

Preface	xv		
Acknowledgments	xvii		
1. Cells: Structure and Functions	1	3. Amino Acids	19
Cells: Structures and Functions	1	L-α-Amino Acids: Structure	19
Properties of “Living” Cells	1	Classification	20
Evolution	2	Nonpolar Amino Acids	20
Structures and Organelles in Eukaryotic Cells	2	Acidic Amino Acids	22
The Plasma Membrane and Cytoskeleton	3	Basic Amino Acids	22
Structures and Organelles Involved in Synthesis, Transport, and Degradation of Molecules	4	Neutral Amino Acids	24
Mitochondria Provide Cells with Energy	5	Unusual Amino Acids	25
The Nucleus Controls a Cell’s Development and Chemical Activities	5	Amino Acids and Their Derivatives are Used as Drugs	25
The Body of an Adult Consists of More Than Two Hundred Specialized Types of Cells	6	Electrolyte and Acid–Base Properties	25
Stem Cells Are a Renewable Source of Specialized Cells	6	4. Three-Dimensional Structure of Proteins	29
2. Water, Acids, Bases, and Buffers	9	Covalent and Non-covalent Interactions	30
Properties of Water	9	Covalent Interactions	30
Hydrogen Bonding	9	Non-covalent Interactions–Attractive Forces	30
Physical Properties	10	Non-covalent Interactions	30
Solutes, Micelles, and Hydrophobic Interactions	10	Primary Structure	31
Colligative Properties	10	Peptide Bond	31
Dissociation of Water and the pH Scale	11	Secondary Structure	31
Buffers	12	α -Helix	31
Henderson–Hasselbalch Equation	12	β -Pleated Sheet	32
Buffer Systems of Blood and Exchange of O ₂ and CO ₂	14	β -Turns	32
Blood Buffer Calculations	16	Random Coil	32
Non-Bicarbonate Buffers in Blood	16	Supersecondary Structure	33
H⁺ Concentration and pH	17	Other Types of Secondary Structure	33
		Tertiary Structure	33
		Quaternary Structure	34
		Denaturation	34
		Protein Folding and Associated Diseases	34
		Proteolysis (Protein Degradation) by ATP-Dependent Ubiquitin-Proteasome Complex	35
		Components and the Properties of the Ubiquitin-Proteasome System	36
		5. Energetics of Biological Systems	39
		Thermodynamics	40
		Thermodynamic Relationships for Chemical Reactions	40

Physiological Concentrations and How ΔG can be <0 When $\Delta G^0 >0$	42	9. Heteropolysaccharides I: Glycoconjugates, Glycoproteins, and Glycolipids	75
Thermodynamic Relationships for Binding of Molecules to Each Other and to Cellular Receptors	42	Glycoproteins	75
Thermodynamic Relationships for Oxidation–Reduction (Redox) Reactions	43	Cell Membrane Constituents	78
Standard Free Energy of Hydrolysis of ATP	43	Cell-Surface Glycoproteins	81
Chemical Kinetics	44	Blood Group Antigens	82
Energetic Considerations of Chemical Kinetics	45	Serum Glycoproteins	82
6. Enzymes and Enzyme Regulation	47	Molecular Mimicry of Oligosaccharides and Host Susceptibility	83
Nomenclature	47	10. Connective Tissue: Fibrous and Non-Fibrous Proteins and Proteoglycans	85
Catalysis	48	Protein Fibers	86
Specificity of Enzyme Catalysis	48	Collagen	86
Active Site and Enzyme–Substrate Complex	48	Elastin	90
Factors Governing the Rate of Enzyme-Catalyzed Reactions	48	Proteoglycans	92
Michaelis–Menten Model for Enzyme-Catalyzed Reactions	49	Types, Structures, and Functions of Glycosaminoglycans	93
Kinetics of Enzymes Catalyzing Two-Substrate Reactions	51	Turnover of Proteoglycans and Role of Lysosomes	95
Inhibition	51	Mucopolysaccharidosis	96
Reversible Inhibition	51	Peptidoglycans	96
Use of Competitive Substrates for Treatment of Intoxication	54	Lectins	96
Irreversible Inhibition	54	11. Gastrointestinal Digestion and Absorption	97
