GUYTON & HALL

TEXTBOOK OF MEDICAL PHYSIOLOGY

TENTH EDITION

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MEDICAL PHYSIOLOGY

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TEXTBOOK OF MEDICAL PHYSIOLOGY

To

MY FATHER
For the Uncompromising Principles That Guided His Life

MY MOTHER
For Leading Her Children into Intellectual Pursuits

MY WIFE
For Her Magnificent Devotion to Her Family

MY CHILDREN
For Making Everything Worthwhile

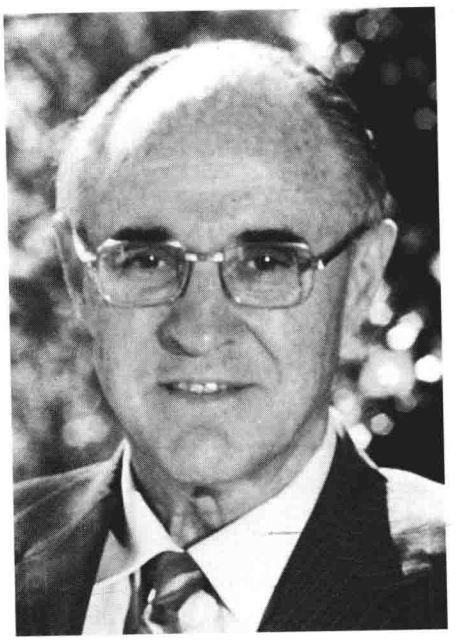
A.C.G.

To

MY TEACHERS
For Showing Me the Excitement and Joy of Physiology

MY FAMILY
For Their Abundant Support, for Their Patience and Understanding, and for Their Love.

J.E.H.



Arthur C. Guyton, M.D.

FOREWORD

Arthur Guyton is a giant of a man. In virtually all dimensions, he stands tall above the crowd. When he contracted polio after Harvard Medical School while training in neurosurgery, he found himself unable to walk on his own. He conquered this problem, adapting to crutches, and decided to go into physiology instead of neurosurgery.

For this he returned to Jackson, Mississippi, where he launched his new career in physiology. In this mode his work revolutionized physiological thinking and put Ole Miss on the biological map as a premier intellectual learning center for physiology.

Because he could not write by hand for any period of time, Arthur learned to dictate almost perfect prose to create, single-handedly, the most complete, sophisticated, au courant, and best-selling textbooks of physiology of his era, in which he authoritatively described and analyzed the whole physiology landscape.

And Arthur developed a new science of integrative physiology to describe and discover the many different servocontrols that regulate blood pressure, cardiac performance, sodium-volume homeostasis, local tissue pressure and flow, and whole-body autoregulation, for all of which multiple feedback control signals are required. For this work Arthur designed and built a detailed computerized model of the entire circulatory system to plan new experiments that test his new hypotheses. His model correctly predicted and described the central role of abnormal kidney function for sustaining the abnormal sodium-volume excretion that maintains hypertension, and his model also describes how plasma renin angiotensin shifts the relationship between blood pressure and salt-excretion.

Arthur loves mechanical and physical problems, but he also appreciates the importance of the biochemical signals that transduce the physical phenomena that produce the physiologic changes. His new-fangled approaches met the usual stiff resistance from establishment thinkers. Undaunted, Guyton invented, exploited, or defined new cardiovascular concepts such as the mean circulatory blood pressure and whole-body autoregulation. He even suggested that interstitial fluid pressures could be negative in the axillae and scrotum.

Needless to say, those physical and chemical biologic passions pervaded his whole life, including his spare time. Thus, crutches included, Arthur with the help of his wife and sons literally designed and built his own beautiful home in Jackson.

I first met Arthur when I heard him speak at a physiology meeting. Immediately I sensed a need to rearrange my thinking and concepts about the signals that control blood pressure. Arthur's perceptions came at the right time for me because our group was being attacked for claiming (correctly) that a normal plasma renin level is not "normal" in any person with high blood pressure.

This is because of a key feedback control system. Thus, whenever blood pressure is raised in a normal person it promptly turns off kidney release of renin and therefore plasma renin levels fall quickly to near zero. The hypertensive person, therefore, has something wrong. Unlike normals, he cannot fully turn off his plasma renin level despite his sustained high arterial blood pressure, so renin levels in the blood remain "normal" by traditional criteria. However, when you block or reduce this "normal" renin with a specific antirenin system drug, the patient promptly becomes normotensive.

I can tell you that this phenomenon, and its exact reciprocals whenever blood pressure falls, could and did become the basis for hours and hours of discussion enjoyed by my research group on our annual 2 to 3 day visits to the Guyton group in Jackson. In this process we got to know John Hall, Arthur's pupil and chosen successor, whose work is taking the field of integrative whole-body physiology and pathophysiology to new heights.

Today the importance of whole-body physiology for understanding organ and cellular physiology and for designing meaningful cellular or molecular biologic experiments cannot be overemphasized. Nor can the relevance of whole-body physiology to understanding whole-body phenomena in humans in health and in major diseases be overemphasized. These diseases often involve abnormal distant hormonal or nervous signals, which may either cause or sustain the disease. Time and time again, whole-body physiology has taught molecular, cellular, and tissue biologists to focus outside their turf before drawing any conclusions. Understanding whole-body physiology, of course, is also the basic prerequisite for physicians practicing clinical medicine.

The future for this approach, which has also been my approach to analysis of my patients, has never shone more brightly.

I hope this foreword will encourage readers to savor every word of the Guyton-Hall viewpoint and philosophy. As you read and reflect on pieces of it, remember that, by reflecting as you read, you can have the same advantage that I gained from my direct contacts with Arthur and John.

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New York, New York

PREFACE

We come now to the tenth edition of the *Textbook of Medical Physiology*. Publication of this book has continued long beyond what we expected when its first edition was written almost 50 years ago. Yet, the project becomes more exciting each year, especially because our increasing knowledge of physiology unravels many new bodily mysteries.

