

Table of Contents

Preface		xiii
Authors		xv
1. Introduction	<i>Victor W. Rodwell, PhD</i>	1
Stereoisomers 1	Functional Groups Important in Biochemistry 4	
2. Water	<i>Victor W. Rodwell, PhD</i>	7
Introduction 7	The Concept of pH 9	
Molecular Structure of Water 7	Protonic Equilibria of Functional Groups That	
Macromolecular Structure of Water 7	Are Weak Acids or Bases 10	
Hydrogen Bonds 8	Henderson-Hasselbalch Equation 12	
Dissociation of Water 8	Buffers & Buffering 13	
3. Amino Acids & Peptides	<i>Victor W. Rodwell, PhD</i>	14
Introduction 14	Separatory Techniques for Amino Acids	
Amino Acids 14	& Peptides 23	
Ionic Forms of Amino Acids 14	Determination of the Amino Acid Composition	
Structures of Amino Acids 16	of Peptides 27	
Solubility of Amino Acids 20	Determination of the Primary Structure of	
General Chemical Reactions 20	Polypeptides 27	
Properties of Individual Amino Acids 21	Automated Edman Technique for Determination	
Peptides 21	of Polypeptide Structures 28	
Physiologically Active Peptides 23	Synthesis by Automated Techniques 30	
4. Proteins	<i>Victor W. Rodwell, PhD</i>	32
Classification of Proteins 32	Denaturation 37	
Bonds Responsible for Protein Structure 33	Determination of Primary Structure 38	
Ordered Conformations of Polypeptides 34	Determination of Secondary & Tertiary	
Less Highly Ordered Conformations of	Structure 39	
Polypeptides 37	Determination of Quaternary Structure 39	
Four Orders, or Levels, of Protein Structure 37		
5. Structure & Function of a Protein—Hemoglobin	<i>David W. Martin, Jr., MD</i>	41
Heme-Oxygen Interaction 41	The Hemoglobin Molecule 43	
Myoglobin 41	Insights From Mutant Hemoglobins 48	
6. General Properties of Enzymes	<i>Victor W. Rodwell, PhD</i>	52
Catalysis 52	Quantitative Measurement of Enzyme Activity 56	
Enzyme Classification & Nomenclature 52	Isolation of Enzymes 58	
Coenzymes 54	Intracellular Distribution of Enzymes 59	
Three-Point Attachment 55	Isozymes 59	
Enzyme Specificity 55	Enzymes in Clinical Diagnosis 61	

7. Bioenergetics	<i>Peter A. Mayes, PhD, DSc</i>	65
Introduction 65	Role of High-Energy Phosphates in Bioenergetics & Energy Capture 67	
8. Kinetic Properties of Enzymes	<i>Victor W. Rodwell, PhD</i>	72
Energy Barriers for Chemical Reactions; Forma- tion of Transition States During the Overall Reaction 72	The Catalytic Site 75	
Representation of Free Energy Changes Associ- ated With Formation & Decay of Transi- tion States 72	Effect of Reactant Concentration 80	
Role of Catalysts in Formation of Productive Transition States 73	The Equilibrium Constant 81	
Effect of Temperature 73	Enzyme Concentration 82	
Role of Enzymes in the Rupture & Formation of Covalent Bonds 73	Substrate Concentration 82	
	Limitations of the Michaelis-Menten Model 85	
	Inhibition of Enzyme Activity 85	
	Ordered & Random Binding of Substrates 87	
	Enzymes as General Acid or General Base Catalysts 88	
9. Regulation of Enzyme Activity	<i>Victor W. Rodwell, PhD</i>	91
Metabolic Regulation 91	Regulation of the Catalytic Efficiency of Enzymes 95	
Regulation of Enzyme Quantity by Control of the Rates of Enzyme Synthesis & Degradation 92		
10. Water-Soluble Vitamins	<i>David W. Martin, Jr., MD</i>	101
The Vitamins of the B Complex 101	The Vitamins of the B Complex (cont'd)	
Thiamin 101	Biotin 110	
Riboflavin 103	Vitamin B ₁₂ 111	
Niacin & Niacinamide 104	Folate or Folacin 113	
Pyridoxine 105	Vitamin C (Ascorbic Acid) 116	
Pantothenic Acid 109		
11. Fat-Soluble Vitamins	<i>David W. Martin, Jr., MD</i>	118
Vitamin A (Retinoids) 118	Vitamin E (α-Tocopherol) 123	
Vitamin D 121	Vitamin K 125	
12. Biologic Oxidation	<i>Peter A. Mayes, PhD, DSc</i>	128
Enzymes & Coenzymes Involved in Oxidation & Reduction 129	Mechanisms of Oxidative Phosphorylation 139	
The Respiratory Chain 134	The Chemiosmotic Theory 139	
The Role of the Respiratory Chain in Energy Capture 137	Transport of Substances Into & Out of Mitochondria 143	
13. Carbohydrates	<i>Peter A. Mayes, PhD, DSc</i>	147
Monosaccharides 149	Amino Sugars (Hexosamines) 151	
Hexoses 149	Disaccharides 153	
Glycosides 151	Polysaccharides 155	
Deoxy Sugars 151	Carbohydrates of Cell Membranes 156	