Irreversible Proteinase Inhibitors and Their Clinical Significance	54	Anatomy and Physiology of the Gastrointestinal Tract	98
Mechanisms of Enzyme Action	55	Mouth and Esophagus	98
Coenzymes, Prosthetic Groups, and Cofactors	55	Stomach	98
Regulation	55	Small Intestine	98
Types of Regulation	56	Formation, Secretion, and Composition of Bile	99
Allosteric Enzyme Regulation	57	Exocrine Pancreatic Secretion	101
Kinetics of Allosteric Proteins	57	Large Intestine	102
7. Clinical Enzymology and Biomarkers of Tissue Injury	59	Gastrointestinal (GI) Hormones	102
Diagnosis and Prognosis of Disease	59	Digestion and Absorption of Major Food Substances	103
Factors Affecting Presence and Removal of Intracellular Enzymes from Plasma	60	Carbohydrates	103
Serum Markers in the Diagnosis of Tissue Damage	62	Disorders of Carbohydrate Digestion and Absorption	105
Myocardium	62	Proteins	105
Pancreas	63	Disorders of Protein Digestion and Absorption	106
Liver	64	Lipids	107
Enzymes as Analytical Reagents	64	Disorders of Lipid Digestion and Absorption	108
Enzymes as Therapeutic Agents	64	Absorption of Water and Electrolytes	111
8. Simple Carbohydrates	65	Disorders of Fluid and Electrolyte Absorption	111
Classification	66	Thermic Effect of Food	113
Monosaccharides	66		

12. Carbohydrate Metabolism I: Glycolysis and the Tricarboxylic Acid Cycle	115	14. Carbohydrate Metabolism II: Gluconeogenesis, Glycogen Synthesis and Breakdown, and Alternative Pathways	151
Glycolysis	115	Gluconeogenesis	152
Source and Entry of Glucose into Cells	116	Metabolic Role	152
Reactions of Glycolysis	117	Gluconeogenic Precursors	155
Phosphorylation of Glucose	118	Regulation of Gluconeogenesis	156
Alternative Substrates of Glycolysis	123	Abnormalities of Gluconeogenesis	156
Role of Anaerobic Glycolysis in Various Tissues and Cells	123	Glycogen Metabolism	157
Summary of Regulation of Glycolysis	124	Glycogen Synthesis	158
Glycolytic Enzyme Deficiencies in Erythrocytes	124	Glycogen Breakdown	159
Pyruvate Metabolism	125	Regulation of Glycogen Metabolism	159
Oxidation of Pyruvate to Acetyl-CoA	126	Glycogen Storage Diseases	159
Tricarboxylic Acid (TCA) Cycle	128	Alternative Pathways of Glucose	
Reactions of TCA Cycle	129	Metabolism and Hexose Interconversions	162
Stereochemical Aspects of the TCA Cycle	132	Glucuronic Acid Pathway	162
Amphibolic Aspects of the TCA Cycle	132	Fructose and Sorbitol Metabolism	162
Regulation of the TCA Cycle	133	Galactose Metabolism	163
Energetics of the TCA Cycle	133	Metabolism of Amino Sugars	165
13. Electron Transport Chain, Oxidative Phosphorylation, and Other Oxygen-Consuming Systems	135	Pentose Phosphate Pathway	165
Mitochondrial Structure and Properties	137	Phagocytosis and the Pentose Phosphate Pathway	168
Components of the Electron Transport Chain	138	15. Protein and Amino Acid Metabolism	169
Electron Transport Complexes	139	Essential and Nonessential Amino Acids	171
Formation of Reactive Oxygen Species	141	Quality and Quantity of Dietary Protein Requirement	171
Organization of the Electron Transport Chain	142	Protein Energy Malnutrition	171
Oxidative Phosphorylation	142	Transport of Amino Acids into Cells	172
Mechanisms of Oxidative Phosphorylation	143	General Reactions of Amino Acids	172
Uncoupling Agents of Oxidative Phosphorylation	143	Role of Organs in Amino Acid Metabolism	174
Mitochondrial Energy States	143	Metabolism of Ammonia	175
Energy-Linked Functions of Mitochondria Other Than ATP Synthesis	144	Urea Synthesis	176
