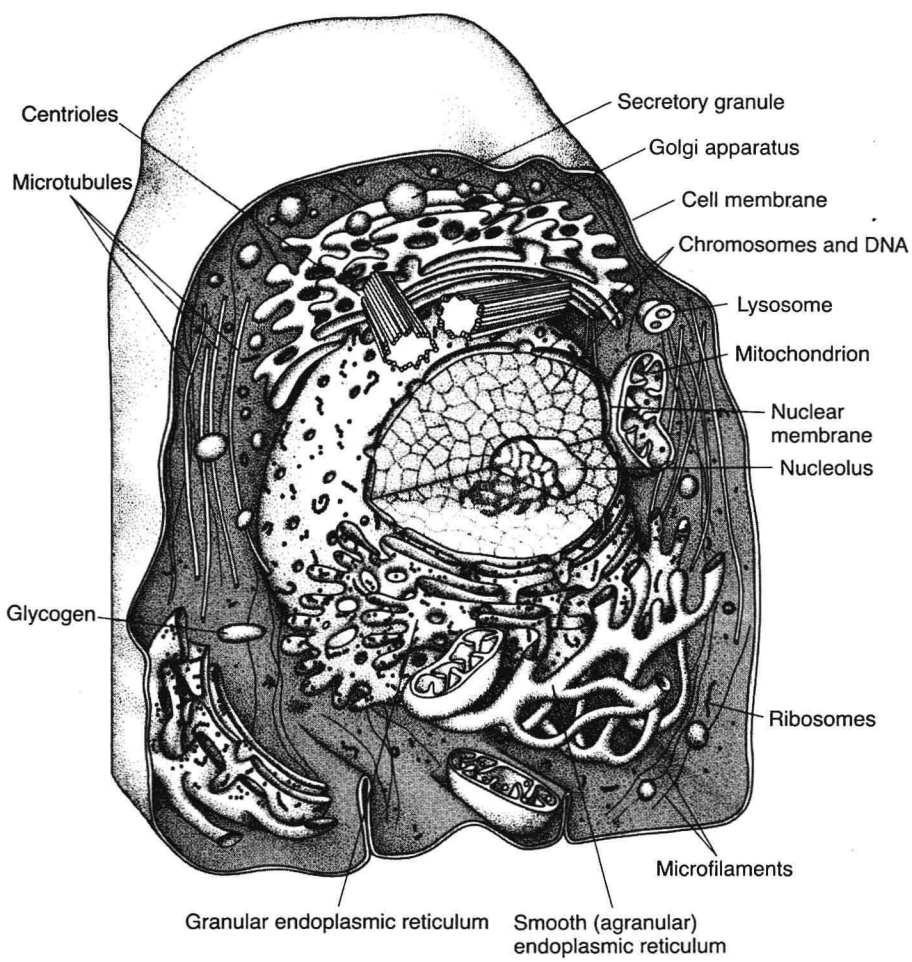


FIGURE 1–1. Diagram of a typical cell. Reproduced, with permission, from A. C. Guyton. *Textbook of Medical Physiology,* 8th ed. Philadelphia, W.B. Saunders Company, 1991, p. 10.

TABLE 1–1. Metabolic Properties of Animal Cell Components

Component	General Properties	Associated Biochemical Processes
Cytosol	Nonsedimentable	Glycolysis, gluconeogenesis, glycogenesis, glycogenolysis, pentose phosphate pathway; fatty acid, steroid, purine, pyrimidine synthesis; copper-zinc superoxide dismutase.
Lysosome	"Wastebasket" of the cell	Acidic compartment containing cathepsins (which degrade several classes of proteins), DNAse, RNAse, hexosaminidase A, β-glucosidase, and sphingomyelinase.
Mitochondrion	"Powerhouse" of the cell, major site of ATP formation	Krebs cycle, β-oxidation of fatty acids, oxidative phosphorylation, and pyruvate dehydrogenase activity; manganese superoxide dismutase.
Nucleus	Repository and expression of genes	DNA replication, RNA synthesis and processing.
Peroxisome	Hydrogen peroxide metabolism	Catalase, D- and L-amino acid oxidase.
Plasma membrane	Boundary between cell exterior and interior	Sodium-potassium ATPase, insulin and glucagon receptors, glucose translocases, LDL receptors, and γ-glutamyl transpeptidase.
Smooth endoplasmic reticulum	Complex lipid biosynthesis	Phospholipid synthesis, steroid hydroxylation, and cytochrome P-450 activity.
Rough endoplasmic reticulum and Golgi	Synthesis of membrane proteins and proteins for export	Protein synthesis and processing.

