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INTERNAL MEDICINE

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VOLUME I



New York Chicago San Francisco Athens London Madrid Mexico City
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ISBN: 978-1-26-426851-1

MHID: 1-26-426851-3

The material in this eBook also appears in the print version of this title: ISBN: 978-1-26-426850-4,
MHID: 1-26-426850-5.

eBook conversion by codeMantra

Version 1.0

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Beginning with the 6th edition, the cover of *Harrison's* has included an image of a bright light—a patient's perception of being examined with an ophthalmoscope. This allegorical symbol of *Harrison's* is a reminder of how the light of knowledge empowers physicians to better diagnose and treat diseases that ultimately afflict all of humankind.

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Contributors	xviii
Preface	xxxix
Harrison's Related Resources	xl

PART 1 The Profession of Medicine

1 The Practice of Medicine	1
<i>The Editors</i>	
2 Promoting Good Health	8
<i>Donald M. Lloyd-Jones, Kathleen M. McKibbin</i>	
3 Vaccine Opposition and Hesitancy	13
<i>Julie A. Bettinger, Hana Mitchell</i>	
4 Decision-Making in Clinical Medicine.....	21
<i>Daniel B. Mark, John B. Wong</i>	
5 Precision Medicine and Clinical Care	30
<i>The Editors</i>	
6 Screening and Prevention of Disease	37
<i>Katrina A. Armstrong, Gary J. Martin</i>	
7 Global Diversity of Health System Financing and Delivery	42
<i>Richard B. Saltman</i>	
8 The Safety and Quality of Health Care.....	50
<i>David W. Bates</i>	
9 Diagnosis: Reducing Errors and Improving Quality.....	54
<i>Gordon Schiff</i>	
10 Racial and Ethnic Disparities in Health Care.....	59
<i>Lenny López, Joseph R. Betancourt</i>	
11 Ethical Issues in Clinical Medicine.....	67
<i>Christine Grady, Bernard Lo</i>	
12 Palliative and End-of-Life Care	72
<i>Ezekiel J. Emanuel</i>	

PART 2 Cardinal Manifestations and Presentation of Diseases

SECTION 1 Pain

13 Pain: Pathophysiology and Management	91
<i>James P. Rathmell, Howard L. Fields</i>	
14 Chest Discomfort	100
<i>David A. Morrow</i>	
15 Abdominal Pain.....	108
<i>Danny O. Jacobs</i>	
16 Headache.....	112
<i>Peter J. Goadsby</i>	
17 Back and Neck Pain	117
<i>John W. Engstrom</i>	

SECTION 2 Alterations in Body Temperature

18 Fever	130
<i>Neeraj K. Surana, Charles A. Dinarello, Reuven Porat</i>	
19 Fever and Rash	133
<i>Elaine T. Kaye, Kenneth M. Kaye</i>	
20 Fever of Unknown Origin	145
<i>Chantal P. Bleeker-Rovers, Catharina M. Mulders-Manders, Jos W. M. van der Meer</i>	

SECTION 3 Nervous System Dysfunction

21 Syncope	152
<i>Roy Freeman</i>	
22 Dizziness and Vertigo.....	159
<i>Mark F. Walker, Robert B. Daroff</i>	
23 Fatigue	162
<i>Jeffrey M. Gelfand, Vanja C. Douglas</i>	
24 Neurologic Causes of Weakness and Paralysis	165
<i>Stephen L. Hauser</i>	
25 Numbness, Tingling, and Sensory Loss	168
<i>Stephen L. Hauser</i>	
26 Gait Disorders, Imbalance, and Falls	173
<i>Jessica M. Baker</i>	
27 Confusion and Delirium	178
<i>S. Andrew Josephson, Bruce L. Miller</i>	
28 Coma.....	183
<i>S. Andrew Josephson, Allan H. Ropper, Stephen L. Hauser</i>	
29 Dementia.....	189
<i>William W. Seeley, Gil D. Rabinovici, Bruce L. Miller</i>	
30 Aphasia, Memory Loss, and Other Cognitive Disorders.....	195
<i>M.-Marsel Mesulam</i>	
31 Sleep Disorders.....	204
<i>Thomas E. Scammell, Clifford B. Saper, Charles A. Czeisler</i>	

SECTION 4 Disorders of Eyes, Ears, Nose, and Throat

32 Disorders of the Eye.....	215
<i>Jonathan C. Horton</i>	
33 Disorders of Smell and Taste	232
<i>Richard L. Doty, Steven M. Bromley</i>	
34 Disorders of Hearing.....	238
<i>Anil K. Lalwani</i>	
35 Upper Respiratory Symptoms, Including Earache, Sinus Symptoms, and Sore Throat.....	247
<i>Rachel L. Amdur, Jeffrey A. Linder</i>	
36 Oral Manifestations of Disease	256
<i>Samuel C. Durso</i>	

SECTION 5 Alterations in Circulatory and Respiratory Functions

37 Dyspnea	263
<i>Rebecca M. Baron</i>	
38 Cough	267
<i>Christopher H. Fanta</i>	
39 Hemoptysis	270
<i>Carolyn M. D'Ambrosio</i>	
40 Hypoxia and Cyanosis.....	272
<i>Joseph Loscalzo</i>	
41 Edema	275
<i>Joseph Loscalzo</i>	
42 Approach to the Patient with a Heart Murmur	278
<i>Patrick T. O'Gara, Joseph Loscalzo</i>	
43 Palpitations.....	286
<i>Joseph Loscalzo</i>	

SECTION 6 Alterations in Gastrointestinal Function

44 Dysphagia.....	287
<i>Ikuo Hirano, Peter J. Kahrilas</i>	
45 Nausea, Vomiting, and Indigestion.....	291
<i>William L. Hasler</i>	
46 Diarrhea and Constipation.....	297
<i>Michael Camilleri, Joseph A. Murray</i>	
47 Unintentional Weight Loss.....	309
<i>J. Larry Jameson</i>	
48 Gastrointestinal Bleeding.....	311
<i>Loren Laine</i>	
49 Jaundice.....	315
<i>Savio John, Daniel S. Pratt</i>	
50 Abdominal Swelling and Ascites.....	321
<i>Lawrence S. Friedman</i>	

SECTION 7 Alterations in Renal and Urinary Tract Function

51 Interstitial Cystitis/Bladder Pain Syndrome.....	325
<i>R. Christopher Doiron, J. Curtis Nickel</i>	
52 Azotemia and Urinary Abnormalities.....	331
<i>David B. Mount</i>	
53 Fluid and Electrolyte Disturbances.....	338
<i>David B. Mount</i>	
54 Hypercalcemia and Hypocalcemia.....	356
<i>Sundeep Khosla</i>	
55 Acidosis and Alkalosis.....	359
<i>Thomas D. DuBose, Jr.</i>	

SECTION 8 Alterations in the Skin

56 Approach to the Patient with a Skin Disorder.....	369
<i>Kim B. Yancey, Thomas J. Lawley</i>	
57 Eczema, Psoriasis, Cutaneous Infections, Acne, and Other Common Skin Disorders.....	374
<i>Leslie P. Lawley, Justin T. Cheeley, Robert A. Swerlick</i>	
58 Skin Manifestations of Internal Disease.....	383
<i>Jean L. Bolognia, Jonathan S. Leventhal, Irwin M. Braverman</i>	
59 Immunologically Mediated Skin Diseases.....	400
<i>Kim B. Yancey, Benjamin F. Chong, Thomas J. Lawley</i>	
60 Cutaneous Drug Reactions.....	407
<i>Robert G. Micheletti, Misha Rosenbach, Bruce U. Wintroub, Kanade Shinkai</i>	
61 Photosensitivity and Other Reactions to Sunlight.....	417
<i>Alexander G. Marneros, David R. Bickers</i>	

SECTION 9 Hematologic Alterations

62 Interpreting Peripheral Blood Smears.....	424
<i>Dan L. Longo</i>	
63 Anemia and Polycythemia.....	431
<i>John W. Adamson, Dan L. Longo</i>	
64 Disorders of Granulocytes and Monocytes.....	439
<i>Steven M. Holland, John I. Gallin</i>	
65 Bleeding and Thrombosis.....	450
<i>Barbara A. Konkle</i>	
66 Enlargement of Lymph Nodes and Spleen.....	457
<i>Dan L. Longo</i>	

PART 3 Pharmacology

67 Principles of Clinical Pharmacology.....	465
<i>Dan M. Roden</i>	
68 Pharmacogenomics.....	474
<i>Dan M. Roden</i>	

PART 4 Oncology and Hematology**SECTION 1 Neoplastic Disorders**

69 Approach to the Patient with Cancer.....	481
<i>Dan L. Longo</i>	
70 Prevention and Early Detection of Cancer.....	490
<i>Jennifer M. Croswell, Otis W. Brawley, Barnett S. Kramer</i>	
71 Cancer Genetics.....	498
<i>Fred Bunz, Bert Vogelstein</i>	
72 Cancer Cell Biology.....	508
<i>Jeffrey W. Clark, Dan L. Longo</i>	
73 Principles of Cancer Treatment.....	529
<i>Edward A. Sausville, Dan L. Longo</i>	
74 Infections in Patients with Cancer.....	556
<i>Robert W. Finberg</i>	
75 Oncologic Emergencies.....	565
<i>Rasim Gucalp, Janice P. Dutcher</i>	
76 Cancer of the Skin.....	578
<i>Brendan D. Curti, John T. Vetto, Sancy A. Leachman</i>	
77 Head and Neck Cancer.....	590
<i>Everett E. Vokes</i>	
78 Neoplasms of the Lung.....	594
<i>Leora Horn, Wade T. Iams</i>	
79 Breast Cancer.....	611
<i>Daniel F. Hayes, Marc E. Lippman</i>	
80 Upper Gastrointestinal Tract Cancers.....	626
<i>David Kelsen</i>	
81 Lower Gastrointestinal Cancers.....	636
<i>Robert J. Mayer</i>	
82 Tumors of the Liver and Biliary Tree.....	643
<i>Josep M. Llovet</i>	
83 Pancreatic Cancer.....	657
<i>Daniel D. Von Hoff</i>	
84 Gastrointestinal Neuroendocrine Tumors.....	663
<i>Matthew H. Kulke</i>	
85 Renal Cell Carcinoma.....	673
<i>Robert J. Motzer, Martin H. Voss</i>	
86 Cancer of the Bladder and Urinary Tract.....	676
<i>Noah M. Hahn</i>	
87 Benign and Malignant Diseases of the Prostate.....	681
<i>Howard I. Scher, James A. Eastham</i>	
88 Testicular Cancer.....	689
<i>David J. Vaughn</i>	
89 Gynecologic Malignancies.....	695
<i>David Spriggs</i>	
90 Primary and Metastatic Tumors of the Nervous System.....	701
<i>Lisa M. DeAngelis, Patrick Y. Wen</i>	
91 Soft Tissue and Bone Sarcomas and Bone Metastases.....	712
<i>Shreyaskumar R. Patel</i>	

92 Carcinoma of Unknown Primary	716
<i>Kanwal Raghav, James L. Abbruzzese, Gauri R. Varadhachary</i>	
93 Paraneoplastic Syndromes: Endocrinologic/ Hematologic	721
<i>J. Larry Jameson, Dan L. Longo</i>	
94 Paraneoplastic Neurologic Syndromes and Autoimmune Encephalitis.....	728
<i>Josep Dalmau, Myrna R. Rosenfeld, Francesc Graus</i>	
95 Cancer Survivorship and the Long-Term Impact of Cancer and Its Treatment	736
<i>Mark Roschewski, Dan L. Longo</i>	