Transport of Cytoplasmic NADH to Mitochondria	145	Metabolism of Some Individual Amino Acids	178
Role of Mitochondria in the Initiation of Programmed Cell Death Known as Apoptosis	145	Arginine	178
The Mitochondrial Genome (see website)	146	Metabolism and Synthesis of Nitric Oxide	178
Nuclear Control of Respiratory Chain Expression	147	Signal Transduction of NO	179
Mitochondrial Diseases	147	Disorders of Glycine Catabolism	181
Other Reducing-Equivalent Transport and Oxygen-Consuming Systems	147	Branched-Chain Amino Acids	182
Oxygen Consumption Linked to Production of Microbicidal Oxygen Species in Phagocytes	148	Sulfur-Containing Amino Acids	183
Protective Mechanisms for Oxygen Toxicity	149	16. Lipids I: Fatty Acids and Eicosanoids	191
Monooxygenases and Dioxygenases	150	Oxidation of Fatty Acids	192
		Activation of Fatty Acids	192
		Transport of Acyl-CoA to the Mitochondrial Matrix	193
		β -Oxidation	193
		Energetics of β -Oxidation	197
		Regulation of Fatty Acid Oxidation	197
		Peroxisomal Fatty Acid Oxidation	197

Other Pathways of Fatty Acid Oxidation	198	Hyperlipidemias	236
Propionyl-CoA Oxidation	198	Hypercholesterolemias	236
α -Oxidation	199	Hypolipidemias	236
Metabolism of Ketone Bodies	199	Atherosclerosis and Coronary Heart Disease	237
Physiological and Pathological Aspects of		Lipid-Lowering Methods	239
Metabolism of Ketone Bodies	200		
Synthesis of Long-Chain Saturated Fatty Acids	202	19. Contractile Systems	241
Sources of NADPH for Fatty Acid Synthesis	204	Introduction	242
Source and Transport of Acetyl-CoA	204	Muscle Systems	242
Regulation of Fatty Acid Synthase	204	Review of the Structure and Genesis	
Fatty Acid Elongation	205	of Muscle	242
Metabolism of Unsaturated Fatty Acids	205	Origin of Muscle Cells	242
Structure and Nomenclature of		Structure of Skeletal Muscle	243
Unsaturated Fatty Acids	205	Myofibrils	244
Functions of Unsaturated Fatty Acids	205	Sarcomeres and Costameres	244
Trans-Fatty Acids	206	Thin Myofilaments	244
Essential Fatty Acids	206	Thick Myofilaments	245
Deficiency of Essential Fatty Acids	206	Myofibrils Contain Numerous	
Metabolism of Eicosanoids	206	Accessory Proteins	246
		Muscle Function: Mechanism and	
		Control of Contraction	246
17. Lipids II: Phospholipids,		Mechanism of Muscle Contraction:	
Glycosphingolipids, and Cholesterol	209	Overview	246
Phospholipids	209	Mechanism of Contraction: Excitation/	
Phosphatidylcholines	210	Contraction Coupling	246
Phosphosphingolipids	212	Mechanism of Contraction: Activation of	
Phospholipids and Glycosphingolipids		Contraction	247
in Clinical Medicine	212	Mechanism of Contraction: Cross-Bridge	
Pulmonary Surfactant Metabolism		Cycling	247
and Respiratory Distress Syndrome	212	Relaxation	248
Biochemical Determinants of Fetal		Diversity and Plasticity in Skeletal Muscle	249
Lung Maturity	214	Multigene Families Encoding Muscle	
Cholesterol	214	Proteins	249
Conversion of Acetyl-CoA to HMG-CoA	215	Differentiation of Fiber Types and Muscle	
Conversion of HMG-CoA to Mevalonate	215	Plasticity	249
Conversion of Mevalonate to Isoprenyl		Energy Supply in Muscle	250
Pyrophosphate	219	Regulation of Smooth and Cardiac Muscle	252
Utilization of Cholesterol	219	Inherited Diseases of Muscle	253
Bile Acids	220	Non-Muscle Systems	254
Regulation of Bile Acid Synthesis	221	Actin	254
Disposition of Bile Acids in the Intestine		Cilia	255
and Their Enterohepatic Circulation	222	Drugs Affecting Microtubules	258