Most important, many new techniques for learning about cellular and molecular physiology have been developed recently. Therefore, more and more can we present physiologic principles in the terminology of molecular and physical science rather than merely as a series of separate unexplained biological phenomena. This change we all welcome, but it also makes revision of almost every section of each chapter a necessity.

To help in this job of revision, Dr. John Hall joined as coauthor in preparing the ninth edition of the *Textbook of Medical Physiology*. In the tenth edition he has doubled the number of chapters for which he is primarily responsible.

The two of us, Drs. Guyton and Hall, have worked very closely together for more than 25 years, so it has been possible to maintain a unified organization of the text that is especially useful to students, yet at the same time keeps the book comprehensive enough that students will wish to use it in later life as a basis for professional careers. As can be expected, Dr. Hall has brought many new insights and new bodies of knowledge that have helped immensely in achieving these goals.

The beauty of studying human physiology is that it integrates the individual functions of all the body's different organs and cells into a functional whole, the human body. Indeed, life relies upon this total function, not on function of individual body parts in isolation from the others.

This brings us to another subject: How are the separate organs and systems controlled so that no one overfunctions while others fail to do their share? Fortunately, our bodies are endowed with a vast network of feedback controls that achieve the necessary balances without which we would not be able to live. Physiologists call this high level of internal bodily control *homeostasis*. In disease states, functional balances are often seriously disturbed—that is, homeostasis becomes very poor. And, when even a single disturbance reaches a limit, the whole body can no longer live. Therefore, one of the principal goals of any medical physiology text is to emphasize the effectiveness and beauty of the body's homeostasis mechanisms as well as to present their abnormal function in disease.

Another goal of this text is to be as accurate as possible. Suggestions and critiques from many physiologists, students, and clinicians throughout the world have been sought and then used for checking factual accuracy as well as balance in the text. Even so, because of the likelihood of error in sorting through thousands of bits of information, we wish to issue still a further invitation—in fact, much more than merely an invitation, actually a request—to all readers to send along notations of error or inaccuracy. Indeed, physiologists perhaps as much as any other scholars understand how important feedback is to proper function of the human body; so, too, is feedback important for progressive development of a textbook of physiology. To those many persons who have already helped, we send our sincerest thanks.

A word of explanation is needed about two features of the text—first, the references, and second, the two print sizes. The sources referenced have been chosen primarily for their presentation of physiologic principles and for the quality of their own references. Use of these, as well as cross-references from them, can give the student almost complete coverage of the entire field of physiology.

The print is set in two sizes. The material in small print is of several different kinds: first, anatomical, chemical, and other information that is needed for immediate discussion but that most students will learn in more detail in other courses; second, physiologic information of special importance to certain fields of clinical medicine; and, third, information that will be of value to those students who may wish to study particular physiologic mechanisms more deeply.

In contrast, the material in large print constitutes the fundamental physiologic information that students will require in virtually all their medical activities and studies.

Again, we wish to express our deepest appreciation to many other persons who have helped in preparing this book. We are particularly grateful to Ivadelle Osberg Heidke, Gwendolyn Harris, and Gerry McAlpin for their excellent secretarial services; to Tomika Mita, Michael Schenk, Angela Gardner, and Myriam Kirkman for their superb work and helpfulness with the illustrations; and to the staff of W.B. Saunders Company for continued editorial and production excellence.

ARTHUR C. GUYTON
JOHN E. HALL

NOTICE

Physiology is an ever-changing field. Standard safety precautions must be followed, but as new research and clinical experience broaden our knowledge, changes in treatment and drug therapy become necessary or appropriate. Readers are advised to check the product information currently provided by the manufacturer of each drug to be administered to verify the recommended dose, the method and duration of administration, and the contraindications. It is the responsibility of the treating physician, relying on experience and knowledge of the patient, to determine dosages and the best treatment for the patient. Neither the publisher nor the editor assumes any responsibility for any injury and/or damage to persons or property.

THE PUBLISHER

CONTENTS

UNIT I
Introduction to Physiology: The Cell and General Physiology

CHAPTER 1
Functional Organization of the Human Body and Control of the "Internal Environment" 2

Cells as the Living Units of the Body 2
Extracellular Fluid—The Internal Environment 2
"Homeostatic" Mechanisms of the Major Functional Systems 3
Homeostasis 3
Extracellular Fluid Transport System—The Circulatory System 3
Origin of Nutrients in the Extracellular Fluid 3
Removal of Metabolic End Products 4
Regulation of Body Functions 4
Reproduction 4
Control Systems of the Body 4
Examples of Control Mechanisms 5
Characteristics of Control Systems 6
Summary—Automaticity of the Body 7

CHAPTER 2
The Cell and Its Function 9

Organization of the Cell 9
Physical Structure of the Cell 10
Membranous Structures of the Cell 10
Cytoplasm and Its Organelles 12
Nucleus 14
Nuclear Membrane 15
Nucleoli and Formation of Ribosomes 15
Comparison of the Animal Cell with Precellular Forms of Life 15
Functional Systems of the Cell 16
Ingestion by the Cell—Endocytosis 16
Digestion of Pinocytic and Phagocytic Foreign Substances in the Cell—Function of the Lysosomes 17
Synthesis and Formation of Cellular Structures by the Endoplasmic Reticulum and the Golgi Apparatus 18
Extraction of Energy from Nutrients—Function of the Mitochondria—19
Locomotion of Cells 21

CHAPTER 3
Genetic Control of Protein Synthesis, Cell Function, and Cell Reproduction 24

The Genes 24
Genetic Code 25
The DNA Code Is Transferred to an RNA Code—The Process of Transcription 25
Synthesis of RNA 26
Assembly of the RNA Molecule from Activated Nucleotides Using the DNA Strand as a Template—The Process of Transcription 27
Messenger RNA—The Codons 27
Transfer RNA—The Anticodons 27
Ribosomal RNA 28
Formation of Proteins on the Ribosomes—The Process of "Translation" 29
Synthesis of Other Substances in the Cell 30
Control of Genetic Function and Biochemical Activity in Cells 30
Genetic Regulation 30
Control of Intracellular Function by Enzyme Regulation 32
The DNA–Genetic System Also Controls Cell Reproduction 32
Cell Reproduction Begins with Replication of the DNA 33
Chromosomes and Their Replication 34
Cell Mitosis 34
Control of Cell Growth and Cell Reproduction 35
Cell Differentiation 35
Cancer 36