(2) The stages of mitosis include prophase, metaphase, anaphase, and telophase
(3) Chromosomes form discrete and identifiable bodies during metaphase

2. Meiosis
   a. Meiosis is the type of cell division that reduces the diploid number (2N) of chromosomes to the haploid number (1N) of the gamete (egg or sperm)
   b. The possession of three copies of human chromosome 21 (trisomy 21) results in Down syndrome and is the most common abnormality of the number of autosomes in live-born infants
   c. Trisomy results from meiotic nondisjunction
      (1) **Nondisjunction** is the failure of two members of a chromosome pair to disjoin during meiosis I, or of two chromatids of a chromosome to disjoin during meiosis II
      (2) Both chromosomes pass to one daughter cell and the other daughter cell receives neither

V. Prokaryotes
   A. General properties
      1. Structure
         a. Prokaryotes, including bacteria, lack a well-defined nucleus
         b. Bacterial cells are surrounded by a plasma membrane and cell wall
         c. Bacteria lack an intracellular membrane network, and they lack intracellular organelles
      2. Size
         a. Bacterial cells are much smaller than human cells
         b. The size of a typical bacterium is about 1 μm (diameter) by 2 μm (length)—about the size of a mitochondrion
   B. Cell division
      1. Under optimal nutritional conditions, prokaryotes can divide every 20 minutes
      2. Prokaryotes divide by binary fission

Objective 4: To classify bacteria as gram positive and gram negative.

VI. Bacteria
   A. Gram-positive bacteria
      1. The gram-positive bacteria have a thick cell wall that retains crystal violet
      2. Many common pathogens are gram-positive bacteria
         a. *Staphylococcus aureus* is a common cause of boils, wound infections, and pneumonia
         b. *Streptococcus pneumoniae,* which is a common cause of middle ear infection and meningitis, is the most common cause of gram-positive pneumonia
         c. *Streptococcus mutans* can produce dental caries
   B. Gram-negative bacteria
      1. The gram-negative bacteria have a thin outer membrane, a peptidoglycan layer, and an intermembrane space; lacking the thick cell wall, gram-negative organisms are unable to retain crystal violet
      2. Many common pathogens are gram-negative bacteria
         a. *Escherichia coli* can cause diarrhea, urinary tract infection, and peritonitis
         b. *Helicobacter pylori* is associated with gastritis and peptic ulcer
         c. *Haemophilus influenzae* is a common cause of meningitis, middle ear infection, pharyngitis, and pneumonia
         d. *Salmonella typhi* is the causative agent of typhoid fever
         e. *Chlamydia pneumoniae* can produce atypical pneumonia

Objective 5: To compare DNA- and RNA-containing viruses.

VII. Viruses
   A. All viruses are incapable of independent existence and are obligate cellular parasites
   B. **DNA viruses** have DNA as their genome
      1. Adenovirus is a common cause of upper respiratory and lower respiratory infections
      2. Hepatitis B virus is the causative agent of hepatitis B, which is common throughout the world
   C. **RNA viruses** have RNA as their genome
      1. Retroviruses, including HIV (the causative agent of AIDS), have an RNA genome and a DNA intermediate in their replication cycle
      2. Poliovirus is an RNA virus, but it lacks a DNA intermediate in its replication cycle

QUESTIONS

DIRECTIONS. (Items 1–7): Each of the numbered items or incomplete statements in this section is followed by answers or by completions of the statement. Select the ONE lettered answer or completion that is BEST in each case. Correct answers and explanations are given at the end of the chapter.