14. The Citric Acid Cycle—The Catabolism of Acetyl-CoA	158
<i>Peter A. Mayes, PhD, DSc</i>	
Significance of the Citric Acid Cycle 158	Energetics of the Citric Acid Cycle 163
Reactions of the Citric Acid Cycle 159	Amphibolic Role of the Citric Acid Cycle 164
15. Metabolism of Carbohydrate	166
<i>Peter A. Mayes, PhD, DSc</i>	
Intermediary Metabolism of Carbohydrate 166	Glycogen Synthase Activation & Inactivation 178
Glycolysis 167	The Hexose Monophosphate Shunt, or Pentose Phosphate Pathway 181
Oxidation of Pyruvate to Acetyl-CoA 171	Gluconeogenesis 185
Glycogen Formation & Degradation 174	Metabolism of Hexoses 187
Glycogenesis 174	Minor Pathways of Glucose Metabolism 188
Glycogenolysis 176	The Uronic Acid Pathway 188
Control Mechanisms of Glycogenolysis & Glycogenesis 176	Metabolism of Fructose 189
Phosphorylase Activation & Inactivation 176	Metabolism of Galactose 191
16. Lipids	194
<i>Peter A. Mayes, PhD, DSc</i>	
Fatty Acids 194	The Plasma Lipids & Lipoproteins 202
Triacylglycerols (Triglycerides) 197	Properties & Reactions of Lipids 203
Phospholipids 198	Methods for Separating & Identifying Lipids in Biologic Material 205
Glycolipids (Glycosphingolipids) 199	The Cell Membranes 206
Steroids 200	
17. Metabolism of Lipids: I. Fatty Acids	208
<i>Peter A. Mayes, PhD, DSc</i>	
Oxidation of Fatty Acids 209	Metabolism of Acylglycerols 222
Biosynthesis of Saturated Fatty Acids 213	Metabolism of Sphingolipids 227
Metabolism of Unsaturated Fatty Acids 218	Phospholipids & Sphingolipids in Disease (Lipidoses) 230
The Essential Fatty Acids (EFA) 220	
18. Metabolism of Lipids: II. Role of the Tissues	232
<i>Peter A. Mayes, PhD, DSc</i>	
Metabolism of Adipose Tissue & Mobiliza- tion of Fat 233	Role of the Liver in Lipid Metabolism 243
Metabolism of the Plasma Lipoproteins 238	Ketosis 246
	Cholesterol Metabolism 249
19. Regulation of Carbohydrate & Lipid Metabolism	257
<i>Peter A. Mayes, PhD, DSc</i>	
General Principles of Regulation of Metabolic Pathways 257	Regulation of Lipid Metabolism 267
Metabolic Control of an Enzyme-Catalyzed Reaction 257	Regulation of Fatty Acid Synthesis (Lipogenesis) 267
Regulation of Carbohydrate Metabolism 258	Regulation of Ketogenesis 268
Regulation of Carbohydrate Metabolism at the Cellular & Enzymatic Level 259	Interconversion of Major Foodstuffs 271
The Blood Glucose 264	The Economics of Carbohydrate & Lipid Metabolism in the Whole Body 273
	Starvation 273