UNIT II
Membrane Physiology, Nerve, and Muscle

CHAPTER 4
Transport of Substances Through the Cell Membrane 40

The Lipid Barrier of the Cell Membrane and Cell Membrane Transport Proteins 40
Diffusion 40
Diffusion Through the Cell Membrane 41
Diffusion Through Protein Channels and "Gating" of These Channels 42
Facilitated Diffusion 43
Factors That Affect Net Rate of Diffusion 44
Osmosis Across Selectively Permeable Membranes—"Net Diffusion" of Water 45
Active Transport 47
Primary Active Transport 47
Secondary Active Transport—Co-transport and Counter-transport 49
Active Transport Through Cellular Sheets 49

CHAPTER **5**
Membrane Potentials and Action Potentials 52

Basic Physics of Membrane Potentials 52
Membrane Potentials Caused by Diffusion 52
Measuring the Membrane Potential 53
Resting Membrane Potential of Nerves 54
Origin of the Normal Resting Membrane Potential 54
Nerve Action Potential 55
Voltage-Gated Sodium and Potassium Channels 56
Summary of the Events That Cause the Action Potential 58
Roles of Other Ions During the Action Potential 59
Initiation of the Action Potential 59
Propagation of the Action Potential 59
Re-establishing Sodium and Potassium Ionic Gradients After Action Potentials Are Completed—Importance of Energy Metabolism 60
Plateau in Some Action Potentials 61
Rhythmicity of Some Excitable Tissues—Repetitive Discharge 61
Special Aspects of Signal Transmission in Nerve Trunks 62
Excitation—The Process of Eliciting the Action Potential 63
"Refractory Period" After an Action Potential During Which a New Stimulus Cannot Be Elicited 64
Inhibition of Excitability—"Stabilizers" and Local Anesthetics 64
Recording Membrane Potentials and Action Potentials 64

CHAPTER **6**
Contraction of Skeletal Muscle 67

Physiologic Anatomy of Skeletal Muscle 67
The Skeletal Muscle Fiber 67
General Mechanism of Muscle Contraction 68
Molecular Mechanism of Muscle Contraction 70
Molecular Characteristics of the Contractile Filaments 70
Effect of Actin and Myosin Filament Overlap on Tension Developed by the Contracting Muscle 72
Relation of Velocity of Contraction to Load 73
Energetics of Muscle Contraction 74
Work Output During Muscle Contraction 74
Sources of Energy for Muscle Contraction 74
Characteristics of Whole Muscle Contraction 74
Mechanics of Skeletal Muscle Contraction 76
Remodeling of Muscle to Match Function 77
Rigor Mortis 78

CHAPTER **7**
Excitation of Skeletal Muscle: A. Neuromuscular Transmission and B. Excitation-Contraction Coupling 80

Transmission of Impulses from Nerves to Skeletal Muscle Fibers: The Neuromuscular Junction 80
Secretion by Acetylcholine by the Nerve Terminals 80
Molecular Biology of Acetylcholine Formation and Release 82
Drugs That Affect Transmission at the Neuromuscular Junction 83
Myasthenia Gravis 83
Muscle Action Potential 83
Spread of the Action Potential to the Interior of the Muscle Fiber by Way of a Transverse Tubule System 84
Excitation-Contraction Coupling 84
Transverse Tubule—Sarcoplasmic Reticulum System 84
Release of Calcium Ions by the Sarcoplasmic Reticulum 85

CHAPTER **8**
Contraction and Excitation of Smooth Muscle 87

Contraction of Smooth Muscle 87
Types of Smooth Muscle 87
Contractile Mechanism in Smooth Muscle 87
Regulation of Contraction by Calcium Ions 89
Neural and Hormonal Control of Smooth Muscle Contraction 90
Neuromuscular Junctions of Smooth Muscle 90
Membrane Potentials and Action Potentials in Smooth Muscle 90
Effect of Local Tissue Factors and Hormones to Cause Smooth Muscle Contraction Without Action Potentials 92
Source of Calcium Ions That Cause Contraction: (1) Through the Cell Membrane and (2) from the Sarcoplasmic Reticulum 93

UNIT **III**
The Heart

CHAPTER **9**
Heart Muscle; The Heart as a Pump 96

Physiology of Cardiac Muscle 96
Physiologic Anatomy of Cardiac Muscle 96
Action Potentials in Cardiac Muscle 97
The Cardiac Cycle 99
Diastole and Systole 99
Relationship of the Electrocardiogram to the Cardiac Cycle 100
Function of the Atria as Primer Pumps 100
Function of the Ventricles as Pumps 100
Emptying of the Ventricles During Systole 100
Function of the Valves 101
The Aortic Pressure Curve 101
Relationship of the Heart Sounds to Heart Pumping 102
Work Output of the Heart 102
Chemical Energy Required for Cardiac Contraction: Oxygen Utilization by the Heart 103
Regulation of Heart Pumping 103
Intrinsic Regulation of Heart Pumping—The Frank-Starling Mechanism 103
Effect of Potassium and Calcium Ions on Heart Function 106
Effect of Temperature on Heart Function 106

CHAPTER **10**
Rhythmical Excitation of the Heart 107

Specialized Excitatory and Conductive System of the Heart 107
Sinus Node (Sinoatrial Node) 107
Internodal Pathways and Transmission of the Cardiac Impulse Through the Atria 109
Atrioventricular Node, and Delay of Impulse Conduction from the Atria to the Ventricles 109
Rapid Transmission in the Ventricular Purkinje System 109
Transmission of the Cardiac Impulse in the Ventricular Muscle 110
Summary of the Spread of the Cardiac Impulse Through the Heart 110