1. An individual with cholera can die within 24 hours because of the loss of which of the following body components?

   (A) Carbohydrate
   (B) Nucleic acid
   (C) Protein
   (D) Water
   (E) Lipid

2. Lipmann's law states that the common currency of energy exchange is

   (A) acetyl-CoA
   (B) ATP
   (C) glucose
   (D) heat
   (E) oxygen

3. Which of the following virus particles contains RNA?

   (A) Adenovirus
   (B) Hepatitis B virus
   (C) Herpes simplex
   (D) Human immunodeficiency virus (HIV)
   (E) Variola virus

4. Which of the following is a true statement regarding a composite virus containing the DNA from Epstein-Barr virus and the protein envelope of the varicella virus?

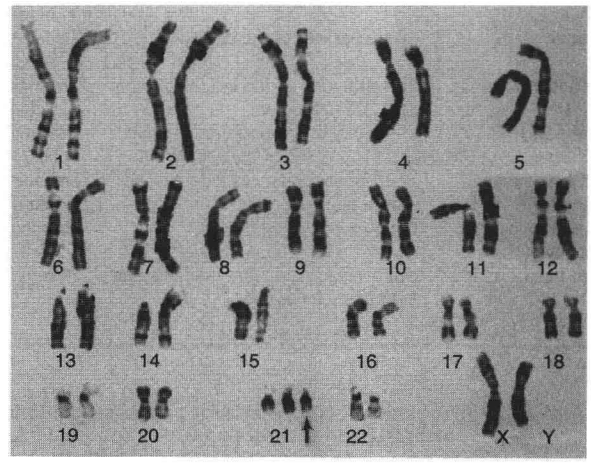
   (A) The progeny would be Epstein-Barr virus
   (B) The progeny would be varicella virus
   (C) The progeny would be a composite virus
   (D) The host-cell range of the composite virus would be the same as that of Epstein-Barr virus
   (E) Mutant forms of varicella virus would be formed

5. A 19-year-old woman in the third trimester of pregnancy develops pyuria, dysuria, and flank pain. The organism most likely to be isolated on urine culture is

   (A) *Escherichia coli*
   (B) *Neisseria gonorrhoeae*
   (C) *Staphylococcus aureus*
   (D) *Streptococcus mutans*
   (E) *Streptococcus pyogenes*

6. Which one of the following cellular mechanisms causes the production of cells with the karyotype illustrated at the top of the next column?

   (A) Cytokinesis (cell division) without karyokinesis (nuclear division)
   (B) Crossing-over of chromatids during mitosis
   (C) Nondisjunction during meiosis
   (D) Chromosomal translocation
   (E) Normal mitosis and meiosis



7. At the time when these chromosomes were harvested, the cell from which they were taken was in which of the following phases?

   (A) S phase
   (B) G_1 phase
   (C) G_2 phase
   (D) interphase
   (E) metaphase

DIRECTIONS. (Items 8–15): Each set of matching questions in this section consists of a list of lettered options followed by several numbered items. For each numbered item, select the ONE lettered option that is most closely associated with it. Each lettered option may be selected once, more than once, or not at all.

Items 8–12

(A) Cytosol
(B) Lysosome
(C) Mitochondrion
(D) Nucleus
(E) Peroxisome
(F) Plasma membrane
(G) Rough endoplasmic reticulum and Golgi
(H) Smooth endoplasmic reticulum

For each description of a biochemical process, select the most appropriate cellular component.