SECTION 2 Hematopoietic Disorders

96 Hematopoietic Stem Cells.....	743
<i>David T. Scadden, Dan L. Longo</i>	
97 Iron Deficiency and Other Hypoproliferative Anemias	747
<i>John W. Adamson</i>	
98 Disorders of Hemoglobin.....	754
<i>Martin H. Steinberg</i>	
99 Megaloblastic Anemias	766
<i>A. Victor Hoffbrand</i>	
100 Hemolytic Anemias	776
<i>Lucio Luzzatto, Lucia De Franceschi</i>	
101 Anemia Due to Acute Blood Loss	791
<i>Dan L. Longo</i>	
102 Bone Marrow Failure Syndromes Including Aplastic Anemia and Myelodysplasia.....	792
<i>Neal S. Young</i>	
103 Polycythemia Vera and Other Myeloproliferative Neoplasms	802
<i>Jerry L. Spivak</i>	
104 Acute Myeloid Leukemia	809
<i>William Blum</i>	
105 Chronic Myeloid Leukemia.....	818
<i>Hagop Kantarjian, Elias Jabbour, Jorge Cortes</i>	
106 Acute Lymphoid Leukemia.....	828
<i>Dieter Hoelzer</i>	
107 Chronic Lymphocytic Leukemia	834
<i>Jennifer A. Woyach, John C. Byrd</i>	
108 Non-Hodgkin's Lymphoma	841
<i>Caron A. Jacobson, Dan L. Longo</i>	
109 Hodgkin's Lymphoma.....	852
<i>Caron A. Jacobson, Dan L. Longo</i>	
110 Less Common Lymphoid and Myeloid Malignancies	855
<i>Ayalew Tefferi, Dan L. Longo</i>	
111 Plasma Cell Disorders.....	866
<i>Nikhil C. Munshi, Dan L. Longo, Kenneth C. Anderson</i>	
112 Amyloidosis	878
<i>John L. Berk, Vaishali Santhorawala</i>	
113 Transfusion Therapy and Biology	884
<i>Pierre Tiberghien, Olivier Garraud, Jacques Chironi</i>	
114 Hematopoietic Cell Transplantation.....	897
<i>Frederick R. Appelbaum</i>	

SECTION 3 Disorders of Hemostasis

115 Disorders of Platelets and Vessel Wall.....	903
<i>Barbara A. Konkle</i>	

116 Coagulation Disorders	910
<i>Jean M. Connors</i>	
117 Arterial and Venous Thrombosis	919
<i>Jane E. Freedman, Joseph Loscalzo</i>	
118 Antiplatelet, Anticoagulant, and Fibrinolytic Drugs	924
<i>Jeffrey I. Weitz</i>	

PART 5 Infectious Diseases

SECTION 1 Basic Considerations in Infectious Diseases

119 Approach to the Patient with an Infectious Disease.....	941
<i>Neeraj K. Surana, Dennis L. Kasper</i>	
120 Molecular Mechanisms of Microbial Pathogenesis.....	948
<i>Thomas E. Wood, Marcia B. Goldberg</i>	
121 Microbial Genomics and Infectious Disease	960
<i>Roby P. Bhattacharyya, Yonatan H. Grad, Deborah T. Hung</i>	
122 Approach to the Acutely Ill Infected Febrile Patient.....	973
<i>Tamar F. Barlam</i>	
123 Immunization Principles and Vaccine Use	981
<i>Sarah Mbaeyi, Amanda Cohn, Nancy Messonnier</i>	
124 Health Recommendations for International Travel	989
<i>Jesse Waggoner, Henry M. Wu</i>	
125 Climate Change and Infectious Disease.....	1001
<i>Aaron S. Bernstein</i>	

SECTION 2 Clinical Syndromes: Community-Acquired Infections

126 Pneumonia	1009
<i>Lionel A. Mandell, Michael S. Niederman</i>	
127 Lung Abscess.....	1020
<i>Rebecca M. Baron, Beverly W. Baron, Miriam Baron Barshak</i>	
128 Infective Endocarditis	1022
<i>Sara E. Cosgrove, Adolf W. Karchmer</i>	
129 Infections of the Skin, Muscles, and Soft Tissues	1034
<i>Dennis L. Stevens, Amy E. Bryant</i>	
130 Infectious Arthritis	1040
<i>Lawrence C. Madoff, Nongnooch Poowanawittayakom</i>	
131 Osteomyelitis.....	1046
<i>Werner Zimmerli</i>	
132 Intraabdominal Infections and Abscesses	1054
<i>Miriam Baron Barshak, Dennis L. Kasper</i>	
133 Acute Infectious Diarrheal Diseases and Bacterial Food Poisoning.....	1061
<i>Richelle C. Charles, Regina C. LaRocque</i>	
134 <i>Clostridioides difficile</i> Infection, Including Pseudomembranous Colitis.....	1066
<i>Dale N. Gerding, Stuart Johnson</i>	
135 Urinary Tract Infections, Pyelonephritis, and Prostatitis	1070
<i>Kalpna Gupta, Barbara W. Trautner</i>	
136 Sexually Transmitted Infections: Overview and Clinical Approach.....	1078
<i>Jeanne M. Marrazzo, King K. Holmes</i>	
137 Encephalitis	1094
<i>Karen L. Roos, Michael R. Wilson, Kenneth L. Tyler</i>	
138 Acute Meningitis	1100
<i>Karen L. Roos, Kenneth L. Tyler</i>	

- 139 Chronic and Recurrent Meningitis 1110
Avindra Nath, Walter J. Koroshetz, Michael R. Wilson
- 140 Brain Abscess and Empyema 1117
Karen L. Roos, Kenneth L. Tyler
- 141 Infectious Complications of Bites 1124
Sandeep S. Jubbal, Florencia Pereyra Segal, Lawrence C. Madoff

SECTION 3 Clinical Syndromes: Health Care–Associated Infections

- 142 Infections Acquired in Health Care Facilities 1128
Robert A. Weinstein
- 143 Infections in Transplant Recipients 1136
Robert W. Finberg

SECTION 4 Therapy for Bacterial Diseases

- 144 Treatment and Prophylaxis of Bacterial Infections 1148
David C. Hooper, Erica S. Shenoy, Ramy H. Elshaboury
- 145 Bacterial Resistance to Antimicrobial Agents 1163
David C. Hooper

SECTION 5 Diseases Caused by Gram-Positive Bacteria

- 146 Pneumococcal Infections 1169
David Goldblatt, Katherine L. O'Brien
- 147 Staphylococcal Infections 1178
Franklin D. Lowy
- 148 Streptococcal Infections 1188
Michael R. Wessels
- 149 Enterococcal Infections 1197
William R. Miller, Cesar A. Arias, Barbara E. Murray
- 150 Diphtheria and Other Corynebacterial Infections 1203
William R. Bishai, John R. Murphy
- 151 *Listeria monocytogenes* Infections 1208
Jennifer P. Collins, Patricia M. Griffin
- 152 Tetanus 1211
C. Louise Thwaites, Lam Minh Yen
- 153 Botulism 1214
Carolina Lúquez, Jeremy Sobel
- 154 Gas Gangrene and Other Clostridial Infections 1220
Amy E. Bryant, Dennis L. Stevens

SECTION 6 Diseases Caused by Gram-Negative Bacteria

- 155 Meningococcal Infections 1225
Manish Sadarangani, Andrew J. Pollard
- 156 Gonococcal Infections 1234
Sanjay Ram, Peter A. Rice
- 157 *Haemophilus* and *Moraxella* Infections 1241
Timothy F. Murphy
- 158 Infections Due to the HACEK Group and Miscellaneous Gram-Negative Bacteria 1246
Tamar F. Barlam
- 159 *Legionella* Infections 1249
Steven A. Pergam, Thomas R. Hawn
- 160 Pertussis and Other *Bordetella* Infections 1257
Karina A. Top, Scott A. Halperin
- 161 Diseases Caused by Gram-Negative Enteric Bacilli 1261
Thomas A. Russo, James R. Johnson
- 162 *Acinetobacter* Infections 1275
Rossana Rosa, L. Silvia Munoz-Price

- 163 *Helicobacter pylori* Infections 1279
John C. Atherton, Martin J. Blaser
- 164 Infections Due to *Pseudomonas*, *Burkholderia*, and *Stenotrophomonas* Species 1284
Reuben Ramphal
- 165 Salmonellosis 1291
David A. Pegues, Samuel I. Miller
- 166 Shigellosis 1298
Philippe J. Sansonetti, Jean Bergounioux
- 167 Infections Due to *Campylobacter* and Related Organisms 1302
Martin J. Blaser
- 168 Cholera and Other Vibrios 1305
Matthew K. Waldor, Edward T. Ryan
- 169 Brucellosis 1310
Nicholas J. Beeching
- 170 Tularemia 1314
Max Maurin, Didier Raoult
- 171 Plague and Other *Yersinia* Infections 1320
Michael B. Prentice
- 172 *Bartonella* Infections, Including Cat-Scratch Disease 1328
Michael Giladi, Moshe Ephros
- 173 Donovanosis 1334
Nigel O'Farrell

SECTION 7 Miscellaneous Bacterial Infections

- 174 Nocardiosis 1335
Gregory A. Filice
- 175 Actinomycosis 1340
Thomas A. Russo
- 176 Whipple's Disease 1344
Thomas A. Russo, Seth R. Glassman
- 177 Infections Due to Mixed Anaerobic Organisms 1347
Neeraj K. Surana, Dennis L. Kasper

SECTION 8 Mycobacterial Diseases

- 178 Tuberculosis 1357
Mario C. Raviglione, Andrea Gori
- 179 Leprosy 1382
Jan H. Richardus, Hemanta K. Kar, Zoica Bakirtzief, Wim H. van Brakel
- 180 Nontuberculous Mycobacterial Infections 1392
Steven M. Holland
- 181 Antimycobacterial Agents 1397
Divya Reddy, Sebastian G. Kurz, Max R. O'Donnell

SECTION 9 Spirochetal Diseases

- 182 Syphilis 1406
Sheila A. Lukehart
- 183 Endemic Treponematoses 1413
Sheila A. Lukehart, Lorenzo Giacani
- 184 Leptospirosis 1417
Jiri F. P. Wagenaar, Marga G.A. Goris
- 185 Relapsing Fever and *Borrelia miyamotoi* Disease 1421
Alan G. Barbour
- 186 Lyme Borreliosis 1425
Allen C. Steere

SECTION 10 Diseases Caused by Rickettsiae, Mycoplasmas, and Chlamydiae

- 187 Rickettsial Diseases 1431
*David H. Walker, J. Stephen Dumler, Lucas S. Blanton,
 Chantal P. Bleeker-Rovers*
- 188 Infections Due to Mycoplasmas 1441
R. Doug Hardy
- 189 Chlamydial Infections 1444
Charlotte A. Gaydos, Thomas C. Quinn