Bile Acid Metabolism and Clinical Medicine	223		
18. Lipids III: Plasma Lipoproteins	225	20. Perturbations of Energy Metabolism:	
Structure and Composition	226	Obesity and Diabetes Mellitus	261
Metabolism	229	Energy Metabolism	261
Chylomicrons	230	Mediators of Feeding Behavior	262
Very Low Density Lipoproteins (VLDL) and		Obesity	263
Formation of Low Density Lipoproteins (LDL)	230	Diabetes Mellitus	264
Low Density Lipoprotein Uptake	232	Endocrine Pancreas and Pancreatic	
High Density Lipoproteins	233	Hormones	265
Lipoproteins and Coronary Heart Disease (CHD),		Insulin	265
(also known as Coronary Artery Disease)	235	Diabetes Mellitus	271

21. Structure and Properties of DNA	275	Prokaryotic Transcription	305
Introduction	275	Lifetime of Prokaryotic mRNA	306
Components of DNA	275	Transcription in Eukaryotes	306
Base Pairing of Bases in DNA Double Helixes	275	Eukaryotic RNA Polymerases	306
Phosphodiester Backbone of DNA	276	RNA Polymerase II Promoters	307
Base Analogues	277	Eukaryotic mRNA Synthesis	307
Modifications of DNA Bases	278	Genetic Code	309
Physical and Chemical Structure of DNA	278	“Universal” Genetic Code	309
Conformational Changes of the DNA Double Helix	279	Attachment of Amino Acid to tRNA Molecule	310
Intercalating Agents	280	Initiator tRNA Molecules and Selection of Initiation Codon	311
Denaturation of DNA	280	Ribosomes	312
Renaturation of DNA	281	Chemical Composition of Prokaryotic Ribosomes	312
Chromosomes and Chromatin	281	Ribosomes are Ribozymes	312
Repetitive DNA Sequences	282	Chemical Composition of Eukaryotic Ribosomes	313
Recombinant DNA Technology	282	Protein Synthesis	313
Enzymes in Recombinant DNA Technology	283	Stages of Protein Synthesis	313
DNA Cloning Vectors	283	Role of GTP	315
Polymerase Chain Reaction (PCR)	283	Post-Translational Modification of Proteins	315
Nucleic Acid Hybridization	284	Coupled Transcription and Translation	316
Applications of Recombinant DNA Technology	285	Endoplasmic Reticulum	316
22. DNA Replication, Repair, and Mutagenesis	287	Compartment Disorders	318
General Features of DNA Replication	287	Inhibitors of Protein Synthesis and Related Disorders	318
DNA Replication is Semi-Conservative	287	24. Regulation of Gene Expression	321
DNA Replication is Bi-Directional	287	Introduction	321
DNA Replication is Semi-Discontinuous	289	Regulation of mRNA Synthesis	321
The Enzymology of DNA Replication	289	Gene Regulation in Prokaryotes	322
DNA Polymerases	289	Lactose (lac) Operon	322
Other Enzymes in DNA Replication	289	Tryptophan (Trp) Operon	324
Three Steps of DNA Replication: Initiation, Elongation, and Termination	290	Gene Regulation in Eukaryotes	326
Fidelity of DNA Replication	291	Mechanisms of Gene Regulation in Eukaryotes	326
Reverse Transcriptase	292	Chromatin Structure Remodeling and Genetic Imprinting (Epigenetic Regulation)	327
Eukaryotic DNA Replication	292	Genomic Imprinting and Epigenetics	328
Inhibitors of DNA Replication	294	Chromatin Remodeling by Covalent Histone Modifications	328
DNA Mutations and DNA Repair	294	Transcriptional Initiation by Transcription Factors	329
Types of Mutations	294	Regulation of Translation by miRNAs and siRNAs	330
Types of DNA Damage	295	Alternative RNA Splicing and Editing	332
Types of DNA Repair	295	25. Nucleotide Metabolism	333
Human Diseases of DNA Repair Deficiency	298	One-Carbon Metabolism	333
23. RNA and Protein Synthesis	301	Inhibitors of Dihydrofolate Reductase	335