Control of Excitation and Conduction in the Heart 111
The Sinus Node as the Pacemaker of the Heart 111
Role of the Purkinje System in Causing Synchronous Contraction of the Ventricular Muscle 111
Control of Heart Rhythmicity and Impulse Conduction by the Cardiac Nerves: The Sympathetic and Parasympathetic Nerves 112

CHAPTER **11**
The Normal Electrocardiogram 114

Characteristics of the Normal Electrocardiogram 114
Depolarization Waves Versus Repolarization Waves 114
Relationship of Atrial and Ventricular Contraction to the Waves of the Electrocardiogram 115
Voltage and Time Calibration of the Electrocardiogram 115
Methods for Recording Electrocardiograms 116
Pen Recorder 116
Flow of Current Around the Heart During the Cardiac Cycle 116
Recording Electrical Potentials from a Partially Depolarized Mass of Syncytial Cardiac Muscle 116
Flow of Electrical Currents in the Chest Around the Heart 116
Electrocardiographic Leads 117
Three Bipolar Limb Leads 117
Chest Leads (Precordial Leads) 118
Augumented Unipolar Limb Leads 119

CHAPTER **12**
Electrocardiographic Interpretation of Cardiac Muscle and Coronary Blood Flow Abnormalities: Vectorial Analysis 120

Principles of Vectorial Analysis of Electrocardiograms 120
Use of Vectors to Represent Electrical Potentials 120
Denoting the Direction of a Vector in Terms of Degrees 120
Axis of Each of the Standard Bipolar Leads and for Each Unipolar Limb Lead 120
Vectorial Analysis of Potentials Recorded in Different Leads 121
Vectorial Analysis of the Normal Electrocardiogram 122
Vectors That Occur at Successive Intervals During Depolarization of the Ventricles—The QRS Complex 122
Electrocardiogram During Repolarization—The T Wave 123
Depolarization of the Atria—The P Wave 124
Vectorcardiogram 124
Mean Electrical Axis of the Ventricular QRS—And Its Significance 125
Determining the Electrical Axis from Standard Lead Electrocardiograms 125
Abnormal Ventricular Conditions That Cause Axis Deviation 125
Conditions That Cause Abnormal Voltages of the QRS Complex 127
Increased Voltage in the Standard Bipolar Limb Leads 127
Decreased Voltage of the Electrocardiogram 127
Prolonged and Bizarre Patterns of the QRS Complex 128
Prolonged QRS Complex as a Result of Cardiac Hypertrophy or Dilatation 128
Prolonged QRS Complex Resulting from Purkinje System Blocks 128
Conditions That Cause Bizarre QRS Complexes 128
Current of Injury 128
Effect of Current of Injury on the QRS Complex 128
The J Point—The Zero Reference Potential for Analyzing Current of Injury 129
Coronary Ischemia as a Cause of Current of Injury 130
Abnormalities in the T Wave 132
Effect of Slow Conduction of the Depolarization Wave on the Characteristics of the T Wave 132
Prolonged Depolarization in Portions of the Ventricular Muscle as a Cause of Abnormalities in the T Wave 132

CHAPTER **13**
Cardiac Arrhythmias and Their Electrocardiographic Interpretation 134

Abnormal Sinus Rhythms 134
Tachycardia 134
Bradycardia 134
Sinus Arrhythmia 134
Abnormal Rhythms That Result from Impulse Conduction Block 135
Sinoatrial Block 135
Atrioventricular Block 135
Incomplete Intraventricular Block—Electrical Alternans 136
Premature Contractions 136
Premature Atrial Contractions 137
A-V Nodal or A-V Bundle Premature Contractions 137
Premature Ventricular Contractions 137
Paroxysmal Tachycardia 138
Atrial Paroxysmal Tachycardia 138
Ventricular Paroxysmal Tachycardia 138
Ventricular Fibrillation 138
Phenomenon of Re-entry—"Circus Movements" as the Basis for Ventricular Fibrillation 139
Atrial Fibrillation 141
Atrial Flutter 142
Cardiac Arrest 142

UNIT **IV**
The Circulation

CHAPTER **14**
Overview of the Circulation; Medical Physics of Pressure, Flow, and Resistance 144

Physical Characteristics of the Circulation 144
Basic Theory of Circulatory Function 146
Interrelationships Among Pressure, Flow, and Resistance 146
Blood Flow 147
Blood Pressure 148
Resistance to Blood Flow 149
Effects of Pressure on Vascular Resistance and Tissue Blood Flow 151

CHAPTER **15**
Vascular Distensibility, and Functions of the Arterial and Venous Systems 152

Vascular Distensibility 152
Vascular Compliance (or Capacitance) 152

Volume-Pressure Curves of the Arterial and Venous Circulations 152
Delayed Compliance (Stress-Relaxation) of Vessels 153
Arterial Pressure Pulsations 153
Transmission of Pressure Pulses to the Peripheral Arteries 154
Clinical Methods for Measuring Systolic and Diastolic Pressures 155
Veins and Their Functions 156
Venous Pressures—Right Atrial Pressure (Central Venous Pressure) and Peripheral Venous Pressures 156
Blood Reservoir Function of the Veins 160

CHAPTER **16**
The Microcirculation and the Lymphatic System: Capillary Fluid Exchange, Interstitial Fluid, and Lymph Flow 162

Structure of the Microcirculation and Capillary System 162
Flow of Blood in the Capillaries—Vasomotion 163
Average Function of the Capillary System 163
Exchange of Nutrients and Other Substances Between the Blood and Interstitial Fluid 164
Diffusion Through the Capillary Membrane 164
The Interstitium and Interstitial Fluid 165
Proteins in the Plasma and Interstitial Fluid Are Especially Important in Controlling Plasma and Interstitial Fluid Volumes 166
Capillary Pressure 166
Interstitial Fluid Pressure 167
Plasma Colloid Osmotic Pressure 168
Interstitial Fluid Colloid Osmotic Pressure 169
Exchange of Fluid Volume Through the Capillary Membrane 169
Starling Equilibrium for Capillary Exchange 170
Lymphatic System 170
Lymph Channels of the Body 170
Formation of Lymph 171
Rate of Lymph Flow 172
Role of the Lymphatic System in Controlling Interstitial Fluid Protein Concentration, Interstitial Fluid Volume, and Interstitial Fluid Pressure 173