8. Major site of ATP production and the target of cyanide poisoning
9. Site of functional LDL receptor, which is missing or defective in familial hypercholesterolemia
10. Major site of catalase activity
11. Site of complex lipid biosynthesis and cytochrome P-450
12. Site of action of sphingomyelinase (defective in Niemann-Pick disease), a hydrolase with an acid pH optimum

Items 13–15

(A) *Bordetella pertussis*
(B) *Campylobacter jejuni*
(C) *Helicobacter pylori*
(D) *Legionella pneumophila*
(E) *Neisseria gonorrhoeae*
(F) *Staphylococcus aureus*
(G) *Streptococcus mutans*
(H) *Streptococcus pyogenes*

For each description, select the most appropriate bacterium.

13. Gram-positive bacterium that can cause dental caries
14. Gram-negative bacterium that can cause peptic ulcers
15. Gram-negative bacterium that can cause whooping cough

Items 16–18

History

The patient is a 54-old accountant who was in excellent health until 2 days ago when he noticed the onset of myalgias (muscle pain) and fever. He awoke on the second day with marked left anterior chest pain. The pain was greatest during inspiration. He recorded his temperature at 39.7 °C (103.5 °F).

Physical Examination

Temperature, 39.4 °C (103 °F); pulse, 95/min and regular; respirations, 22/min and shallow; blood pressure, 122/82 mm Hg. The patient appeared moderately ill and uncomfortable because of pain. The lungs were clear to percussion, but rales (abnormal sounds heard through a stethoscope) were heard over the left anterior chest.

Laboratory

Chest x-ray, left upper lobar infiltration
Electrocardiogram, normal
White blood cell count, 25,200/μL (normal, 4500–11,000/μL)
Neutrophils, 85% (normal, 54–62%)
Lymphocytes, 11% (normal, 23–33%)
Monocytes, 4% (normal, 3–7%)
Red blood count, 5.1 million/μL (normal ♂, 4.3–5.7 million/μL)
Hematocrit, 44% (normal ♂, 39–49%)
Arterial oxygen saturation, 96% (normal, 95–100%)
Lactate dehydrogenase (LDH), 260 U/L (normal, 210–380 U/L)
Creatine phosphokinase (CPK), 56 U/L (normal ♂, 40–175 U/L)
Aspartate aminotransferase (AST, SGOT), 18 U/L (normal, 10–30 U/L)
Serum glucose, 82 mg/dL (normal, 70–105 mg/dL)
Sputum yielded scant material that was taken for a Gram stain.
Blood cultures were also taken.

16. Which one of the following findings helps exclude diagnoses other than bacterial pneumonia that might be responsible for left anterior chest pain?
    (A) Chest x-ray
    (B) Creatine phosphokinase
    (C) Temperature
    (D) White blood cell count
    (E) Serum glucose

Items 17–18

(A) Adenovirus
(B) *Chlamydia pneumoniae*
(C) *Haemophilus influenzae*
(D) *Mycobacterium tuberculosis*
(E) *Streptococcus pneumoniae*

Correlate the most likely cause of typical bacterial pneumonia in this patient with the Gram stain finding.

17. Lancet-shaped gram-positive diplococci
18. Gram-negative organism

ANSWERS AND EXPLANATIONS

1. The answer is D: water. Death from cholera is a result of dehydration and circulatory collapse. Nearly all biochemical reactions occur in water, the most abundant constituent in the body (55% by mass). Protein (19%) and lipid are the most abundant organic constituents. The percentage of fat varies considerably in human populations with an average value of about 19%. Well-trained athletes have a body composition that is only 10% fat. The amount of carbohydrate and nucleic acid is small (≈1%). Of the inorganic minerals, calcium (a constituent of bones and teeth) is the most abundant. *Biochemistry,* p. 2.
2. The answer is B: ATP. ATP is the common currency of energy exchange for all organisms (Lipmann's law). Life is concerned with the production and utilization of ATP. Acetyl-CoA is the substrate for the Krebs cycle, and its oxidative metabolism provides reducing substrates for oxidative phosphorylation and ATP formation. Glucose and fats are fuels for oxidative metabolism, which generates ATP. Humans and other organisms are unable to use heat as a source of metabolic energy. The reaction of oxygen with reductants yields ATP, the biological unit of energy, but oxygen *per se* does not energize muscle contraction, ion transport, or anabolic reactions. *Biochemistry,* p. 3.
3. The answer is D: HIV. Although adenovirus, hepatitis B virus, herpes simplex, and variola virus (a poxvirus) contain DNA as their genetic material, a few viruses, such as human immunodeficiency virus (HIV) and poliovirus, contain RNA. HIV is replicated via a DNA intermediate. Because information is transferred from RNA to DNA