Structure of RNA	302	Formation of One-Carbon Derivatives of Folate	336
Ribosomal RNA (rRNA)	302	Formation of 5-Phosphoribosyl-1-Pyrophosphate	336
Transfer RNA (tRNA)	302		
Other Non-Coding RNAs	303		
Messenger RNA	303		
Enzymatic Synthesis of RNA	304		

Biosynthesis of Purine Nucleotides	337	Carbon Dioxide (CO₂) Transport	360
<i>De Novo</i> Synthesis	337	Erythropoietin	361
Salvage Pathways	337	Inherited Disorders of Hemoglobin	
Dietary Purines	338	Structure and Synthesis	362
Conversion of Nucleoside Monophosphates to Diphosphates and Triphosphates	339	Normal Hemoglobins	362
Formation of Purine Deoxyribonucleotides	339	Thalassemias	363
Regulation of Purine Biosynthesis	341	Hemoglobinopathies	364
PRPP Synthetase Reaction	341	Derivatives of Hemoglobin	366
Amidophosphoribosyltransferase Reaction	341	Carbon Monoxide-Hemoglobin	366
Regulation of Formation of AMP and GMP from IMP	341		
Inhibitors of Purine Biosynthesis	342	27. Metabolism of Iron and Heme	369
Inhibitors of Folate Biosynthesis	342	Iron Metabolism	369
Inhibitors of Formation of IMP	342	Iron Absorption, Transport, Utilization, and Storage	369
Inhibitors of Formation of AMP and GMP	342	Plasma Iron Transport	370
Inhibitors of Multiple Steps: Purine Analogues	342	Storage of Iron	370
Inhibition of Conversion of Ribonucleoside Diphosphate to Deoxyribonucleoside Diphosphate	343	Coordinate Regulation of Iron Uptake and Storage in Non-Erythroid Cells	370
Catabolism of Purine Nucleotides	343	Alterations of Plasma Transferrin Concentration	371
Xanthine Oxidase Reduction	344	Regulation of Iron Metabolism	371
Disorders of Purine Nucleotide Metabolism	345	Disorders of Iron Metabolism	372
Gout	345	Iron Storage Disorders	373
Lesch-Nyhan Syndrome	347	Heme Biosynthesis	373
Adenine Phosphoribosyltransferase (APRT) Deficiency	347	Formation of δ -Aminolevulinic Acid	374
Adenosine Deaminase (ADA) Deficiency and Purine Nucleoside Phosphorylase (PNP) Deficiency	347	Formation of Porphobilinogen	374
Myoadenylate Deaminase Deficiency	348	Formation of Uroporphyrinogen III	374
Biosynthesis of Pyrimidine Nucleotides	348	Formation of Coproporphyrinogen III	374
<i>De Novo</i> Synthesis	349	Formation of Protoporphyrinogen IX	374
Formation of UMP	349	Formation of Protoporphyrin IX and Heme	374
Formation of Other Pyrimidine Nucleotides	350	Disorders of Heme Biosynthesis	375
Salvage Pathways	352	Heme Catabolism	376
Pyrimidine Analogues	352	Formation of Bilirubin	377
Regulation of <i>de Novo</i> Pyrimidine Biosynthesis	352	Circulatory Transport of Bilirubin	378
Coordination of Purine and Pyrimidine Nucleotide Biosynthesis	353	Hepatic Uptake, Conjugation, and Secretion of Bilirubin	379
Catabolism of Pyrimidine Nucleotides	354	Bilirubin in the Intestinal Tract	381
Abnormalities of Pyrimidine Metabolism	354	Disorders of Bilirubin Metabolism	381
		Unconjugated Hyperbilirubinemias	381
		Conjugated Hyperbilirubinemias	381
		Neonatal Hyperbilirubinemia	382
26. Hemoglobin	355	28. Endocrine Metabolism I: Introduction and Signal Transduction	383
Structure of Hemoglobins	356	Hormonal Amines	384
Globin Chains	356	Peptide, Protein, and Glycoprotein Hormones	384
Heme Group	357	Steroid Hormones	385
Functional Aspects of Hemoglobin	357	Organization of the Endocrine System	385
Oxygen Transport	357	Feedback Regulation of the Endocrine System	386
Mechanism of Oxygenation	358	Additional Properties of Hormones	386
Function, Metabolism, and Regulation of Organic Phosphates in Erythrocytes	360	Mechanism of Hormone Action and Signal Transduction	386