20. Biosynthesis of Amino Acids	275
<i>Victor W. Rodwell, PhD</i>	
Amino Acid Metabolism 275	Biosynthesis of Nutritionally Nonessential Amino Acids (cont'd)
Nutritionally Essential & Nutritionally Non-essential Amino Acids 275	From Nutritionally Essential Amino Acids 280
Biosynthesis of Nutritionally Nonessential Amino Acids 276	Biosynthesis of Nutritionally Essential Amino Acids 281
From Amphibolic Intermediates 276	From Glutamate 281
From Other Nutritionally Nonessential Amino Acids 278	From Aspartate 281
	From Amphibolic Intermediates 281
21. Catabolism of Amino Acid Nitrogen	283
<i>Victor W. Rodwell, PhD</i>	
Overall View 283	Interorgan Amino Acid Exchange in the Fed State 288
Transamination 284	Urea Synthesis 289
Oxidative Deamination 285	Regulation of Urea Synthesis 290
Formation of Ammonia 285	Metabolic Disorders of the Urea Cycle 291
Transport of Ammonia 286	
Interorgan Amino Acid Exchange in the Post-absorptive State 287	
22. Catabolism of the Carbon Skeletons of Amino Acids	293
<i>Victor W. Rodwell, PhD</i>	
Conversion of Carbon Skeletons of Common L- α -Amino Acids to Amphibolic Intermediates 293	Amino Acids Forming α -Ketoglutarate 296
Amino Acids Forming Oxaloacetate 296	Amino Acids Forming Pyruvate 297
	Amino Acids Forming Acetyl-Coenzyme A 303
	Amino Acids Forming Succinyl-Coenzyme A 311
23. Conversion of Amino Acids to Specialized Products	319
<i>Victor W. Rodwell, PhD</i>	
Glycine 319	Histidine 322
α -Alanine 320	Arginine 322
β -Alanine 320	Ornithine 322
β -Alanyl & Related Dipeptides 320	Tryptophan 325
Serine 321	Melanins 327
Threonine 321	Tyrosine 327
Methionine 322	Creatine & Creatinine 327
Cysteine 322	γ -Aminobutyrate 329
24. Porphyrins & Bile Pigments	331
<i>David W. Martin, Jr., MD</i>	
Porphyryns 331	Metabolism of Bilirubin in the Intestine 343
The Porphyrias 338	Hyperbilirubinemia 344
Catabolism of Heme; Formation of Bile Pigments 341	
25. Nucleotides	348
<i>David W. Martin, Jr., MD</i>	
Nucleosides & Nucleotides 350	Synthetic Derivatives 354
Naturally Occurring Nucleotides 352	
26. Metabolism of Purine & Pyrimidine Nucleotides	357
<i>David W. Martin, Jr., MD</i>	
Digestion 357	Clinical Disorders of Purine Metabolism 370
Purines 359	Clinical Disorders of Pyrimidine Metabolism 373
Pyrimidines 366	