(opposite to the usual direction of information flow), HIV and related viruses are called retroviruses. Poliovirus is an RNA virus that does not go through a DNA intermediate, hence poliovirus is not a retrovirus. Hepatitis B virus is a DNA virus whose replication involves an RNA intermediate that serves as a template for DNA synthesis. *Biochemistry,* p. 12.

4. The answer is A: the progeny will be Epstein-Barr virus. It is possible to package viral nucleic acids in the protein coats of different viruses in favorable cases. It is the genetic material or nucleic acid that codes for the proteins required for replication; thus, it is the Epstein-Barr viral DNA that determines the progeny. Crick's law states that information cannot go from protein to nucleic acid (PRINCIPLE 25 OF BIOCHEMISTRY). The protein coat of a virus is recognized by plasma membrane receptors, and it is the coat protein that determines the host range that a viral particle can infect. *Biochemistry,* p. 270.
5. The answer is A: *Escherichia coli.* This bacterium, although a physiological inhabitant of the large bowel, can also cause disease, one of the most common of which is urinary tract infection, especially in women. The other bacteria listed are not common causes of urinary tract infection. *Pseudomonas aeruginosa* is another gram-negative organism that often causes urinary tract infection. *Biochemistry,* p. 11.
6. The answer is C: nondisjunction during meiosis. The most common mechanism for producing trisomy is the failure of sister chromatids to separate during meiosis (nondisjunction). Cytokinesis refers to the division of one cell into two cells, and karyokinesis is nuclear division. Crossing-over is the exchange of part of one homologous chromosome with another during meiosis. Translocation refers to the joining of a part of one chromosome to another, as occurs frequently in chronic myelogenous leukemia with the formation of the Philadelphia chromosome by reciprocal translocation of chromosomes 9 and 22. *Biochemistry,* p. 9.
7. The answer is E: metaphase. Prophase, metaphase, anaphase, and telophase are the subdivisions of mitosis when individual chromosomes are visible. Individual chromosomes are not visible during interphase. The subdivisions of interphase are G_1, S, and G_2. *Biochemistry,* p. 9.
8. The answer is C: mitochondrion. This is the location of the enzymes of the Krebs cycle, β-oxidation of fatty acids, and oxidative phosphorylation. The mitochondrion is the powerhouse of the cell. Cyanide is a potent inhibitor of cytochrome oxidase, a component of the mitochondrial electron transport chain. *Biochemistry,* p. 6.
9. The answer is F: plasma membrane. Familial hypercholesterolemia results from defects in the LDL receptor that is localized in the plasma membrane, and more than 20 separate mutations have been described. As a result of impaired uptake, affected individuals have elevated LDL in plasma. These patients have xanthomas (nodular swellings of various tendons due to cholesteryl ester deposition in macrophages) and premature atherosclerosis. The disease is autosomal dominant, and most patients are heterozygotes with about half the normal amount of functional receptors. *Biochemistry,* p. 200; *Nelson,* p. 355.
10. The answer is E: peroxisome. The peroxisome is an organelle that is active in hydrogen peroxide generation and metabolism. It contains D-amino acid oxidase and L-amino acid oxidase, which produce hydrogen peroxide, and the peroxisome contains catalase, the enzyme that converts hydrogen peroxide to oxygen and water. *Biochemistry,* p. 6.
11. The answer is H: smooth endoplasmic reticulum. This organelle is the membrane network inside the cell that does not have attached ribosomes. Many aspects of lipid metabolism involve this organelle because of the poor solubility of lipids in the hydrophilic cytosol and their greater solubility in the membrane. Cytochrome P-450, which is a family of more than 30 molecular entities, forms an electron transport chain that participates in the desaturation of fatty acids; steroid hormone hydroxylation; and barbiturate, drug, and ethanol metabolism. *Biochemistry,* p. 6.