Types of Hormone Receptors	387	Adrenal Medulla	418
Nuclear Receptors	387	Regulation of Release	419
Steroid Hormone Receptors	388	Synthesis of Epinephrine	419
Cell Surface Receptors	389	Regulation of Catecholamine Secretion	420
G-Protein-Coupled Receptors (GPCR)		Biological Actions of Catecholamines	421
and G-Proteins	389	Disturbances in Adrenal Medullary Function	421
Heterotrimeric G-Protein-Coupled			
Adenylate Cyclase-cAMP System	389	31. Endocrine Metabolism IV:	
Abnormalities in Initiation of G-Protein Signal	391	Thyroid Gland	425
G-Protein-Coupled Phosphatidylinositol-		Introduction	426
Ca ²⁺ Pathway	392	Thyroid Hormone Synthesis	426
Mechanism of the Calcium Messenger		Regulation of Thyroid Hormone Synthesis	428
System	392	Transport and Metabolism of Thyroid	
Monomeric Guanine Nucleotide-Binding		Hormones	430
Proteins with GTPase Activity	392	Biological Actions of Thyroid Hormones	431
Receptors that Initiate Tyrosine Kinase (TK)		Physiological Effects	431
Activity	393		
Receptors for Insulin and Growth Factors	394	32. Endocrine Metabolism V:	
Receptors for Growth Hormone and Prolactin	394	Reproductive System	435
Non-Receptor Tyrosine Kinases	395	Sex Determination	436
Signal Transduction Mediated via the		Testes	437
Guanylyl Cyclases	395	Regulation of Spermatogenesis: Sertoli–	
		Neuroendocrine Axis	437
29. Endocrine Metabolism II:		Regulation of Testicular Steroidogenesis:	
Hypothalamus and Pituitary	397	Leydig–Neuroendocrine Axis	439
Hypothalamus	397	Metabolism of Testosterone	439
Neurohypophyseal Peptide Hormones	399	Biological Effects of Androgens	441
Neuroregulatory Peptides	400	Female Reproductive System	441
Pituitary Gland (Hypophysis)	400	Menstrual Cycle	441
Somatomammotropin	401	Endocrine Control of Folliculogenesis	441
Growth Hormone (GH Somatotropin)	401	Hormonal Control of Follicle Growth	442
Actions of GH	401	Hormonal Control of Luteal Function	442
Regulation of GH Release	402	Pregnancy	443
Insulin-Like Growth Factors (IGFs)	403	Human Placental Lactogen (hPL)	444
Disturbances in GH and IGF	403	Parturition	445
Prolactin	405	Lactation	445
Disturbances in Prolactin	405	Biological Effects of Estrogens	445
The Opiomelanocortin Family	405	Selective Estrogen Receptor Modulators (SERM)	446
Pituitary Independent Cutaneous POMC		Biological Effects of Progesterone	446
Production and Ultraviolet-induced			
Formation of Melanin	407	33. Immunology	449
Glycoprotein Hormones	407	Introduction	449
		What Generates the Immune Response?	450
30. Endocrine Metabolism III:		Components of the Immune System	450
Adrenal Glands	409	Communication within the Immune Response	452
Synthesis of Corticosteroids	411	HLA Class I Antigens	456
Regulation of Corticosteroid Secretion	413	The Complement System and Inflammation	457
Metabolism of Corticosteroids	415	Antibodies	460
Synthetic Corticosteroids	415	B Cell Development and Antibody Diversity	463
Biological Actions of Aldosterone	415	T Cell Development and T Cell Receptor	
Biological Actions of Cortisol	415	Diversity	465
Disturbances in Adrenocortical Function	417		

T Cell Activation and Differentiation	466	Calcium and Phosphate Homeostasis	490
The Adaptive Immune Response: Specific Antibody Response	467	Parathyroid Hormone-Related Protein	496
The Adaptive Immune Response: Cell Mediated Immune Response	470	Disorders of Calcium and Phosphorus Homeostasis	497
34. Biochemistry of Hemostasis	473	Magnesium	499