27. Nucleic Acid Structure & Function	376
<i>David W. Martin, Jr., MD</i>	
DNA 376	RNA (cont'd)
Chemical Nature of DNA 376	Biologic Function of RNA 382
Structure of DNA 378	Structural Organization of RNA 382
Function of DNA 379	Ribosomal RNA 384
RNA 381	Small Stable RNA 385
Chemical Nature of RNA 381	
28. DNA Organization & Replication	386
<i>David W. Martin, Jr., MD</i>	
Chromatin 386	DNA Synthesis & Replication 394
Genetic Organization of the Mammalian Genome 390	Recombinant DNA Technology 402
Alteration & Rearrangement of Genetic Material 391	
29. RNA Synthesis & Processing	405
<i>David W. Martin, Jr., MD</i>	
RNA Synthesis 405	Processing of RNA Molecules (cont'd)
Transcriptional Signals 407	Transfer RNA (tRNA) 413
Processing of RNA Molecules 410	Ribosomal RNA (rRNA) 414
Messenger RNA (mRNA) 412	Nucleases 415
30. Protein Synthesis & the Genetic Code	416
<i>David W. Martin, Jr., MD</i>	
Transfer RNA Function 418	Protein Synthesis 425
Mutations 419	
31. Regulation of Gene Expression	431
<i>David W. Martin, Jr., MD</i>	
Regulation in Prokaryotes 432	Regulation in Eukaryotes (cont'd)
The Lac Operon 432	V-J Joining 441
Bacteriophage Lambda 435	Class Switching 442
Attenuation in the Tryptophan Operon 438	Transcription Control 443
Regulation in Eukaryotes 440	Differential RNA Processing 446
Gene Amplification During Development 440	Messenger RNA Stability 446
Immunoglobulin Gene Rearrangement 441	Differential mRNA Translation 446
32. Membranes	448
<i>David W. Martin, Jr., MD</i>	
Lipid Composition 448	Membrane Assembly 456
Organization of Membrane Lipids 449	Transport Across Membranes 458
Membrane Proteins 453	Intercellular Contact & Communication 460
The Fluid Mosaic Model of Membrane Structure 454	
33. Glycoproteins, Proteoglycans, & Glycosaminoglycans	464
<i>David W. Martin, Jr., MD</i>	
Glycoproteins 464	Degradation of the Polysaccharide Moieties of Glycoproteins & Proteoglycans 476
Blood Group Antigens 470	
Proteoglycans 473	
34. Contractile & Structural Proteins	480
<i>David W. Martin, Jr., MD</i>	
Muscle 480	Collagen 493
Cell Motility & the Cytoskeleton 488	

35. Characteristics of Hormone Systems	497
<i>Daryl K. Granner, MD</i>	
General Features 497	Feedback Control Concept 499
Diversity of the Endocrine System 497	Hormone Receptors 500
Target Gland Concept 499	Hormone Receptors & Disease 503
36. Hormone Action	505
<i>Daryl K. Granner, MD</i>	
Classification of Hormones 505	Mechanism of Action of Group II (Peptide) Hormones 507
Mechanism of Action of Group I Hormones 506	cAMP as the Second Messenger 507
Sterol-Derived Hormones 506	Hormones That Act Through Calcium or Phosphatidylinositides 512
Iodothyronine Hormones 507	Hormones for Which the Intracellular Messenger Is Unknown 514
37. Pituitary & Hypothalamic Hormones	515
<i>Daryl K. Granner, MD</i>	
General Structure of the Pituitary 515	Anterior Pituitary Hormones (cont'd)
Hypothalamic Hormones 516	The Pro-opiomelanocortin (POMC) Peptide Family 523
Anterior Pituitary Hormones 517	Posterior Pituitary Hormones 527
The Growth Hormone-Prolactin-Chorionic Somatomammotropin Group 517	Oxytocin 527
The Glycoprotein Hormone Group 521	Antidiuretic Hormone (ADH; Vasopressin) 528
38. The Thyroid Hormones	530
<i>Daryl K. Granner, MD</i>	
Structure & General Features 530	Regulation of Thyroid Hormone Synthesis & Release 534
Thyroid Hormone Biosynthesis 530	Mechanism of Action of Thyroid Hormones 535
Thyroglobulin Metabolism 530	Pathophysiology 536
Iodide Metabolism 531	Goiter 536
Transport & Metabolism of Thyroid Hormones 533	Hypothyroidism 536
	Hyperthyroidism 536
39. Hormones That Regulate Calcium Metabolism	537
<i>Daryl K. Granner, MD</i>	
General Features 537	Hormones Involved in Calcium Homeostasis (cont'd)
Calcium Homeostasis 538	Calcitriol (1,25[OH] ₂ -D ₃) 543
Hormones Involved in Calcium Homeostasis 539	Calcitonin (CT) 546
Parathyroid Hormone (PTH) 539	
40. Hormones of the Adrenal Gland	548
<i>Daryl K. Granner, MD</i>	
Structure of the Adrenal Gland 548	The Adrenal Cortex (cont'd)
Vascular Anatomy 548	Classification & Mechanism of Action of Adrenal Steroid Hormones 559
Zones of the Adrenal Cortex 548	Pathophysiology of the Adrenal Cortex 562
The Adrenal Medulla 548	The Adrenal Medulla 562
The Adrenal Cortex 548	The Sympathoadrenal System 562
Hormones 548	Origin & Structure of the Adrenal Medulla 563
Nomenclature & Chemistry of Steroids 549	Biosynthesis of Catecholamines 563
Biosynthesis of Adrenal Steroid Hormones 549	Storage & Release of Catecholamines 565
Secretion, Transport, & Metabolism of Adrenal Steroid Hormones 553	Metabolism of Catecholamines 566
Regulation of Synthesis of Adrenal Steroid Hormones 554	Regulation of Synthesis of Catecholamines 567
Metabolic Effects of Adrenal Steroid Hormones 556	Classification & Mechanism of Action of Catecholamines 567
	Pathophysiology of the Adrenal Medulla 568