CHAPTER **17**
Local Control of Blood Flow by the Tissues; and Humoral Regulation 175

Local Control of Blood Flow in Response to Tissue Needs 175
Mechanisms of Blood Flow Control 175
Acute Control of Local Blood Flow 176
Long-Term Blood Flow Regulation 179
Development of Collateral Circulation—A Phenomenon of Long-Term Local Blood Flow Regulation 180
Humoral Regulation of the Circulation 181
Vasoconstrictor Agents 181
Vasodilator Agents 181
Effects of Ions and Other Chemical Factors on Vascular Control 182

CHAPTER **18**
Nervous Regulation of the Circulation, and Rapid Control of Arterial Pressure 184

Nervous Regulation of the Circulation 184
Autonomic Nervous System 184
Role of the Nervous System for Rapid Control of Arterial Pressure 187
Increase in Arterial Pressure During Muscle Exercise and Other Types of Stress 188
Reflex Mechanisms for Maintaining Normal Arterial Pressure 188
Central Nervous System Ischemic Response—Control of Arterial Pressure by the Brain's Vasomotor Center in Response to Diminished Brain Blood Flow 191
Special Features of Nervous Control of Arterial Pressure 192
Role of the Skeletal Nerves and Skeletal Muscles in Increasing Cardiac Output and Arterial Pressure 192
Respiratory Waves in the Arterial Pressure 193
Arterial Pressure "Vasomotor" Waves—Oscillation of the Pressure Reflex Control Systems 193

CHAPTER **19**
Dominant Role of the Kidney in Long-Term Regulation of Arterial Pressure and in Hypertension: The Integrated System for Pressure Control 195

The Renal–Body Fluid System for Arterial Pressure Control 195
Quantitation of Pressure Diuresis as a Basis for Arterial Pressure Control 195
Hypertension (High Blood Pressure): This Is Often Caused by Excess Extracellular Fluid Volume 199
The Renin-Angiotensin System: Its Role in Pressure Control and in Hypertension 201
Components of the Renin-Angiotensin System 201
Types of Hypertension in Which Angiotensin Is Involved: Hypertension Caused by a Renin-Secreting Tumor or by Infusion of Angiotensin II 203
Other Types of Hypertension Caused by Combinations of Volume-Loading and Vasoconstriction 205
"Essential Hypertension" in Human Beings 205
Summary of the Integrated, Multifaceted System for Arterial Pressure Regulation 207

CHAPTER **20**
Cardiac Output, Venous Return, and Their Regulation 210

Normal Values for Cardiac Output at Rest and During Activity 210
Control of Cardiac Output by Venous Return—Role of the Frank-Starling Mechanism of the Heart 210
Cardiac Output Regulation Is the Sum of Blood Flow Regulation in All the Local Tissues of the Body—Tissue Metabolism Regulates Most Local Blood Flow 211
The Heart Has Limits for the Cardiac Output That It Can Achieve 212
What Is the Role of the Nervous System in Controlling Cardiac Output? 212
Pathologically High and Pathologically Low Cardiac Outputs 213

High Cardiac Output Is Almost Always Caused by Reduced Total Peripheral Resistance 213
Low Cardiac Output 214
A More Quantitative Analysis of Cardiac Output Regulation 214
Cardiac Output Curves Used in Quantitative Analysis 215
Venous Return Curves 215
Analysis of Cardiac Output and Right Atrial Pressure, Using Simultaneous Cardiac Output and Venous Return Curves 218
Methods for Measuring Cardiac Output 220
Pulsatile Output of the Heart as Measured by an Electromagnetic or Ultrasonic Flowmeter 220
Measurement of Cardiac Output by the Oxygen Fick Method 220
Indicator Dilution Method 221

CHAPTER **21**
Muscle Blood Flow and Cardiac Output During Exercise; the Coronary Circulation and Ischemic Heart Disease 223

Blood Flow in Skeletal Muscle and Its Regulation During Exercise 223
Rate of Blood Flow Through the Muscles 223
Control of Blood Flow Through the Skeletal Muscles 223
Circulatory Readjustments During Exercise 224
Coronary Circulation 226
Physiologic Anatomy of the Coronary Blood Supply 226
Normal Coronary Blood Flow 226
Control of Coronary Blood Flow 227
Special Features of Cardiac Muscle Metabolism 228
Ischemic Heart Disease 229
Causes of Death After Acute Coronary Occlusion 230
Stages of Recovery from Acute Myocardial Infarction 231
Function of the Heart After Recovery from Myocardial Infarction 232
Pain in Coronary Disease 232
Surgical Treatment of Coronary Disease 233

CHAPTER **22**
Cardiac Failure 235

Dynamics of the Circulation in Cardiac Failure 235
Acute Effects of Moderate Cardiac Failure 235
Chronic Stage of Failure–Fluid Retention Helps to Compensate Cardiac Output 236
Summary of the Changes That Occur After Acute Cardiac Failure—"Compensated Heart Failure" 237
Dynamics of Severe Cardiac Failure—Decompensated Heart Failure 237
Unilateral Left Heart Failure 239
Low-Output Cardiac Failure—Cardiogenic Shock 239
Edema in Patients with Cardiac Failure 239
Cardiac Reserve 241
Appendix 241
Quantitative Graphical Method for Analysis of Cardiac Failure 241

CHAPTER **23**
Heart Valves and Heart Sounds; Dynamics of Valvular and Congenital Heart Defects 245

Heart Sounds 245
Normal Heart Sounds 245
Valvular Lesions 247
Abnormal Circulatory Dynamics in Valvular Heart Disease 248
Dynamics of the Circulation in Aortic Stenosis and Aortic Regurgitation 248
Dynamics of Mitral Stenosis and Mitral Regurgitation 248
Circulatory Dynamics During Exercise in Patients with Valvular Lesions 249
Abnormal Circulatory Dynamics in Congenital Heart Defects 249
Patent Ductus Arteriosus—A Left-to-Right Shunt 249
Tetralogy of Fallot—A Right-to-Left Shunt 251
Causes of Congenital Anomalies 251
Use of Extracorporeal Circulation During Cardiac Surgery 251
Hypertrophy of the Heart in Valvular and Congenital Heart Disease 252