Hemostasis is a Two-Phase Process	473	Essential Trace Elements	499
Platelets and Hemostatic Plug Formation	474	Copper	499
Clotting Factors and the Coagulation Cascade	474	Zinc	502
Clot Dissolution: Fibrinolysis	475	Molybdenum	502
Hemostatic System Factors (Proteins) and Their Properties	475	36. Vitamin Metabolism	503
Protease Precursors	475	Fat Soluble Vitamins	504
Cofactor Proteins	476	Vitamin A	504
Protease Inhibitors	477	Water Soluble Vitamins	509
Other Proteins of the Hemostatic System	477	Thiamine (Vitamin B ₁)	509
Membrane Phospholipid Surfaces	478	Riboflavin (Vitamin B ₂)	510
The Clotting Process and the Formation of Fibrin	478	Pyridoxine (Vitamin B ₆)	511
Reactions of the Coagulation Cascade: The Procoagulant Subsystem	478	Cobalamin (Vitamin B ₁₂)	511
Activation of Prothrombin	479	Folic Acid (Pteroylglutamic Acid)	512
The Extrinsic Pathway: Injury and Tissue Factor Exposure	479	Niacin	513
Initiation of the Procoagulant Subsystem and Activation of Factor VII	479	Pantothenic Acid (Pantoyl- β -Alanine)	513
The Intrinsic Pathway: <i>In Vitro</i> and <i>In Vivo</i> Processes	480	Biotin	513
The Contact Phase of the <i>In Vitro</i> Intrinsic Pathway of Coagulation	480	Ascorbic Acid (Vitamin C)	514
The Anticoagulant Subsystem	480	37. Water, Electrolytes, and Acid-Base Balance	517
Activation of Protein C and Inactivation of Factors Va and VIIIa	480	Water Metabolism	517
Anticoagulant Subsystem: Protease Inhibitors	481	Homeostatic Controls	519
Mechanism of Action of Heparin as a Therapeutic Anticoagulant	481	Water and Osmolality Controls	519
Inhibitors of the Contact Phase Proteases	482	Electrolyte Balance	521
Fibrinolytic Subsystem	482	Sodium	521
Plasminogen Activation	482	Potassium	521
Degradation of Fibrin (Fibrinolysis)	483	Chloride	521
Vitamin K, Oral Anticoagulants, and Their Mechanisms of Action	483	Acid-Base Balance	522
Action of Warfarin and Other Vitamin K Antagonists	483	Disorders of Acid-Base Balance	523
Thrombosis: Hemostatic System Dysfunction	484	38. Case Studies	527
35. Mineral Metabolism	487	Clinical Case Study 1: A Disorder of Fission of Organelles, Mitochondria, and Peroxisomes	527
Calcium and Phosphorus	487	Clinical Case Study 2: Paternal Inheritance of Mitochondrial DNA	527
Distribution and Function	487	Clinical Case Study 3: Treatment of Acetaminophen Toxicity with N-Acetylcysteine	528
Bone Structure, Formation, and Turnover	488	Clinical Case Study 4: Alzheimer's Disease (AD)	528
		Clinical Case Study 5: Methanol Toxicity	529
		Clinical Case Study 6: Consequences of α_1 -Antitrypsin Deficiency and Management	530
		Clinical Case Study 7: Complement Deficiency	532
		Clinical Case Study 8: Defects in Intracellular Killing by Phagocytes	532

Clinical Case Study 9: IgA Deficiency	533	for Severe Neonate Hyperbilirubinemia (Neonatal Jaundice)	554
Clinical Case Study 10: Impaired Development of T Cells and B Cells	533	Clinical Case Study 25: L-Dihydroxy-Phenylalanine (L-DOPA, also known as Levodopa) Responsive Dystonia	555
Clinical Case Study 11: Biochemistry of Hemostasis	534	Clinical Case Study 26: Hereditary Hemochromatosis (Chapter 27)	556
Vignette 1: Fibrinogen	534	References for Additional Clinical Case Studies and Enrichment	
Vignette 2: Factor XIII	534	Clinical Case Studies on Porphyrrias	557
Vignette 3: Activated Protein C Resistance	534	Clinical Case Studies and Supplemental Enrichment References for Electron Transport and Oxidative Phosphorylation: Chapter 13	557