SECTION 11 Viral Diseases: General Considerations

- 190 Principles of Medical Virology 1453
David M. Knipe
- 191 Antiviral Chemotherapy, Excluding Antiretroviral
 Drugs 1460
Jeffrey I. Cohen, Eleanor Wilson

SECTION 12 Infections Due to DNA Viruses

- 192 Herpes Simplex Virus Infections 1470
Lawrence Corey
- 193 Varicella-Zoster Virus Infections..... 1479
Richard J. Whitley
- 194 Epstein-Barr Virus Infections, Including Infectious
 Mononucleosis 1483
Jeffrey I. Cohen
- 195 Cytomegalovirus and Human Herpesvirus
 Types 6, 7, and 8..... 1487
Camille Nelson Kotton, Martin S. Hirsch
- 196 Molluscum Contagiosum, Monkeypox, and
 Other Poxvirus Infections 1492
Inger K. Damon
- 197 Parvovirus Infections 1495
Kevin E. Brown
- 198 Human Papillomavirus Infections 1498
Darron R. Brown, Aaron C. Ermel

SECTION 13 Infections Due to DNA and RNA Respiratory Viruses

- 199 Common Viral Respiratory Infections, Including
 COVID-19..... 1504
James E. Crowe, Jr.
- 200 Influenza 1515
Kathleen M. Neuzil, Peter F. Wright

SECTION 14 Infections Due to Human Immunodeficiency Virus and Other Human Retroviruses

- 201 The Human Retroviruses 1521
Dan L. Longo, Anthony S. Fauci
- 202 Human Immunodeficiency Virus Disease:
 AIDS and Related Disorders..... 1527
Anthony S. Fauci, Gregory K. Folkers, H. Clifford Lane

SECTION 15 Infections Due to RNA Viruses

- 203 Viral Gastroenteritis 1597
Umesh D. Parashar, Roger I. Glass
- 204 Enterovirus, Parechovirus, and Reovirus Infections 1602
Jeffrey I. Cohen
- 205 Measles (Rubeola)..... 1608
Kaitlin Rainwater-Lovett, William J. Moss

- 206 Rubella (German Measles)..... 1612
Laura A. Zimmerman, Susan E. Reef

- 207 Mumps 1615
Jessica Leung, Mariel Marlow

- 208 Rabies and Other Rhabdovirus Infections 1618
Alan C. Jackson

- 209 Arthropod-Borne and Rodent-Borne Virus
 Infections 1624
Jens H. Kuhn, Ian Crozier

- 210 Ebolavirus and Marburgvirus Infections..... 1645
Jens H. Kuhn, Ian Crozier

SECTION 16 Fungal Infections

- 211 Pathogenesis, Diagnosis, and Treatment of
 Fungal Infections 1652
Michail S. Lionakis, John E. Edwards Jr.

- 212 Histoplasmosis..... 1658
Chadi A. Hage, L. Joseph Wheat

- 213 Coccidioidomycosis 1661
Neil M. Ampel

- 214 Blastomycosis 1664
Gregory M. Gauthier, Bruce S. Klein

- 215 Cryptococcosis..... 1668
Arturo Casadevall

- 216 Candidiasis 1671
*Michail S. Lionakis, Shakti Singh, Ashraf S. Ibrahim,
 John E. Edwards, Jr.*

- 217 Aspergillosis 1677
David W. Denning

- 218 Mucormycosis..... 1681
Brad Spellberg, Ashraf S. Ibrahim

- 219 Less Common Systemic Mycoses and Superficial
 Mycoses..... 1686
Carol A. Kauffman

- 220 *Pneumocystis* Infections..... 1691
Alison Morris, Henry Masur

SECTION 17 Protozoal and Helminthic Infections: General Considerations

- 221 Introduction to Parasitic Infections 1696
Sharon L. Reed

- 222 Agents Used to Treat Parasitic Infections..... 1701
Thomas A. Moore

SECTION 18 Protozoal Infections

- 223 Amebiasis and Infection with Free-Living Amebae..... 1714
Rosa M. Andrade, Sharon L. Reed

- 224 Malaria 1720
Nicholas J. White, Elizabeth A. Ashley

- 225 Babesiosis 1736
Edouard Vannier, Jeffrey A. Gelfand

- 226 Leishmaniasis 1741
Shyam Sundar

- 227 Chagas Disease and African Trypanosomiasis..... 1748
François Chappuis, Yves Jackson

- 228 *Toxoplasma* Infections..... 1757
Kami Kim

- 229 Protozoal Intestinal Infections and Trichomoniasis..... 1764
Peter F. Weller

SECTION 19 Helminthic Infections

- 230 Introduction to Helminthic Infections..... 1768
Peter F. Weller
- 231 Trichinellosis and Other Tissue Nematode Infections 1770
Peter F. Weller
- 232 Intestinal Nematode Infections 1773
Thomas B. Nutman, Peter F. Weller
- 233 Filarial and Related Infections..... 1778
Thomas B. Nutman, Peter F. Weller
- 234 Schistosomiasis and Other Trematode Infections..... 1784
Birgitte Jyding Vennervald
- 235 Cestode Infections 1790
A. Clinton White, Jr., Peter F. Weller

PART 6 Disorders of the Cardiovascular System**SECTION 1 Introduction to Cardiovascular Disorders**

- 236 Approach to the Patient with Possible Cardiovascular Disease 1797
Joseph Loscalzo
- 237 Basic Biology of the Cardiovascular System 1799
Joseph Loscalzo, John F. Keaney, Jr., Calum A. MacRae
- 238 Epidemiology of Cardiovascular Disease 1810
Thomas A. Gaziano, J. Michael Gaziano

SECTION 2 Diagnosis of Cardiovascular Disorders

- 239 Physical Examination of the Cardiovascular System..... 1815
Patrick T. O'Gara, Joseph Loscalzo
- 240 Electrocardiography..... 1824
Ary L. Goldberger
- 241 Noninvasive Cardiac Imaging: Echocardiography, Nuclear Cardiology, and Magnetic Resonance/Computed Tomography Imaging..... 1832
Marcelo F. Di Carli, Raymond Y. Kwong, Scott D. Solomon
- 242 Diagnostic Cardiac Catheterization and Coronary Angiography 1859
Jane A. Leopold, David P. Faxon

SECTION 3 Disorders of Rhythm

- 243 Principles of Clinical Cardiac Electrophysiology 1866
William H. Sauer, Bruce A. Koplan, Paul C. Zei
- 244 The Bradyarrhythmias: Disorders of the Sinoatrial Node..... 1873
William H. Sauer, Bruce A. Koplan
- 245 The Bradyarrhythmias: Disorders of the Atrioventricular Node..... 1880
William H. Sauer, Bruce A. Koplan
- 246 Approach to Supraventricular Tachyarrhythmias 1888
William H. Sauer, Paul C. Zei
- 247 Physiologic and Nonphysiologic Sinus Tachycardia..... 1891
William H. Sauer, Paul C. Zei
- 248 Focal Atrial Tachycardia..... 1893
William H. Sauer, Paul C. Zei
- 249 Paroxysmal Supraventricular Tachycardias..... 1894
William H. Sauer, Paul C. Zei

- 250 Common Atrial Flutter and Macroreentrant and Multifocal Atrial Tachycardias..... 1899
William H. Sauer, Paul C. Zei
- 251 Atrial Fibrillation..... 1903
William H. Sauer, Paul C. Zei
- 252 Approach to Ventricular Arrhythmias 1910
William H. Sauer, Usha B. Tedrow
- 253 Premature Ventricular Contractions, Nonsustained Ventricular Tachycardia, and Accelerated Idioventricular Rhythm..... 1915
William H. Sauer, Usha B. Tedrow
- 254 Sustained Ventricular Tachycardia 1919
William H. Sauer, Usha B. Tedrow
- 255 Polymorphic Ventricular Tachycardia and Ventricular Fibrillation 1923
William H. Sauer, Usha B. Tedrow
- 256 Electrical Storm and Incessant Ventricular Tachycardia..... 1927
William H. Sauer, Usha B. Tedrow

SECTION 4 Disorders of the Heart, Muscles, Valves, and Pericardium

- 257 Heart Failure: Pathophysiology and Diagnosis..... 1930
Michael M. Givertz, Mandeep R. Mehra
- 258 Heart Failure: Management 1940
Akshay S. Desai, Mandeep R. Mehra
- 259 Cardiomyopathy and Myocarditis..... 1954
Neal K. Lakdawala, Lynne Warner Stevenson, Joseph Loscalzo
- 260 Cardiac Transplantation and Prolonged Assisted Circulation 1973
Mandeep R. Mehra
- 261 Aortic Stenosis..... 1978
Patrick T. O'Gara, Joseph Loscalzo
- 262 Aortic Regurgitation 1986
Patrick T. O'Gara, Joseph Loscalzo
- 263 Mitral Stenosis 1991
Patrick T. O'Gara, Joseph Loscalzo
- 264 Mitral Regurgitation 1995
Patrick T. O'Gara, Joseph Loscalzo
- 265 Mitral Valve Prolapse 1999
Patrick T. O'Gara, Joseph Loscalzo
- 266 Tricuspid Valve Disease..... 2001
Patrick T. O'Gara, Joseph Loscalzo
- 267 Pulmonic Valve Disease..... 2004
Patrick T. O'Gara, Joseph Loscalzo
- 268 Multiple and Mixed Valvular Heart Disease..... 2005
Patrick T. O'Gara, Joseph Loscalzo
- 269 Congenital Heart Disease in the Adult 2008
Anne Marie Valente, Michael J. Landzberg
- 270 Pericardial Disease 2019
Joseph Loscalzo
- 271 Atrial Myxoma and Other Cardiac Tumors..... 2025
Eric H. Awtry
- 272 Cardiac Trauma 2028
Eric H. Awtry

SECTION 5 Coronary and Peripheral Vascular Disease

- 273 Ischemic Heart Disease..... 2030
Elliott M. Antman, Joseph Loscalzo

274 Non-ST-Segment Elevation Acute Coronary Syndrome (Non-ST-Segment Elevation Myocardial Infarction and Unstable Angina)	2046
<i>Robert P. Giugliano, Christopher P. Cannon, Eugene Braunwald</i>	
275 ST-Segment Elevation Myocardial Infarction	2053
<i>Elliott M. Antman, Joseph Loscalzo</i>	
276 Percutaneous Coronary Interventions and Other Interventional Procedures	2066
<i>David P. Faxon, Deepak L. Bhatt</i>	
277 Hypertension.....	2072
<i>Theodore A. Kotchen</i>	
278 Renovascular Disease.....	2088
<i>Stephen C. Textor</i>	
279 Deep-Venous Thrombosis and Pulmonary Thromboembolism	2091
<i>Samuel Z. Goldhaber</i>	
280 Diseases of the Aorta.....	2101
<i>Mark A. Creager, Joseph Loscalzo</i>	
281 Arterial Diseases of the Extremities.....	2107
<i>Mark A. Creager, Joseph Loscalzo</i>	
282 Chronic Venous Disease and Lymphedema	2115
<i>Mark A. Creager, Joseph Loscalzo</i>	
283 Pulmonary Hypertension	2121
<i>Bradley A. Maron, Joseph Loscalzo</i>	