12. The answer is B: lysosome. The lysosome contains the enzyme that is defective in Niemann-Pick and a wide variety of other lipid storage diseases. Because of the inability to degrade sphingolipid substrate, the lysosomes and cells become engorged and dysfunctional. Lysosomes are intracellular organelles that contain a variety of hydrolases (cathepsins or proteases, DNAse, RNAse, lipases, and glycosidases) that function at slightly acidic pH ($\approx$5). These enzymes catalyze the degradation of a variety of molecules and have gained the distinction of being the "wastebasket" of the cell because of their role in degrading cellular molecules. *Biochemistry,* p. 6.
13. The answer is G: *Streptococcus mutans.* This is a gram-positive organism, lacking an electron transport chain, that derives its energy by converting glucose to lactic acid by anaerobic glycolysis. Lactic acid dissolves enamel, producing dental caries. *Biochemistry,* p. 10.
14. The answer is C: *Helicobacter pylori.* Researchers recognized in the 1990s that this organism is a causative agent in some forms of peptic ulcer. The necessity of treating peptic ulcer with antibiotics in addition to histamine receptor blockers or proton pump inhibitors is undergoing evaluation. *Biochemistry,* p. 11.
15. The answer is A: *Bordetella pertussis.* DPT (diphtheria, pertussis, and tetanus) form the classical triad used in childhood immunization. Vaccines for polio and measles have been added to the triad. Pertussis toxin is a protein that catalyzes the ADP ribosylation and inactivation of the α-subunit of G_i, a G-protein involved in signal transduction. *Biochemistry,* p. 11.
16. The answer is B: creatine phosphokinase. Elevation of serum creatine phosphokinase occurs 6–12 hours after a myocardial infarction, and the enzyme remains elevated for a few days after the initial insult. Creatine phosphokinase is not present in lungs and is not elevated because of bacterial pneumonia. A normal electrocardiogram and normal creatine phosphokinase rule cardiac problems unlikely in this patient. An elevated white blood cell count with an increased percentage of polymorphonuclear leukocytes and fever occur with most systemic bacterial infections. The chest x-ray points to a pulmonary infection (pneumonia). Left anterior chest pain can also result from a myocardial infarction (heart attack), but such pain does not vary with respiration. A normal blood glucose does not aid in the diagnosis of bacterial pneumonia. Sometimes systemic infections will aggravate latent diabetes mellitus and produce an elevated serum glucose. *Biochemistry,* p. 64.
17. The answer is E: *Streptococcus pneumoniae.* This organism is a gram-positive agent that can cause pneumonia. Typical pneumonia is characterized by sudden onset, high fever, often accompanied by chills and rigors, ill appearance, and few or no upper respiratory symptoms. The elevated white blood count with an increase in the

proportion of segmented neutrophils is indicative of an acute inflammatory disease. *Biochemistry,* p. 11; *Cecil,* pp. 409 and 1608.

18. The answer is C: *Haemophilus influenzae.* This organism is gram negative and frequently causes typical pneumonia. Both gram-negative and gram-positive organisms can produce bacterial pneumonia as seen in this patient, and a Gram stain of the sputum, sputum culture, or blood cultures is performed to make the diagnosis. *Mycobacterium tuberculosis,* which gives a characteristic acid-fast stain, produces a pulmonary infection that is more chronic in its course and is not accompanied by high fever and a markedly elevated white blood cell count. The chest x-ray in tuberculosis characteristically reveals cavitary lesions, and these were not observed in this patient. *Chlamydia pneumoniae,* a gram-negative bacterium, and adenovirus (not a bacterium) can produce atypical pneumonia, a disease in which the signs and symptoms are less severe than described in this patient. *Biochemistry,* p. 11.

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