Vignette 4: Antibiotic-Induced Vitamin K Deficiency	534	Clinical Case Studies and Supplemental Enrichment References for Chapter 14	557
Vignette 5: Hemophilia	534	Clinical Case Study: A Defective Glucose-6-Phosphatase	557
Vignette 6: Von Willebrand Disease	535	Clinical Case Study: McArdle's Disease	557
Vignette 7: Laboratory-Created Artifacts	535	Clinical Case Studies and Supplemental Enrichment References for Chapter 15	557
Clinical Case Study 12: Deficiency of Glycogenin-1 Leading to Glycogen Depletion in Skeletal Muscle Fibers and Cardiac Myocytes	537	Clinical Case Studies and Supplemental Enrichment References for Chapter 19	558
Clinical Case Study 13: Acute Pancreatitis	538	Clinical Case Studies and Supplemental Enrichment References for Chapter 20	558
Clinical Case Study 14: Precocious Puberty	538	Clinical Case Study References for Activating (Gain-of-Function) Mutations of SUR1 and Kir6.2 Genes	558
Clinical Case Study 15: Lack of Physiologically Functioning Growth Hormone due to Disruption of the Intracellular Signalling Pathway	539	Additional Clinical Case Studies on Diabetes Mellitus	558
Clinical Case Study 16: Xeroderma Pigmentosum, a nucleotide Excision Repair Defect	540	Clinical Case Studies on Insulinoma Resulting in Hypoglycemia, a Diagnostically Challenging Problem	558
Clinical Case Study 17: Disorders of Collagen Biosynthesis	540	Clinical Case Studies on Obesity and Anorexia Nervosa (Chapter 20 Energy Homeostasis)	559
Vignette 1: Ehlers–Danlos syndrome	540	A Clinical Case Study on Anorexia Nervosa	559
Vignette 2: Osteogenesis Imperfecta	540	Clinical Case Studies and Supplemental Enrichment References for Chapter 25: Nucleotide Metabolism	559
Vignette 3: Scurvy	541	Clinical Case Studies and Supplemental Enrichment References on Signal Transduction (Chapter 23)	559
Clinical Case Study 18: Use of Serum Electrophoretic and Related Studies for the Diagnosis of Multiple Myeloma and Small B-cell Neoplasms (Waldenström Macroglobulinemia)	541	Clinical Case Study 2: Secondary Cushing's Syndrome Due to Metastatic Small-Cell Carcinoma of Prostatic Origin	560
Vignette 1: IgG(K) MM	541	Clinical Case Study 3: Adrenal Insufficiency	560
Vignette 2: Nonsecretory MM	541	Clinical Case Study 4: 21-Hydroxylase Deficiency	560
Vignette 3: Wadenström's macroglobulinemia	542	Clinical Case Study 5: Pheochromocytoma	560
Clinical Case Study 19: Celiac Disease	547		
Clinical Case Study 20: A Neonatal Death due to Medium-Chain Acyl-CoA Dehydrogenase (MCAD) Deficiency	548		
Clinical Case Study 21: Acute Coronary Syndromes	549		
Clinical Case Study 22: Hemoglobin Related Abnormalities	550		
Vignette 1: Hemoglobin (Hb) Disorder with Hbs/O _{arab} Disease	550		
Clinical Case Study 23: Methemoglobinemia (MBMHb)	553		
Clinical Case Study 24: Sn-Mesoporphyrin Therapy Instead of Exchange of Transfusion			

Clinical Case Studies and Supplemental Enrichment References on the Thyroid (Chapter 31)	560	Clinical Case Studies and Supplemental Enrichment References for Water, Electrolytes, and Acid-Base Balance (Chapter 37)	561
Clinical Case Studies and Supplemental Enrichment References for Mineral Metabolism (Chapter 35)	560	Appendix	563
Clinical Case Study for Copper Metabolism	561	Acronyms and Abbreviations Found in This Text	563
Clinical Case Study for Zinc Deficiency	561		
Clinical Case Studies and Supplemental Enrichment References for Vitamin Metabolism (Chapter 36)	561	Index	569