PART 7 Disorders of the Respiratory System

SECTION 1 Diagnosis of Respiratory Disorders

284 Approach to the Patient with Disease of the Respiratory System	2131
<i>Bruce D. Levy</i>	
285 Disturbances of Respiratory Function	2133
<i>Edward T. Naureckas, Julian Solway</i>	
286 Diagnostic Procedures in Respiratory Disease	2140
<i>George R. Washko, Hilary J. Goldberg, Majid Shafiq</i>	

SECTION 2 Diseases of the Respiratory System

287 Asthma.....	2147
<i>Elliot Israel</i>	
288 Hypersensitivity Pneumonitis and Pulmonary Infiltrates with Eosinophilia	2160
<i>Praveen Akuthota, Michael E. Wechsler</i>	
289 Occupational and Environmental Lung Disease	2166
<i>John R. Balmes</i>	
290 Bronchiectasis.....	2173
<i>Rebecca M. Baron, Beverly W. Baron, Miriam Baron Barshak</i>	
291 Cystic Fibrosis	2176
<i>Eric J. Sorscher</i>	
292 Chronic Obstructive Pulmonary Disease.....	2180
<i>Edwin K. Silverman, James D. Crapo, Barry J. Make</i>	
293 Interstitial Lung Disease	2190
<i>Gary M. Hunninghake, Ivan O. Rosas</i>	
294 Disorders of the Pleura.....	2197
<i>Richard W. Light</i>	
295 Disorders of the Mediastinum.....	2200
<i>Richard W. Light</i>	
296 Disorders of Ventilation	2201
<i>John F. McConville, Julian Solway, Babak Mokhlesi</i>	

297 Sleep Apnea.....	2204
<i>Andrew Wellman, Daniel J. Gottlieb, Susan Redline</i>	
298 Lung Transplantation	2209
<i>Hilary J. Goldberg, Hari R. Mallidi</i>	
299 Interventional Pulmonary Medicine.....	2214
<i>Lonny Yarmus, David Feller-Kopman</i>	

PART 8 Critical Care Medicine

SECTION 1 Respiratory Critical Care

300 Approach to the Patient with Critical Illness.....	2217
<i>Rebecca M. Baron, Anthony F. Massaro</i>	
301 Acute Respiratory Distress Syndrome	2225
<i>Rebecca M. Baron, Bruce D. Levy</i>	
302 Mechanical Ventilatory Support.....	2230
<i>Scott Schissel</i>	

SECTION 2 Shock and Cardiac Arrest

303 Approach to the Patient with Shock	2235
<i>Anthony F. Massaro</i>	
304 Sepsis and Septic Shock	2241
<i>Emily B. Brant, Christopher W. Seymour, Derek C. Angus</i>	
305 Cardiogenic Shock and Pulmonary Edema.....	2250
<i>David H. Ingbar, Holger Thiele</i>	
306 Cardiovascular Collapse, Cardiac Arrest, and Sudden Cardiac Death	2257
<i>Christine Albert, William H. Sauer</i>	

SECTION 3 Neurologic Critical Care

307 Nervous System Disorders in Critical Care.....	2267
<i>J. Claude Hemphill, III, Wade S. Smith, S. Andrew Josephson, Daryl R. Gress</i>	

PART 9 Disorders of the Kidney and Urinary Tract

308 Approach to the Patient with Renal Disease or Urinary Tract Disease.....	2279
<i>Julian L. Seifter</i>	
309 Cell Biology and Physiology of the Kidney	2287
<i>Alfred L. George, Jr., Eric G. Neilson</i>	
310 Acute Kidney Injury.....	2296
<i>Sushrut S. Waikar, Joseph V. Bonventre</i>	
311 Chronic Kidney Disease	2309
<i>Joanne M. Bargman, Karl Skorecki</i>	
312 Dialysis in the Treatment of Kidney Failure	2320
<i>Kathleen D. Liu, Glenn M. Chertow</i>	
313 Transplantation in the Treatment of Renal Failure	2325
<i>Jamil Azzi, Naoka Murakami, Anil Chandraker</i>	
314 Glomerular Diseases	2331
<i>Julia B. Lewis, Eric G. Neilson</i>	
315 Polycystic Kidney Disease and Other Inherited Disorders of Tubule Growth and Development.....	2350
<i>Jing Zhou, Martin R. Pollak</i>	
316 Tubulointerstitial Diseases of the Kidney.....	2357
<i>Laurence H. Beck Jr., David J. Salant</i>	
317 Vascular Injury to the Kidney	2364
<i>Ronald S. Go, Nelson Leung</i>	

- 318 Nephrolithiasis 2368
Gary C. Curhan
- 319 Urinary Tract Obstruction 2373
Julian L. Seifter
- 320 Interventional Nephrology 2377
Dirk M. Hentschel

PART 10 Disorders of the Gastrointestinal System

SECTION 1 Disorders of the Alimentary Tract

- 321 Approach to the Patient with Gastrointestinal Disease 2381
William L. Hasler, Chung Owyang
- 322 Gastrointestinal Endoscopy 2387
Louis Michel Wong Kee Song, Mark Topazian
- 323 Diseases of the Esophagus 2423
Peter J. Kahrilas, Ikuo Hirano
- 324 Peptic Ulcer Disease and Related Disorders 2434
John Del Valle
- 325 Disorders of Absorption 2458
Deborah C. Rubin
- 326 Inflammatory Bowel Disease 2469
Sonia Friedman, Richard S. Blumberg
- 327 Irritable Bowel Syndrome 2490
Chung Owyang
- 328 Diverticular Disease and Common Anorectal Disorders 2497
Susan L. Gearhart
- 329 Mesenteric Vascular Insufficiency 2506
Maryam Ali Khan, Jaideep Das Gupta, Mahmoud Malas
- 330 Acute Intestinal Obstruction 2508
Danny O. Jacobs
- 331 Acute Appendicitis and Peritonitis 2513
Danny O. Jacobs

SECTION 2 Nutrition

- 332 Nutrient Requirements and Dietary Assessment 2517
Johanna T. Dwyer
- 333 Vitamin and Trace Mineral Deficiency and Excess 2523
Paolo M. Suter
- 334 Malnutrition and Nutritional Assessment 2534
Gordon L. Jensen
- 335 Enteral and Parenteral Nutrition 2539
L. John Hoffer, Bruce R. Bistrian, David F. Driscoll

SECTION 3 Liver and Biliary Tract Disease

- 336 Approach to the Patient with Liver Disease 2546
Marc G. Ghany, Jay H. Hoofnagle
- 337 Evaluation of Liver Function 2553
Emily D. Bethea, Daniel S. Pratt
- 338 The Hyperbilirubinemias 2557
Allan W. Wolkoff
- 339 Acute Viral Hepatitis 2562
Jules L. Dienstag
- 340 Toxic and Drug-Induced Hepatitis 2584
William M. Lee, Jules L. Dienstag
- 341 Chronic Hepatitis 2591
Jules L. Dienstag

- 342 Alcohol-Associated Liver Disease 2617
Bernd Schnabl
- 343 Nonalcoholic Fatty Liver Diseases and Nonalcoholic Steatohepatitis 2619
Manal F. Abdelmalek, Anna Mae Diehl
- 344 Cirrhosis and Its Complications 2624
Alex S. Befeler, Bruce R. Bacon
- 345 Liver Transplantation 2633
Raymond T. Chung, Jules L. Dienstag
- 346 Diseases of the Gallbladder and Bile Ducts 2641
Norton J. Greenberger, Gustav Paumgartner, Daniel S. Pratt

SECTION 4 Disorders of the Pancreas

- 347 Approach to the Patient with Pancreatic Disease 2652
Somashekar G. Krishna, Darwin L. Conwell, Phil A. Hart
- 348 Acute and Chronic Pancreatitis 2657
Phil A. Hart, Darwin L. Conwell, Somashekar G. Krishna

PART 11 Immune-Mediated, Inflammatory, and Rheumatologic Disorders

SECTION 1 The Immune System in Health and Disease

- 349 Introduction to the Immune System 2671
Barton F. Haynes, Kelly A. Soderberg, Anthony S. Fauci
- 350 Mechanisms of Regulation and Dysregulation of the Immune System 2701
Barton F. Haynes, Kelly A. Soderberg, Anthony S. Fauci
- 351 Primary Immune Deficiency Diseases 2709
Alain Fischer

SECTION 2 Disorders of Immune-Mediated Injury

- 352 Urticaria, Angioedema, and Allergic Rhinitis 2719
Katherine L. Tuttle, Joshua A. Boyce
- 353 Anaphylaxis 2727
David Hong, Joshua A. Boyce
- 354 Mastocytosis 2729
Matthew P. Giannetti, Joshua A. Boyce
- 355 Autoimmunity and Autoimmune Diseases 2731
Betty Diamond, Peter E. Lipsky
- 356 Systemic Lupus Erythematosus 2736
Bevra Hannahs Hahn, Maureen McMahon
- 357 Antiphospholipid Syndrome 2749
Haralampos M. Moutsopoulos, Clio P. Mavragani
- 358 Rheumatoid Arthritis 2751
Ankoor Shah, E. William St. Clair
- 359 Acute Rheumatic Fever 2766
Joseph Kado, Jonathan Carapetis
- 360 Systemic Sclerosis (Scleroderma) and Related Disorders 2771
John Varga
- 361 Sjögren's Syndrome 2787
Haralampos M. Moutsopoulos, Clio P. Mavragani
- 362 Spondyloarthritis 2790
Joel D. Taurog, Lianne S. Gensler, Nilig Haroon
- 363 The Vasculitis Syndromes 2802
Carol A. Langford, Anthony S. Fauci
- 364 Behçet Syndrome 2817

365 Inflammatory Myopathies.....	2819
<i>Steven A. Greenberg, Anthony A. Amato</i>	
366 Relapsing Polychondritis.....	2826
<i>Carol A. Langford</i>	
367 Sarcoidosis.....	2829
<i>Robert P. Baughman, Elyse E. Lower</i>	
368 IgG4-Related Disease.....	2837
<i>John H. Stone</i>	
369 Familial Mediterranean Fever and Other Hereditary Autoinflammatory Diseases.....	2840
<i>Daniel L. Kastner</i>	

SECTION 3 Disorders of the Joints and Adjacent Tissues

370 Approach to Articular and Musculoskeletal Disorders.....	2844
<i>John J. Cush</i>	
371 Osteoarthritis.....	2854
<i>David T. Felson, Tuhina Neogi</i>	
372 Gout and Other Crystal-Associated Arthropathies.....	2862
<i>Hyon K. Choi</i>	
373 Fibromyalgia.....	2868
<i>Leslie J. Crofford</i>	
374 Arthritis Associated with Systemic Disease, and Other Arthritides.....	2871
<i>Carol A. Langford, Brian F. Mandell</i>	
375 Periarticular Disorders of the Extremities.....	2878
<i>Carol A. Langford</i>	