CHAPTER **24**
Circulatory Shock and Physiology of Its Treatment 253

Physiologic Causes of Shock 253
Circulatory Shock Caused by Decreased Cardiac Output 253
Circulatory Shock That Occurs Without Diminished Cardiac Output 253
What Happens to the Arterial Pressure in Circulatory Shock? 253
Tissue Deterioration Is the End Stage of Circulatory Shock, Whatever the Cause 253
Stages of Shock 254
Shock Caused by Hypovolemia—Hemorrhagic Shock 254
Relationship of Bleeding Volume to Cardiac Output and Arterial Pressure 254
Progressive and Nonprogressive Hemorrhagic Shock 255
Irreversible Shock 258
Hypovolemic Shock Caused by Plasma Loss 259
Hypovolemic Shock Caused by Trauma 259
Neurogenic Shock—Increased Vascular Capacity 259
Anaphylactic Shock and Histamine Shock 259
Septic Shock 260
Physiology of Treatment in Shock 260
Replacement Therapy 260
Treatment of Shock with Sympathomimetic Drugs—Sometimes Useful, Sometimes Not 261
Other Therapy 261
Circulatory Arrest 261
Effect of Circulatory Arrest on the Brain 261

UNIT **V**
The Kidneys and Body Fluids

CHAPTER **25**
The Body Fluid Compartments: Extracellular and Intracellular Fluids; Interstitial Fluid and Edema 264

Fluid Intake and Output Are Balanced During Steady-State Conditions 264

Daily Intake of Water 264
Daily Loss of Body Water 264
Body Fluid Compartments 265
Intracellular Fluid Compartment 265
Extracellular Fluid Compartment 266
Blood Volume 266
Constituents of Extracellular and Intracellular Fluids 266
Ionic Compositions of Plasma and Interstitial Fluid Are Similar 266
Important Constituents of the Intracellular Fluid 267
Measurement of Fluid Volumes in the Different Body Fluid Compartments; the Indicator-Dilution Principle 268
Determination of Volumes of Specific Body Fluid Compartments 268
Regulation of Fluid Exchange and Osmotic Equilibria Between Intracellular and Extracellular Fluid 269
Basic Principles of Osmosis and Osmotic Pressure 269
Osmotic Equilibrium Is Maintained Between Intracellular and Extracellular Fluids 271
Volumes and Osmolalities of Extracellular and Intracellular Fluid in Abnormal States 272
Effect of Adding Saline Solution to the Extracellular Fluid 272
Glucose and Other Solutions Administered for Nutritive Purposes 273
Clinical Abnormalities of Fluid Volume Regulation: Hyponatremia and Hypernatremia 273
Causes of Hyponatremia: Excess Water or Loss of Sodium 274
Causes of Hypernatremia: Water Loss or Excess Sodium 274
Edema: Excess Fluid in the Tissues 274
Intracellular Edema 274
Extracellular Edema 274
Safety Factors That Normally Prevent Edema 276
Fluids in the "Potential Spaces" of the Body 277

CHAPTER **26**
Urine Formation by the Kidneys: I. Glomerular Filtration, Renal Blood Flow, and Their Control 279

Multiple Functions of the Kidneys in Homeostasis 279
Physiologic Anatomy of the Kidneys 280
General Organization of the Kidneys and Urinary Tract 280
Renal Blood Supply 281
The Nephron Is the Functional Unit of the Kidney 281
Urine Formation Results from Glomerular Filtration, Tubular Reabsorption, and Tubular Secretion 282
Filtration, Reabsorption, and Secretion of Different Substances 283
Glomerular Filtration—The First Step In Urine Formation 284
Composition of the Glomerular Filtrate 284
GFR Is About 20 Per Cent of the Renal Plasma Flow 284
Glomerular Capillary Membrane 284
Determinants of the Glomerular Filtration Rate 286
Increased Glomerular Capillary Filtration Coefficient (K_f) Increases GFR 286
Increased Bowman's Capsule Hydrostatic Pressure Decreases GFR 287
Increased Glomerular Capillary Colloid Osmotic Pressure Decreases GFR 287
Increased Glomerular Capillary Hydrostatic Pressure Increases GFR 287
Renal Blood Flow 288
Determinants of Renal Blood Flow 288
Blood Flow in the Vasa Recta of the Renal Medulla Is Very Low Compared with Flow in the Renal Cortex 289
Physiologic Control of Glomerular Filtration and Renal Blood Flow 289
Sympathetic Nervous System Activation Decreases GFR 289
Hormonal and Autacoid Control of Renal Circulation 289
Autoregulation of GFR and Renal Blood Flow 290
Importance of GFR Autoregulation in Preventing Extreme Changes in Renal Excretion 291
Role of Tubuloglomerular Feedback in Autoregulation of GFR 291
Myogenic Autoregulation of Renal Blood Flow and GFR 293
Other Factors That Increase Renal Blood Flow and GFR: High Protein Intake and Increased Blood Glucose 293

CHAPTER **27**
Urine Formation by the Kidneys: II. Tubular Processing of the Glomerular Filtrate 295

Reabsorption and Secretion by the Renal Tubules 295
Tubular Reabsorption Is Selective and Quantitatively Large 295
Tubular Reabsorption Includes Passive and Active Mechanisms 295
Active Transport 296
Passive Water Reabsorption by Osmosis Is Coupled Mainly to Sodium Reabsorption 299
Reabsorption of Chloride, Urea, and Other Solutes by Passive Diffusion 300
Reabsorption and Secretion Along Different Parts of the Nephron 300
Proximal Tubular Reabsorption 300
Solute and Water Transport in the Loop of Henle 302
Distal Tubule 303
Late Distal Tubule and Cortical Collecting Tubule 303
Medullary Collecting Duct 304
Summary of Concentrations of Different Solutes in the Different Tubular Segments 304
Regulation of Tubular Reabsorption 305
Glomerulotubular Balance—The Ability of the Tubules to Increase Reabsorption Rate in Response to Increased Tubular Load 305
Peritubular Capillary and Renal Interstitial Fluid Physical Forces 306
Effect of Arterial Pressure on Urine Output—The Pressure-Natriuresis and Pressure-Diuresis Mechanisms 308
Hormonal Control of Tubular Reabsorption 308
Use of Clearance Methods to Quantify Kidney Function 309
PAH Clearance Can Be Used to Estimate Renal Plasma Flow 311
Filtration Fraction Is Calculated from GFR Divided by Plasma Renal Flow 311
Calculation of Tubular Reabsorption or Secretion from Renal Clearances 311