41. Hormones of the Gonads	570
<i>Daryl K. Granner, MD</i>	
Hormones of the Testes 570	Hormones of the Ovaries (cont'd)
Biosynthesis & Metabolism of Testicular Hormones 570	Regulation and Physiologic Actions of Ovarian Hormones 578
Regulation of Testicular Function 572	Mechanism of Action of Ovarian Hormones 583
Physiologic Action of Testicular Hormones 573	Pathophysiology of the Female Reproductive System 583
Mechanism of Action of Testicular Hormones 575	Gonadal Hormones & Sexual Differentiation 583
Pathophysiology of the Male Reproductive System 575	Chromosomal Sex 583
Hormones of the Ovaries 575	Gonadal Sex 584
Biosynthesis & Metabolism of Ovarian Hormones 576	Phenotypic Sex 584
42. Hormones of the Pancreas & Gastrointestinal Tract	587
<i>Daryl K. Granner, MD</i>	
Pancreatic Hormones 587	Gastrointestinal Hormones 603
Insulin 587	The Secretin Family 606
Insulinlike Growth Factors 601	The Gastrin-Cholecystokinin Family 606
Glucagon 602	Other Gastrointestinal Peptides 608
Somatostatin 603	
Pancreatic Polypeptide 603	
43. The Chemistry of Respiration	610
<i>David W. Martin, Jr., MD</i>	
Chemical & Physiologic Events Affecting Diffusion of Oxygen & Carbon Dioxide 610	Transport of CO ₂ in Blood 615
Transport of Oxygen in Blood 613	Respiratory Regulation of Acid-Base Balance 617
44. Digestion/Absorption in the Gastrointestinal Tract	621
<i>Peter A. Mayes, PhD, DSc</i>	
Digestion in the Oral Cavity 621	The Bile 622
Digestion in the Stomach 621	Absorption From the Gastrointestinal Tract 629
Pancreatic & Intestinal Digestion 622	Intestinal Putrefaction & Fermentation 633
45. Blood Plasma & Clotting	635
<i>David W. Martin, Jr., MD</i>	
Blood Plasma 635	Blood Clotting 642
The Plasma Proteins 635	
46. Water & Minerals	649
<i>David W. Martin, Jr., MD</i>	
Water 649	Minerals (cont'd)
Body Water 649	Trace Elements 655
Water Balance 649	Cobalt 655
Water Losses 649	Copper 655
Water Intake 650	Iron 655
Minerals 651	Molybdenum 659
Calcium 651	Selenium 659
Phosphorus 652	Manganese 659
Magnesium 653	Zinc 659
Sodium 653	Chromium 660
Potassium 654	

47. Nutrition **661**

Marion Nestle, PhD

Nutritional Requirements in Humans 661
Composition of Foods 663
Food Energy 666
Sources of Energy 668
Vitamins 673
Minerals 675

Water 677
Nutritional Supplements 677
Food Toxins & Additives 677
Nutrition & Health 677
Dietary Recommendations 679

Abbreviations Encountered in Biochemistry **681**

Index **683**