PART 12 Endocrinology and Metabolism

SECTION 1 Endocrinology

376 Approach to the Patient with Endocrine Disorders.....	2881
<i>J. Larry Jameson</i>	
377 Mechanisms of Hormone Action.....	2884
<i>J. Larry Jameson</i>	
378 Physiology of Anterior Pituitary Hormones.....	2891
<i>Shlomo Melmed, J. Larry Jameson</i>	
379 Hypopituitarism.....	2896
<i>Shlomo Melmed, J. Larry Jameson</i>	
380 Pituitary Tumor Syndromes.....	2902
<i>Shlomo Melmed, J. Larry Jameson</i>	
381 Disorders of the Neurohypophysis.....	2918
<i>Gary L. Robertson, Daniel G. Bichet</i>	
382 Thyroid Gland Physiology and Testing.....	2926
<i>J. Larry Jameson, Susan J. Mandel, Anthony P. Weetman</i>	
383 Hypothyroidism.....	2933
<i>J. Larry Jameson, Susan J. Mandel, Anthony P. Weetman</i>	
384 Hyperthyroidism and Other Causes of Thyrotoxicosis.....	2938
<i>J. Larry Jameson, Susan J. Mandel, Anthony P. Weetman</i>	
385 Thyroid Nodular Disease and Thyroid Cancer.....	2946
<i>J. Larry Jameson, Susan J. Mandel, Anthony P. Weetman</i>	
386 Disorders of the Adrenal Cortex.....	2955
<i>Wiebke Arlt</i>	
387 Pheochromocytoma.....	2976
<i>Hartmut P. H. Neumann</i>	
388 Multiple Endocrine Neoplasia Syndromes.....	2983

389 Autoimmune Polyendocrine Syndromes.....	2992
<i>Peter A. Gottlieb, Aaron W. Michels</i>	

SECTION 2 Sex- and Gender-Based Medicine

390 Sex Development.....	2997
<i>Courtney Finlayson, J. Larry Jameson, John C. Achermann</i>	
391 Disorders of the Testes and Male Reproductive System.....	3006
<i>Shalender Bhasin, J. Larry Jameson</i>	
392 Disorders of the Female Reproductive System.....	3027
<i>Janet E. Hall, Anuja Dokras</i>	
393 Menstrual Disorders and Pelvic Pain.....	3033
<i>Janet E. Hall, Anuja Dokras</i>	
394 Hirsutism.....	3039
<i>David A. Ehrmann</i>	
395 Menopause and Postmenopausal Hormone Therapy.....	3043
<i>JoAnn E. Manson, Shari S. Bassuk</i>	
396 Infertility and Contraception.....	3050
<i>Anuja Dokras, Janet E. Hall</i>	
397 Sexual Dysfunction.....	3055
<i>Kevin T. McVary</i>	
398 Women's Health.....	3063
<i>Emily Nosova, Andrea Dunaif</i>	
399 Men's Health.....	3069
<i>Shalender Bhasin</i>	
400 Lesbian, Gay, Bisexual, and Transgender (LGBT) Health.....	3078
<i>Baligh R. Yehia, Zachary B. R. McClain</i>	

SECTION 3 Obesity, Diabetes Mellitus, and Metabolic Syndrome

401 Pathobiology of Obesity.....	3080
<i>Stephen O'Rahilly, I. Sadaf Farooqi</i>	
402 Evaluation and Management of Obesity.....	3087
<i>Robert F. Kushner</i>	
403 Diabetes Mellitus: Diagnosis, Classification, and Pathophysiology.....	3094
<i>Alvin C. Powers, Kevin D. Niswender, Carmella Evans-Molina</i>	
404 Diabetes Mellitus: Management and Therapies.....	3104
<i>Alvin C. Powers, Michael J. Fowler, Michael R. Rickels</i>	
405 Diabetes Mellitus: Complications.....	3120
<i>Alvin C. Powers, John M. Stafford, Michael R. Rickels</i>	
406 Hypoglycemia.....	3129
<i>Stephen N. Davis, Philip E. Cryer</i>	
407 Disorders of Lipoprotein Metabolism.....	3135
<i>Daniel J. Rader</i>	
408 The Metabolic Syndrome.....	3150
<i>Robert H. Eckel</i>	

SECTION 4 Disorders of Bone and Mineral Metabolism

409 Bone and Mineral Metabolism in Health and Disease.....	3157
<i>F. Richard Bringhurst, Henry M. Kronenberg, Eva S. Liu</i>	
410 Disorders of the Parathyroid Gland and Calcium Homeostasis.....	3169
<i>John T. Potts, Jr., Harald Jüppner</i>	
411 Osteoporosis.....	3191

Robert Lindsay, Blossom Samuels

- 412 Paget's Disease and Other Dysplasias of Bone 3209
Rajesh K. Jain, Tamara J. Vokes

SECTION 5 Disorders of Intermediary Metabolism

- 413 Heritable Disorders of Connective Tissue..... 3217
Joan C. Marini, Fransiska Malfait
- 414 Hemochromatosis..... 3230
Lawrie W. Powell, David M. Frazer
- 415 Wilson's Disease 3235
Stephen G. Kaler
- 416 The Porphyrias 3237
Robert J. Desnick, Manisha Balwani
- 417 Disorders of Purine and Pyrimidine Metabolism 3248
John N. Mecchella, Christopher M. Burns
- 418 Lysosomal Storage Diseases 3254
Robert J. Hopkin, Gregory A. Grabowski
- 419 Glycogen Storage Diseases and Other Inherited Disorders of Carbohydrate Metabolism 3261
Priya S. Kishnani
- 420 Inherited Disorders of Amino Acid Metabolism in Adults..... 3268
Nicola Longo
- 421 Inherited Defects of Membrane Transport 3274
Nicola Longo

PART 13 Neurologic Disorders

SECTION 1 Diagnosis of Neurologic Disorders

- 422 Approach to the Patient with Neurologic Disease 3277
Daniel H. Lowenstein, S. Andrew Josephson, Stephen L. Hauser
- 423 Neuroimaging in Neurologic Disorders 3282
William P. Dillon
- 424 Pathobiology of Neurologic Diseases 3293
Stephen L. Hauser, Arnold R. Kriegstein, Stanley B. Prusiner

SECTION 2 Diseases of the Central Nervous System

- 425 Seizures and Epilepsy 3305
Vikram R. Rao, Daniel H. Lowenstein
- 426 Introduction to Cerebrovascular Diseases..... 3324
Wade S. Smith, S. Claiborne Johnston, J. Claude Hemphill, III
- 427 Ischemic Stroke 3335
Wade S. Smith, S. Claiborne Johnston, J. Claude Hemphill, III
- 428 Intracranial Hemorrhage..... 3348
Wade S. Smith, J. Claude Hemphill, III, S. Claiborne Johnston
- 429 Subarachnoid Hemorrhage 3353
J. Claude Hemphill, III, Wade S. Smith, Daryl R. Gress
- 430 Migraine and Other Primary Headache Disorders..... 3357
Peter J. Goadsby
- 431 Alzheimer's Disease 3370
Gil D. Rabinovici, William W. Seeley, Bruce L. Miller
- 432 Frontotemporal Dementia 3378
William W. Seeley, Bruce L. Miller
- 433 Vascular Dementia 3381
Steven M. Greenberg, William W. Seeley
- 434 Dementia with Lewy Bodies..... 3385

Irene Litvan, William W. Seeley, Bruce L. Miller

- 435 Parkinson's Disease 3386
C. Warren Olanow, Anthony H.V. Schapira
- 436 Tremor, Chorea, and Other Movement Disorders 3400
C. Warren Olanow, Christine Klein
- 437 Amyotrophic Lateral Sclerosis and Other Motor Neuron Diseases 3410
Robert H. Brown, Jr.
- 438 Prion Diseases 3416
Stanley B. Prusiner, Michael Geschwind
- 439 Ataxic Disorders 3422
Roger N. Rosenberg
- 440 Disorders of the Autonomic Nervous System 3427
Richard J. Barohn, John W. Engstrom
- 441 Trigeminal Neuralgia, Bell's Palsy, and Other Cranial Nerve Disorders 3436
Vanja C. Douglas, Stephen L. Hauser
- 442 Diseases of the Spinal Cord..... 3445
Stephen L. Hauser
- 443 Concussion and Other Traumatic Brain Injuries..... 3456
Geoffrey T. Manley, Benjamin L. Brett, Michael McCrea
- 444 Multiple Sclerosis 3462
Bruce A. C. Cree, Stephen L. Hauser
- 445 Neuromyelitis Optica..... 3477
Bruce A. C. Cree, Stephen L. Hauser

SECTION 3 Nerve and Muscle Disorders

- 446 Peripheral Neuropathy 3480
Anthony A. Amato, Richard J. Barohn
- 447 Guillain-Barré Syndrome and Other Immune-Mediated Neuropathies..... 3501
Stephen L. Hauser, Anthony A. Amato
- 448 Myasthenia Gravis and Other Diseases of the Neuromuscular Junction 3509
Anthony A. Amato
- 449 Muscular Dystrophies and Other Muscle Diseases 3516
Anthony A. Amato, Robert H. Brown, Jr.

SECTION 4 Myalgic Encephalomyelitis/Chronic Fatigue Syndrome

- 450 Myalgic Encephalomyelitis/Chronic Fatigue Syndrome 3532
Elizabeth R. Unger, Jin-Mann S. Lin, Jeanne Bertolli

SECTION 5 Psychiatric and Addiction Disorders

- 451 Biology of Psychiatric Disorders..... 3534
Robert O. Messing, Eric J. Nestler, Matthew W. State
- 452 Psychiatric Disorders 3540
Victor I. Reus
- 453 Alcohol and Alcohol Use Disorders 3556
Marc A. Schuckit
- 454 Nicotine Addiction 3563
David M. Burns
- 455 Marijuana and Marijuana Use Disorders 3567
Nora D. Volkow, Aidan Hampson, Ruben Baler
- 456 Opioid-Related Disorders..... 3569
Thomas R. Kosten, Colin N. Haile
- 457 Cocaine, Other Psychostimulants, and Hallucinogens..... 3573
Karran A. Phillips, Wilson M. Compton

PART 14 Poisoning, Drug Overdose, and Envenomation

- 458 Heavy Metal Poisoning 3579
Howard Hu
- 459 Poisoning and Drug Overdose 3582
Mark B. Mycyk
- 460 Disorders Caused by Venomous Snakebites and Marine Animal Exposures..... 3596
Erik Fisher, Alex Chen, Charles Lei
- 461 Ectoparasite Infestations and Arthropod Injuries 3608
Richard J. Pollack, Scott A. Norton

PART 15 Disorders Associated with Environmental Exposures

- 462 Altitude Illness 3617
Buddha Basnyat, Geoffrey Tabin
- 463 Hyperbaric and Diving Medicine 3623
Michael H. Bennett, Simon J. Mitchell
- 464 Hypothermia and Peripheral Cold Injuries 3630
Daniel F. Danzl
- 465 Heat-Related Illnesses 3635
Daniel F. Danzl

PART 16 Genes, the Environment, and Disease

- 466 Principles of Human Genetics 3639
J. Larry Jameson, Peter Kopp
- 467 The Practice of Genetics in Clinical Medicine 3662
Susan M. Domchek, J. Larry Jameson, Susan Miesfeldt
- 468 Mitochondrial DNA and Heritable Traits and Diseases..... 3668
Karl L. Skorecki, Bruce H. Cohen
- 469 Telomere Disease 3680
Rodrigo T. Calado, Neal S. Young
- 470 Gene- and Cell-Based Therapy in Clinical Medicine 3685
Katherine A. High, Marcela V. Maus
- 471 The Human Microbiome 3690
Neeraj K. Surana, Dennis L. Kasper