CHAPTER **28**
Regulation of Extracellular Fluid Osmolarity and Sodium Concentration 313

The Kidney Excretes Excess Water by Forming a Dilute Urine 313
Antidiuretic Hormone Controls Urine Concentration 313
Renal Mechanisms for Excreting a Dilute Urine 313
The Kidney Conserves Water by Excreting a Concentrated Urine 315
Obligatory Urine Volume 315
Requirements for Excreting a Concentrated Urine—High ADH Levels and Hyperosmotic Renal Medulla 315
The Countercurrent Mechanism Produces a Hyperosmotic Renal Medullary Interstitium 315
Role of the Distal Tubule and Collecting Ducts in Excreting a Concentrated Urine 317
Urea Contributes to Hyperosmotic Renal Medullary Interstitium and to a Concentrated Urine 318
Countercurrent Exchange in the Vasa Recta Preserves Hyperosmolarity of the Renal Medulla 319
Summary of Urine Concentrating Mechanism and Changes in Osmolarity in Different Segments of the Tubules 320
Quantifying Renal Urine Concentration and Dilution: "Free Water" and Osmolar Clearances 321
Disorders of Urinary Concentrating Ability 322
Control of Extracellular Fluid Osmolarity and Sodium Concentration 322
Estimating Plasma Osmolarity from Plasma Sodium Concentration 322
Osmoreceptor-ADH Feedback System 323
ADH Synthesis in Supraoptic and Paraventricular Nuclei of the Hypothalamus and ADH Release from the Posterior Pituitary 323
Cardiovascular Reflex Stimulation of ADH Release by Decreased Arterial Pressure and/or Decreased Blood Volume 324
Quantitative Importance of Cardiovascular Reflexes and Osmolarity in Stimulating ADH Secretion 324
Other Stimuli for ADH Secretion 324
Role of Thirst in Controlling Extracellular Fluid Osmolarity and Sodium Concentration 325
Central Nervous System Centers for Thirst 325
Stimuli for Thirst 325
Threshold for Osmolar Stimulus of Drinking 326
Integrated Responses of Osmoreceptor-ADH and Thirst Mechanisms in Controlling Extracellular Fluid Osmolarity and Sodium Concentration 326
Role of Angiotensin II and Aldosterone in Controlling Extracellular Fluid Osmolarity and Sodium Concentration 327
Salt-Appetite Mechanism for Controlling Extracellular Fluid Sodium Concentration and Volume 327

CHAPTER **29**
Integration of Renal Mechanisms for Control of Blood Volume and Extracellular Fluid Volume; and Renal Regulation of Potassium, Calcium, Phosphate, and Magnesium 329

Control Mechanisms for Regulating Sodium and Water Excretion 329
Sodium Excretion Is Precisely Matched to Intake Under Steady-State Conditions 329
Sodium Excretion Is Controlled by Altering Glomerular Filtration or Tubular Sodium Reabsorption Rates 329
Importance of Pressure Natriuresis and Pressure Diuresis in Maintaining Body Sodium and Fluid Balance 330
Pressure Natriuresis and Diuresis Are Key Components of a Renal–Body Fluid Feedback for Regulating Body Fluid Volumes and Arterial Pressure 330
Precision of Blood Volume and Extracellular Fluid Volume Regulation 331
Distribution of Extracellular Fluid Between the Interstitial Spaces and Vascular System 332
Nervous and Hormonal Factors Increase the Effectiveness of Renal–Body Fluid Feedback Control 332
Sympathetic Nervous System Control of Renal Excretion: The Arterial Baroreceptor and Low-Pressure Stretch Receptor Reflexes 332
Role of Angiotensin II in Controlling Renal Excretion 333
Role of Aldosterone in Controlling Renal Excretion 334
Role of ADH in Controlling Renal Water Excretion 334
Role of Atrial Natriuretic Peptide in Controlling Renal Excretion 335
Integrated Responses to Changes in Sodium Intake 335
Conditions That Cause Large Increases in Blood Volume and Extracellular Fluid Volume 335
Increased Blood Volume and Extracellular Fluid Volume Caused by Heart Diseases 335
Increased Blood Volume Caused by Increased Capacity of the Circulation 336
Conditions That Cause Large Increases in Extracellular Fluid Volume but with Normal Blood Volume 336
Nephrotic Syndrome—Loss of Plasma Proteins in the Urine and Sodium Retention by the Kidneys 336
Liver Cirrhosis—Decreased Synthesis of Plasma Proteins by the Liver and Sodium Retention by the Kidneys 336
Regulation of Potassium Excretion and Potassium Concentration in the Extracellular Fluid 336
Regulation of Internal Potassium Distribution 337
Overview of Renal Potassium Excretion 338
Potassium Secretion in the Principal Cells of the Late Distal and Cortical Collecting Tubules 339
Summary of Factors That Regulate Potassium Secretion: Plasma Potassium Concentration, Aldosterone, Tubular Flow Rate, and Hydrogen Ion 339
Control of Renal Calcium Excretion and Extracellular Calcium Ion Concentration 342
Control of Calcium Excretion by the Kidneys 343
Regulation of Renal Phosphate Excretion 343
Control of Renal Magnesium Excretion and Extracellular Magnesium Ion Concentration 344