PART 17 Global Medicine

- 472 Global Issues in Medicine 3703
Joseph J. Rhatigan, Paul Farmer
- 473 Emerging and Reemerging Infectious Diseases..... 3713
George W. Rutherford, Jaime Sepúlveda
- 474 Primary Care and Global Health 3718
Tim Evans, Kumanan Rasanathan
- 475 Health Effects of Climate Change 3726
Eugene T. Richardson, Maxine A. Burkett, Paul E. Farmer

PART 18 Aging

- 476 Biology of Aging..... 3733
Rafael de Cabo, David Le Couteur
- 477 Caring for the Geriatric Patient..... 3739
Joseph G. Ouslander, Bernardo Reyes

PART 19 Consultative Medicine

- 478 Approach to Medical Consultation..... 3761
Jeffrey Berns, Jack Ende
- 479 Medical Disorders During Pregnancy..... 3762
Sarah Rae Easter, Robert L. Barbieri
- 480 Medical Evaluation of the Surgical Patient 3769
Prashant Vaishnava, Kim A. Eagle

PART 20 Frontiers

- 481 Behavioral Economics and Health..... 3775
Kevin G. Volpp, George Loewenstein, David A. Asch
- 482 Complementary and Integrative Therapies and Practices 3784
Helene M. Langevin
- 483 The Role of Epigenetics in Disease and Treatment..... 3790
Brian C. Capell, Shelley L. Berger
- 484 Applications of Stem Cell Biology in Clinical Medicine 3796
John A. Kessler
- 485 The Role of Circadian Biology in Health and Disease..... 3800
Jonathan Cedernaes, Kathryn Moynihan Ramsey, Joseph Bass
- 486 Network Medicine: Systems Biology in Health and Disease 3812
Joseph Loscalzo
- 487 Emerging Neurotherapeutic Technologies 3819
Jyoti Mishra, Karunesh Ganguly
- 488 Machine Learning and Augmented Intelligence in Clinical Medicine..... 3826
Arjun K. Manrai, Isaac S. Kohane
- 489 Metabolomics 3831
Jared R. Mayers, Mathew G. Vander Heiden
- 490 Circulating Nucleic Acids as Liquid Biopsies and Noninvasive Disease Biomarkers 3836
Ash A. Alizadeh, Kiran K. Khush, Yair J. Blumenfeld
- 491 Protein Folding Disorders 3846
Richard I. Morimoto, G. Scott Budinger
- 492 Novel Approaches to Diseases of Unknown Etiology..... 3851
David Adams, Camilo Toro, Joseph Loscalzo

Index I-1

The following chapters are available online. They can be viewed by opening the table of contents of *Harrison's* 21st edition at www.accessmedicine.com/harrisons.

Video Collection

- V1 Video Library of Gait Disorders**
Gail Kang, Nicholas B. Galifianakis, Michael D. Geschwind
- V2 Primary Progressive Aphasia, Memory Loss, and Other Focal Cerebral Disorders**
Maria Luisa Gorno-Tempini, Jennifer Ogar, Joel Kramer, Bruce L. Miller, Gil D. Rabinovici, Maria Carmela Tartaglia
- V3 Video Library of Neuro-Ophthalmology**
Jonathan C. Horton
- V4 Examination of the Comatose Patient**
S. Andrew Josephson
- V5 Video Atlas of Gastrointestinal Endoscopic Lesions**
Louis Michel Wong Kee Song, Mark Topazian
- V6 The Neurologic Screening Exam**
Daniel H. Lowenstein
- V7 Video Atlas of the Detailed Neurologic Examination**
Martin A. Samuels

Supplementary Topics

- S1 Fluid and Electrolyte Imbalances and Acid-Base Disturbances: Case Examples**
David B. Mount, Thomas D. DuBose, Jr.
- S2 Cerebrospinal Fluid Disturbances: Case Examples**
Prashanth S. Ramachandran, Michael R. Wilson
- S3 Microbial Bioterrorism**
H. Clifford Lane, Anthony S. Fauci
- S4 Chemical Terrorism**
James A. Romano, Jr., Jonathan Newmark
- S5 Radiation Terrorism**
Christine E. Hill-Kayser, Eli Glatstein, Zelig A. Tochner
- S6 Infections in War Veterans**
Andrew W. Artenstein
- S7 Health Care for Military Veterans**
Stephen C. Hunt, Lucile Burgo-Black, Charles W. Hoge
- S8 Primary Immunodeficiencies Associated with (or Secondary to) Other Diseases**
Alain Fischer
- S9 Technique of Lumbar Puncture**
Elizabeth Robbins, Stephen L. Hauser

- S10 The Clinical Laboratory in Modern Health Care**
Anthony A. Killeen
- S11 Laboratory Diagnosis of Infectious Diseases**
Manfred Brigl, Alexander J. McAdam
- S12 Laboratory Diagnosis of Parasitic Infections**
Sharon L. Reed, Sanjay R. Mehta

Atlases

- A1 Atlas of Rashes Associated with Fever**
Kenneth M. Kaye, Elaine T. Kaye
- A2 Atlas of Blood Smears of Malaria and Babesiosis**
Nicholas J. White, Elizabeth A. Ashley
- A3 Atlas of Oral Manifestations of Disease**
Samuel C. Durso, Janet A. Yellowitz
- A4 Atlas of Urinary Sediments and Renal Biopsies**
Agnes B. Fogo, Eric G. Neilson
- A5 Atlas of Skin Manifestations of Internal Disease**
Thomas J. Lawley, Benjamin K. Stoff, Calvin O. McCall
- A6 Atlas of Hematology**
Dan L. Longo
- A7 Atlas of Electrocardiography**
Ary L. Goldberger
- A8 Atlas of Cardiac Arrhythmias**
Ary L. Goldberger
- A9 Atlas of Noninvasive Imaging**
Marcelo F. Di Carli, Raymond Y. Kwong, Scott D. Solomon
- A10 Atlas of Atherosclerosis**
Peter Libby
- A11 Atlas of Percutaneous Revascularization and Adult Structural Heart Interventions**
Jane A. Leopold, Deepak L. Bhatt, David P. Faxon
- A12 Atlas of Chest Imaging**
Samuel Y. Ash, George R. Washko
- A13 Atlas of Liver Biopsies**
Jules L. Dienstag, Atul K. Bhan
- A14 Atlas of the Vasculitic Syndromes**
Carol A. Langford, Anthony S. Fauci
- A15 Atlas of Clinical Manifestations of Endocrine and Metabolic Diseases**
J. Larry Jameson
- A16 Atlas of Neuroimaging**
Michael F. Regner, Andre D. Furtado, Luciano Villarinho, William P. Dillon

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The Editors are pleased to present the 21st edition of *Harrison's Principles of Internal Medicine*. This 21st edition is a true landmark in medicine, spanning 71 years and multiple generations of trainees and practicing clinicians. While medicine and medical education have evolved, readers will appreciate how this classic textbook has retained enduring features that have distinguished it among medical texts—a sharp focus on the clinical presentation of disease, expert in-depth summaries of pathophysiology and treatment, and highlights of emerging frontiers of science and medicine. Indeed, *Harrison's* retains its conviction that, in the profession of medicine, we are all perpetual students with lifelong learning as our common goal.

Harrison's is intended for learners throughout their careers. For *students*, Part 1, Chapter 1 begins with an overview of “The Practice of Medicine.” In this introductory chapter, the editors continue the tradition of orienting clinicians to the *science* and the *art* of medicine, emphasizing the values of our profession while incorporating new advances in technology, science, and clinical care. Part 2, “Cardinal Manifestations and Presentation of Diseases,” is a signature feature of *Harrison's*. These chapters eloquently describe how patients present with common clinical conditions, such as headache, fever, cough, palpitations, or anemia, and provide an overview of typical symptoms, physical findings, and differential diagnosis. Mastery of these topics prepares students for subsequent chapters on specific diseases they will encounter in courses on pathophysiology and in clinical clerkships. For *residents* and *fellows* caring for patients and preparing for board examinations, *Harrison's* remains a definitive source of trusted content written by internationally renowned experts. Trainees will be reassured by the depth of content, comprehensive tables, and illuminating figures and clinical algorithms. Many examination questions are based on key testing points derived from *Harrison's* chapters. A useful companion book, *Harrison's Self-Assessment and Board Review*, includes over 1000 questions, offers comprehensive explanations of the correct answer, and provides links to the relevant chapters in the textbook. *Practicing clinicians* must keep up with an ever-changing knowledge base and clinical guidelines as part of lifelong learning. Clinicians can trust that chapters are updated extensively with each edition of *Harrison's*. The text is an excellent point-of-care reference for clinical questions, differential diagnosis, and patient management. In addition to the expanded and detailed Treatment sections, *Harrison's* continues its tradition of including “Approach to the Patient” sections, which provide an expert's overview of the practical management of common but often complex clinical conditions.

This edition has been modified extensively in its structure as well as its content and offers a more consistently standardized format for each disease chapter. The authors and editors have curated rigorously and synthesized the vast amount of information that comprises general internal medicine—and each of the major specialties—into a highly readable and informative two-volume book. Readers will appreciate the concise writing style and substantive quality that have always characterized *Harrison's*. This book has a sharp focus on essential information with a goal of providing clear and definitive answers to clinical questions.

In the 21st edition, examples of new chapters include “Precision Medicine and Clinical Care,” focusing on the ever-growing pool of “big data” used to provide individualized genotype-phenotype correlations; “Mechanisms of Regulation and Dysregulation of the Immune System,” focusing on the extraordinary advances made over the past 5 years in understanding the complex and subtle mechanisms whereby the immune system is regulated and how perturbations in this regulation lead to disease states as well as targets for therapeutic intervention; new chapters on Alzheimer's disease and related conditions, with a special focus on vascular dementia, a common and treatable cause of cognitive

loss; and a new chapter on marijuana and marijuana use disorders, as well as updated management guidelines for multiple sclerosis and the expanding array of other autoimmune nervous system diseases that can now be identified and treated.

Other new chapters include “Vaccine Opposition and Hesitancy,” “Precision Medicine and Clinical Care,” “Diagnosis: Reducing Errors and Improving Quality,” “Approach to the Patient with Renal or Urinary Tract Disease,” “Interventional Nephrology,” “Health Effects of Climate Change,” and “Circulating Nucleic Acids as Liquid Biopsies and Noninvasive Disease Biomarkers.” In addition, many chapters have new authors.

The chapter, “Vaccine Opposition and Hesitancy,” provides an overview of the current antivaccination crisis, the issues involved, and specific strategies to utilize within the clinical setting to address the lack of confidence that many patients feel toward the health care system. The chapter, “Metabolomics,” outlines an emerging and important new and sensitive approach to measuring perturbations within a system or patient that will likely become a routine part of the clinical armamentarium for diagnosing, monitoring, and treating disease.

In addition to these and other new topics, the 21st edition presents important updates in the established chapters, such as the microbiology and clinical management of SARS-CoV-2 infection, the use of gene editing for sickle cell anemia and thalassemia, gene therapy for hemophilia, new immunotherapies for autoimmune diseases and cancers, and novel approaches to vaccine development, among many others. Our focus on forwarding-looking issues of emerging clinical importance continues with the series of chapters entitled “Frontiers,” which foreshadows cutting-edge science that will change medical practice in the near term. Examples of new Frontier chapters include “Machine Learning and Augmented Intelligence,” “Metabolomics,” “Protein Folding Disorders,” and “Novel Approaches to Disease of Unknown Etiology.”

Harrison's content is available in a variety of print and digital formats, including eBooks, apps, and a popular, widely used online platform available at www.accessmedicine.com.

We have many people to thank for their efforts in producing this book. First, the authors have done a superb job of producing authoritative chapters that synthesize vast amounts of scientific and clinical data to create informative and practical approaches to managing patients. In today's information-rich, rapidly evolving environment, they have ensured that this information is current. We are most grateful to our colleagues who work closely with each editor to facilitate communication with the authors and help us keep *Harrison's* content current. In particular, we wish to acknowledge the expert support of Lauren Bauer, Patricia Conrad, Patricia L. Duffey, Gregory K. Folkers, Julie B. McCoy, Elizabeth Robbins, Marie Scurti, and Stephanie C. Tribuna. Scott Grillo and James Shanahan, our long-standing partners at McGraw Hill's Professional Publishing group, have inspired the creative and dynamic evolution of *Harrison's*, guiding the development of the book and its related products in new formats. Kim Davis, as Managing Editor, has adeptly ensured that the complex production of this multi-authored textbook proceeded smoothly and efficiently. Priscilla Beer oversaw the production of our videos and animations; Jeffrey Herzich, Elleanore Waka, and Rachel Norton, along with other members of the McGraw Hill staff; and Revathi Viswanathan of KnowledgeWorks Global Ltd., shepherded the production of this new edition.

We are privileged to have compiled this 21st edition and are enthusiastic about all that it offers our readers. We learned much in the process of editing *Harrison's* and hope that you will find this edition uniquely valuable as a clinical and educational resource.

The Editors

A complete collection to meet your educational, clinical, and board prep needs.

Harrison's Online

The online edition of *Harrison's* is available at www.accessmedicine.com. It requires an institutional or individual subscription separate from the purchase of the print book. The online edition of *Harrison's* features all the chapters from the print edition, plus more than two dozen supplementary chapters in print, atlas, and video formats. *Harrison's Online* includes numerous monthly updates, from the editors of *Harrison's*, on important new developments in medical research and practice. Easily search across the entire *Harrison's* content set, download images and tables for presentations and lectures, view step-by-step videos on common clinical procedures, access the text of the *Harrison's Manual of Medicine*, set up a personalized test exam for board prep, get access to chapters from new editions of *Harrison's* months before book publication, and more.

The Harrison's Manual of Medicine

The *Harrison's Manual of Medicine* provides high-yield, rapid-access clinical summaries of *Harrison's* content, suitable for use at the bedside. Chapters in the *Manual* reflect those likely to be encountered in both the inpatient and outpatient setting. The format is built for ease of use. The *Manual* is available in print, eBook, and app. In addition, the full text of the *Manual* is available to subscribers at accessmedicine.com. This format provides flexibility of format to customers, who can move back and forth between the full scope of *Harrison's Principles of Internal Medicine* and the high-yield clinical essentials of the *Manual*.

The *Manual* includes more than 200 chapters in 17 sections and covers presenting signs and symptoms and major conditions seen in both inpatient and outpatient settings. The full table of contents is available at www.accessmedicine.com.

The Harrison's Self-Assessment and Board Review

This practical resource provides more than 1000 self-assessment questions, most in board-style clinical vignette format with multiple choice answers. The explanations for the questions are comprehensive and provide detailed guidance on correct and incorrect answers. Question-and-answer sets include references to related chapters in *Harrison's Principles of Internal Medicine* for more comprehensive understanding. Use this very handy resource for primary and recertification exam prep, for rotational shelf exams, and for general assessment of understanding of the principles of clinical medicine. This resource is available as a print book, an eBook, an app, and on accessmedicine.com, where users can create personalized testing experiences and receive instant scores on practice tests.

Harrison's Podclass

Our podcast presents bi-weekly episodes covering clinical vignettes across internal medicine, with two expert discussants reviewing common and challenging patient presentations and a series of self-assessment Q&A choices tied to each case. The hosts work through correct and incorrect answer choices and summarize cases with practical pearls that all students and clinicians will find helpful and interesting. *Harrison's Podclass* is available in most of the common podcast outlets and on www.accessmedicine.com.

1

The Practice of Medicine

The Editors

ENDURING VALUES OF THE MEDICAL PROFESSION

No greater opportunity, responsibility, or obligation can fall to the lot of a human being than to become a physician. In the care of the suffering, [the physician] needs technical skill, scientific knowledge, and human understanding. Tact, sympathy, and understanding are expected of the physician, for the patient is no mere collection of symptoms, signs, disordered functions, damaged organs, and disturbed emotions. [The patient] is human, fearful, and hopeful, seeking relief, help, and reassurance.

—Harrison's Principles of Internal Medicine, 1950

The practice of medicine has changed in significant ways since the first edition of this book was published in 1950. The advent of molecular genetics, sophisticated new imaging techniques, robotics, and advances in bioinformatics and information technology have contributed to an explosion of scientific information that has changed fundamentally the way physicians define, diagnose, treat, and attempt to prevent disease. This growth of scientific knowledge continues to evolve at an accelerated pace.

The widespread use of electronic medical records and the Internet have altered the way physicians and other health care providers access and exchange information as a routine part of medical education and practice (Fig. 1-1). As today's physicians strive to integrate an ever-expanding body of scientific knowledge into everyday practice, it is critically important to remember two key principles: first, the ultimate goal of medicine is to prevent disease and, when it occurs, to diagnose it early and provide effective treatment; and second, despite 70 years of scientific advances since the first edition of this text, a trusting relationship between physician and patient still lies at the heart of effective patient care.

■ THE SCIENCE AND ART OF MEDICINE

Deductive reasoning and applied technology form the foundation for the approach and solution to many clinical problems. Extraordinary advances in biochemistry, cell biology, immunology, and genomics,



FIGURE 1-1 *The Doctor* by Luke Fildes depicts the caring relationship between this Victorian physician and a very ill child. Painted in 1891, the painting reflects the death of the painter's young son from typhoid fever and was intended to reflect the compassionate care provided by the physician even when his tools were not able to influence the course of disease. (Source: History and Art Collection/Alamy Stock Photo.)

coupled with newly developed imaging techniques, provide a window into the most remote recesses of the body and allow access to the innermost parts of the cell. Revelations about the nature of genes and single cells have opened a portal for formulating a new molecular basis for the physiology of systems. Researchers are deciphering the complex mechanisms by which genes are regulated, and increasingly, physicians are learning how subtle changes in many different genes, acting in an integrative contextual way, can affect the function of cells and organisms. Clinicians have developed a new appreciation of the role of stem cells in normal tissue function, in the development of cancer and other disorders, and in the treatment of certain diseases. Entirely new areas of research, including studies of the human microbiome, epigenetics, and noncoding RNAs as regulatory features of the genome, have become important for understanding both health and disease. Information technology enables the interrogation of medical records from millions of individuals, yielding new insights into the etiology, characteristics, prognosis, and stratification of many diseases. With the increasing availability of very large data sets (“big data”) from omic analyses and the electronic medical record, there is now a growing need for machine learning and artificial intelligence for unbiased analyses that enhance clinical predictive accuracy. The knowledge gleaned from the *science of medicine* continues to enhance the understanding by physicians of complex pathologic processes and to provide new approaches to disease prevention, diagnosis, and treatment. With continued refinement of unique omic signatures coupled with nuanced clinical pathophenotypes, the profession moves ever closer to practical precision medicine. Yet, skill in the most sophisticated applications of laboratory technology and in the use of the latest therapeutic modality alone does not make a good physician. Extraordinary advances in vaccine platform technology and the use of cryo-electron microscopy for the structure-based design of vaccine immunogens have transformed the field of vaccinology, resulting in the unprecedented speed and success with which COVID-19 vaccines were developed.

When a patient poses challenging clinical problems, an effective physician must be able to identify the crucial elements in a complex history and physical examination; order the appropriate laboratory, imaging, and diagnostic tests; and extract the key results from densely populated computer screens to determine whether to treat or to “watch.” As the number of tests increases, so does the likelihood that some incidental finding, completely unrelated to the clinical problem at hand, will be uncovered. Deciding whether a clinical clue is worth pursuing or should be dismissed as a “red herring” and weighing whether a proposed test, preventive measure, or treatment entails a greater risk than the disease itself are essential judgments that a skilled clinician must make many times each day. This combination of medical knowledge, intuition, experience, and judgment defines the *art of medicine*, which is as necessary to the practice of medicine and the precision medicine of the future as is a sound scientific base, and as important for contemporary medical practice as it has been in earlier eras.

■ CLINICAL SKILLS

History-Taking The recorded history of an illness should include all the facts of medical significance in the life of the patient. Recent events should be given the most attention. Patients should, at some early point, have the opportunity to tell their own story of the illness without frequent interruption and, when appropriate, should receive expressions of interest, encouragement, and empathy from the physician. Any event related by a patient, however trivial or seemingly irrelevant, may provide the key to solving the medical problem. A methodical review of systems is important to elicit features of an underlying disease that might not be mentioned in the patient's narrative. In general, patients who feel comfortable with the physician will offer more complete information; thus, putting the patient at ease contributes substantially to obtaining an adequate history.

An informative history is more than eliciting an orderly listing of symptoms. By listening to patients and noting the ways in which they describe their symptoms, physicians can gain valuable insight. Inflections of voice, facial expression, gestures, and attitude (i.e., “body language”) may offer important clues to patients’ perception of and reaction to their symptoms. Because patients vary considerably in their medical sophistication and ability to recall facts, the reported medical history should be corroborated whenever possible. The social history also can provide important insights into the types of diseases that should be considered and can identify practical considerations for subsequent management. The family history not only identifies rare genetic disorders or common exposures, but often reveals risk factors for common disorders, such as coronary heart disease, hypertension, autoimmunity, and asthma. A thorough family history may require input from multiple relatives to ensure completeness and accuracy. An experienced clinician can usually formulate a relevant differential diagnosis from the history alone, using the physical examination and diagnostic tests to narrow the list or reveal unexpected findings that lead to more focused inquiry.

The very act of eliciting the history provides the physician with an opportunity to establish or enhance a unique bond that can form the basis for a good patient–physician relationship. This process helps the physician develop an appreciation of the patient’s view of the illness, the patient’s expectations of the physician and the health care system, and the financial and social implications of the illness for the patient. Although current health care settings may impose time constraints on patient visits, it is important not to rush the encounter. A hurried approach may lead patients to believe that what they are relating is not of importance to the physician, and, as a result, they may withhold relevant information. The confidentiality of the patient–physician relationship cannot be overemphasized.

Physical Examination The purpose of the physical examination is to identify physical signs of disease. The significance of these objective indications of disease is enhanced when they confirm a functional or structural change already suggested by the patient’s history. At times, however, physical signs may be the only evidence of disease and may not have been suggested by the history.

The physical examination should be methodical and thorough, with consideration given to the patient’s comfort and modesty. Although attention is often directed by the history to the diseased organ or part of the body, the examination of a new patient must extend from head to toe in an objective search for abnormalities. The results of the examination, like the details of the history, should be recorded at the time they are elicited—not hours later, when they are subject to the distortions of memory. Physical examination skills should be learned under direct observation of experienced clinicians. Even highly experienced clinicians can benefit from ongoing coaching and feedback. Simulation laboratories and standardized patients play an increasingly important role in the development of clinical skills. Although the skills of physical diagnosis are acquired with experience, it is not merely technique that determines success in identifying signs of disease. The detection of a few scattered petechiae, a faint diastolic murmur, or a small mass in the abdomen is not a question of keener eyes and ears or more sensitive fingers, but of a mind alert to those findings. Because physical findings can change with time, the physical examination should be repeated as frequently as the clinical situation warrants.