CHAPTER **30**
Regulation of Acid-Base Balance 346

Hydrogen Ion Concentration Is Precisely Regulated 346
Acids and Bases—Their Definitions and Meanings 346
Defenses Against Changes in Hydrogen Ion Concentration: Buffers, Lungs, and Kidneys 347
Buffering of Hydrogen Ions in the Body Fluids 347
The Bicarbonate Buffer System 348
Quantitative Dynamics of the Bicarbonate Buffer System 348
The Phosphate Buffer System 350
Proteins: Important Intracellular Buffers 350

Isohydric Principle: All Buffers in a Common Solution Are in Equilibrium with the Same Hydrogen Ion Concentration 350
Respiratory Regulation of Acid-Base Balance 351
Pulmonary Expiration of CO_2 Balances Metabolic Formation of CO_2 351
Increasing Alveolar Ventilation Decreases Extracellular Fluid Hydrogen Ion Concentration and Raises pH 351
Increased Hydrogen Ion Concentration Stimulates Alveolar Ventilation 351
Renal Control of Acid-Base Balance 352
Secretion of Hydrogen Ions and Reabsorption of Bicarbonate Ions by the Renal Tubule 353
Hydrogen Ions Are Secreted by Secondary Active Transport in the Early Tubular Segments 353
Filtered Bicarbonate Ions Are Reabsorbed by Interaction with Hydrogen Ions in the Tubules 354
Primary Active Secretion of Hydrogen Ions in the Intercalated Cells of Late Distal and Collecting Tubules 355
Combination of Excess Hydrogen Ions With Phosphate and Ammonia Buffers in the Tubule—A Mechanism for Generating New Bicarbonate Ions 355
The Phosphate Buffer System Carries Excess Hydrogen Ions into the Urine and Generates New Bicarbonate 356
Excretion of Excess Hydrogen Ions and Generation of New Bicarbonate by the Ammonia Buffer System 356
Quantifying Renal Acid-Base Excretion 357
Regulation of Renal Tubular Hydrogen Ion Secretion 357
Renal Correction of Acidosis—Increased Excretion of Hydrogen Ions and Addition of Bicarbonate Ions to the Extracellular Fluid 358
Acidosis Decreases the Ratio of HCO_3^-/H^+ in Renal Tubular Fluid 358
Renal Correction of Alkalosis—Decreased Tubular Secretion of Hydrogen Ions and Increased Excretion of Bicarbonate Ions 359
Alkalosis Increases the Ratio of HCO_3^-/H^+ in Renal Tubular Fluid 359
Clinical Causes of Acid-Base Disorders 359
Respiratory Acidosis Is Caused by Decreased Ventilation and Increased P_{CO_2} 359
Respiratory Alkalosis Results from Increased Ventilation and Decreased P_{CO_2} 359
Metabolic Acidosis Results from Decreased Extracellular Fluid Bicarbonate Concentration 360
Metabolic Alkalosis Is Caused by Increased Extracellular Fluid Bicarbonate Concentration 360
Treatment of Acidosis or Alkalosis 360
Clinical Measurements and Analysis of Acid-Base Disorders 361
Complex Acid-Base Disorders and the Use of the Acid-Base Nomogram for Diagnosis 361
Use of Anion Gap to Diagnose Acid-Base Disorders 362

CHAPTER **31**
Micturition, Diuretics, and Kidney Diseases 364
Micturition 364
Physiologic Anatomy and Nervous Connections of the Bladder 364
Innervation of the Bladder 364
Transport of Urine from the Kidney Through the Ureters and Into the Bladder 364
Filling of the Bladder and Bladder Wall Tone; The Cystometrogram 365
Micturition Reflex 366
Facilitation or Inhibition of Micturition by the Brain 366
Abnormalities of Micturition 366
Diuretics and Their Mechanisms of Action 367
Osmotic Diuretics Decrease Water Reabsorption by Increasing Osmotic Pressure of Tubular Fluid 367
"Loop" Diuretics Decrease Active Sodium-Chloride-Potassium Reabsorption in the Thick Ascending Loop of Henle 368
Thiazide Diuretics Inhibit Sodium-Chloride Reabsorption in the Early Distal Tubule 368
Carbonic Anhydrase Inhibitors Block Sodium-Bicarbonate Reabsorption in the Proximal Tubules 368
Competitive Inhibitors of Aldosterone Decrease Sodium Reabsorption from and Potassium Secretion into the Cortical Collecting Tubule 368
Diuretics That Block Sodium Channels in the Collecting Tubules Decrease Sodium Reabsorption 368
Kidney Diseases 369
Acute Renal Failure 369
Prerenal Acute Renal Failure Caused by Decreased Blood Flow to the Kidney 369
Intrarenal Acute Renal Failure Caused by Abnormalities Within the Kidney 369
Postrenal Acute Renal Failure Caused by Abnormalities of the Lower Urinary Tract 370
Physiologic Effects of Acute Renal Failure 370
Chronic Renal Failure: An Irreversible Decrease in the Number of Functional Nephrons 371
Vicious Circle of Chronic Renal Failure Leading to End-Stage Renal Disease 371
Injury to the Renal Vasculature as a Cause of Chronic Renal Failure 371
Injury to the Glomeruli as a Cause of Chronic Renal Failure—Glomerulonephritis 372
Injury to the Renal Interstitium as a Cause of Chronic Renal Failure—Pyelonephritis 373
Nephrotic Syndrome—Excretion of Protein in the Urine Because of Increased Glomerular Permeability 373
Abnormal Nephron Function in Chronic Renal Failure 373
Effects of Renal Failure on the Body Fluids—Uremia 375
Hypertension and Kidney Disease 376
Specific Tubular Disorders 377
Treatment of Renal Failure by Dialysis With an Artificial Kidney 377

UNIT **VI**
Blood Cells, Immunity, and Blood Clotting

CHAPTER **32**
Red Blood Cells, Anemia, and Polycythemia 382
Red Blood Cells (Erythrocytes) 382
Production of Red Blood Cells 382
Formation of Hemoglobin 386
Iron Metabolism 387
Destruction of Red Blood Cells 389
The Anemias 389
Effects of Anemia on the Circulatory System 390