Given the many highly sensitive diagnostic tests now available (particularly imaging techniques), it may be tempting to place less emphasis on the physical examination. Some are critical of physical diagnosis based on perceived low levels of specificity and sensitivity. Indeed, many patients are seen by consultants only after a series of diagnostic tests have been performed and the results are known. This fact should not deter the physician from performing a thorough physical examination since important clinical findings may have escaped detection by diagnostic tests. Especially important, a thorough and thoughtful physical examination may render a laboratory finding unimportant (i.e., certain echocardiographic regurgitant lesions). The act of a hands-on examination of the patient also offers an opportunity

for communication and may have reassuring effects that foster the patient–physician relationship.

Diagnostic Studies Physicians rely increasingly on a wide array of laboratory and imaging tests to make diagnoses and ultimately to solve clinical problems; however, such information does not relieve the physician from the responsibility of carefully observing and examining the patient. It is also essential to appreciate the limitations of diagnostic tests. By virtue of their apparent precision, these tests often gain an aura of certainty regardless of the fallibility of the tests themselves, the instruments used in the tests, and the individuals performing or interpreting the tests. Physicians must weigh the expense involved in laboratory procedures against the value of the information these procedures are likely to provide.

Single laboratory tests are rarely ordered. Instead, physicians generally request “batteries” of multiple tests, which often prove useful and can be performed with a single specimen at relatively low cost. For example, abnormalities of hepatic function may provide the clue to nonspecific symptoms such as generalized weakness and increased fatigability, suggesting a diagnosis of chronic liver disease. Sometimes a single abnormality, such as an elevated serum calcium level, points to a particular disease, such as hyperparathyroidism.

The thoughtful use of screening tests (e.g., measurement of low-density lipoprotein cholesterol) may allow early intervention to prevent disease (Chap. 6). Screening tests are most informative when they are directed toward common diseases and when their results indicate whether other potentially useful—but often costly—tests or interventions are needed. On the one hand, biochemical measurements, together with simple laboratory determinations such as routine serum chemistries, blood counts, and urinalysis, often provide a major clue to the presence of a pathologic process. On the other hand, the physician must learn to evaluate occasional screening-test abnormalities that do not necessarily connote significant disease. An in-depth workup after the report of an isolated laboratory abnormality in a person who is otherwise well is often wasteful and unproductive. Because so many tests are performed routinely for screening purposes, it is not unusual for one or two values to be slightly abnormal. Nevertheless, even if there is no reason to suspect an underlying illness, tests yielding abnormal results ordinarily are repeated to rule out laboratory error. If an abnormality is confirmed, it is important to consider its potential significance in the context of the patient’s condition and other test results.

There is almost continual development of technically improved imaging studies with greater sensitivity and specificity. These tests provide remarkably detailed anatomic information that can be pivotal in informing medical decision-making. MRI, CT, ultrasonography, a variety of isotopic scans, and positron emission tomography (PET) have supplanted older, more invasive approaches and opened new diagnostic vistas. In light of their capabilities and the rapidity with which they can lead to a diagnosis, it is tempting to order a battery of imaging studies. All physicians have had experiences in which imaging studies revealed findings that led to an unexpected diagnosis. Nonetheless, patients must endure each of these tests, and the added cost of unnecessary testing is substantial. Furthermore, investigation of an unexpected abnormal finding may lead to an iatrogenic complication or to the diagnosis of an irrelevant or incidental problem. A skilled physician must learn to use these powerful diagnostic tools judiciously, always considering whether the results will alter management and benefit the patient.

■ MANAGEMENT OF PATIENT CARE

Team-Based Care Medical practice has long involved teams, particularly physicians working with nurses and, more recently, with physician assistants and nurse practitioners. Advances in medicine have increased our ability to manage very complex clinical situations (e.g., intensive care units [ICUs], bone marrow transplantation) and have shifted the burden of disease toward chronic illnesses. Because an individual patient may have multiple chronic diseases, he or she may be cared for by several specialists as well as a primary care physician. In the inpatient setting, care may involve multiple consultants along with

the primary admitting physician. Communication through the medical record is necessary but not sufficient, particularly when patients have complex medical problems or when difficult decisions need to be made about the optimal management plan. Physicians should optimally meet face-to-face or by phone to ensure clear communication and thoughtful planning. It is important to note that patients often receive or perceive different messages from various care providers; thus, attempts should be made to provide consistency among these messages to the patient. Management plans and treatment options should be outlined succinctly and clearly for the patient.

Another dimension of team-based care involves allied health professions. It is not unusual for a hospitalized patient to encounter physical therapists, pharmacists, respiratory therapists, radiology technicians, social workers, dietitians, and transport personnel (among others) in addition to physicians and nurses. Each of these individuals contributes to clinical care as well as to the patient's experience with the health care system. In the outpatient setting, disease screening and chronic disease management are often carried out by nurses, physician assistants, or other allied health professionals.

The growth of team-based care has important implications for medical culture, student and resident training, and the organization of health care systems. Despite diversity in training, skills, and responsibilities among health care professionals, common values need to be espoused and reinforced. Many medical schools have incorporated interprofessional teamwork into their curricula. Effective communication is inevitably the most challenging aspect of implementing team-based care. While communication can be aided by electronic devices, including medical records, apps, or text messages, it is vitally important to balance efficiency with taking the necessary time to speak directly with colleagues.

The Dichotomy of Inpatient and Outpatient Internal Medicine The hospital environment has undergone sweeping changes over the past few decades. Emergency departments and critical care units have evolved to manage critically ill patients, allowing them to survive formerly fatal conditions. In parallel, there is increasing pressure to reduce the length of stay in the hospital and to manage complex disorders in the outpatient setting. This transition has been driven not only by efforts to reduce costs but also by the availability of new outpatient technologies, such as imaging and percutaneous infusion catheters for long-term antibiotics or nutrition, minimally invasive surgical procedures, and evidence that outcomes often are improved by reducing inpatient hospitalization.

In addition to traditional medical beds, hospitals now encompass multiple distinct levels of care, such as the emergency department, procedure rooms, overnight observation units, critical care units, and palliative care units. A consequence of this differentiation has been the emergence of new specialties (e.g., emergency medicine and end-of-life care) and the provision of in-hospital care by hospitalists and intensivists. Most *hospitalists* are board-certified internists who bear primary responsibility for the care of hospitalized patients and whose work is limited entirely to the hospital setting. The shortened length of hospital stay means that most patients receive only acute care while hospitalized; the increased complexities of inpatient medicine make the presence of an internist with specific training, skills, and experience in the hospital environment extremely beneficial. *Intensivists* are board-certified physicians who are further certified in critical care medicine and who direct and provide care for very ill patients in critical care units. Clearly, an important challenge in internal medicine today is to ensure the continuity of communication and information flow between a patient's primary care physician and those who are in charge of the patient's hospital care. Maintaining these channels of communication is frequently complicated by patient "handoffs"—i.e., transitions from the outpatient to the inpatient environment, from the critical care unit to a general medicine floor, from a medical to a surgical service and vice versa, from the hospital environment to the recently developed "home hospital" setting (for select patients with adequate home support), and from the hospital or home hospital to the outpatient environment.

The involvement of many care providers in conjunction with these transitions can threaten the traditional one-to-one relationship between patient and primary care physician. Of course, patients can benefit greatly from effective collaboration among a number of health care professionals; however, *it is the duty of the patient's principal or primary physician to provide cohesive guidance through an illness.* To meet this challenge, primary care physicians must be familiar with the techniques, skills, and objectives of specialist physicians and allied health professionals who care for their patients in the hospital. In addition, primary care physicians must ensure that their patients benefit from scientific advances and the expertise of specialists, both in and out of the hospital. Primary care physicians should explain the role of these specialists to reassure patients that they are in the hands of physicians best trained to manage their current illness. However, the primary care physician should assure patients and their families that decisions are being made in consultation with these specialists. The evolving concept of the "medical home" incorporates team-based primary care with subspecialty care in a cohesive environment that ensures smooth transitions of care.

Mitigating the Stress of Acute Illness Few people are prepared for a new diagnosis of cancer or anticipate the occurrence of a myocardial infarction, stroke, or major accident. The care of a frightened or distraught patient is confounded by these understandable responses to life-threatening events. The physician and other health providers can reduce the shock of life-changing events by providing information in a clear, calm, consistent, and reassuring manner. Often, information and reassurance need to be repeated. Caregivers should also recognize that, for the typical patient, hospital emergency rooms, operating rooms, ICUs, and general medical floors represent an intimidating environment. Hospitalized patients find themselves surrounded by air jets, buttons, and glaring lights; invaded by tubes and wires; and beset by the numerous members of the health care team—hospitalists, specialists, nurses, nurses' aides, physician assistants, social workers, technologists, physical therapists, medical students, house officers, attending and consulting physicians, and many others. They may be transported to special laboratories and imaging facilities replete with blinking lights, strange sounds, and unfamiliar personnel; they may be left unattended at times; and they may be obligated to share a room with other patients who have their own health problems. It is little wonder that patients may find this environment bewildering and stressful. The additive effects of an acute illness, unfamiliar environment, multiple medications, and sleep deprivation can lead to confusion or delirium, especially in older hospitalized patients. Physicians who appreciate the hospital experience from the patient's perspective and who make an effort to guide the patient through this experience may make a stressful situation more tolerable and enhance the patient's chances for an optimal recovery.

Medical Decision-Making Medical decision-making is a fundamental responsibility of the physician and occurs at each stage of the diagnostic and therapeutic process. The decision-making process involves the ordering of additional tests, requests for consultations, decisions about treatment, and predictions concerning prognosis. This process requires an in-depth understanding of the pathophysiology and natural history of disease. Formulating a differential diagnosis requires not only a broad knowledge base but also the ability to assess the relative probabilities of various diseases for a given patient. Application of the scientific method, including hypothesis formulation and data collection, is essential to the process of accepting or rejecting a particular diagnosis. Analysis of the differential diagnosis is an iterative process. As new information or test results are acquired, the group of disease processes being considered can be contracted or expanded appropriately. Whenever possible, decisions should be evidence-based, taking advantage of rigorously designed clinical trials or objective comparisons of different diagnostic tests. *Evidence-based medicine* stands in sharp contrast to anecdotal experience, which is often biased. Unless attuned to the importance of using larger, objective studies for making decisions, even the most experienced physicians can be influenced

to an undue extent by recent encounters with selected patients. Evidence-based medicine has become an increasingly important part of routine medical practice and has led to the publication of many useful practice guidelines. It is important to remember, however, that only a small fraction of the many decisions made in clinical practice are based on rigorous clinical trial evidence; other guideline recommendations are, therefore, predicated on expert consensus and weaker evidentiary support.

Thus, the importance of evidence-based medicine notwithstanding, much medical decision-making still relies on good clinical judgment, an attribute that is difficult to quantify or even to assess qualitatively. Physicians must use their knowledge and experience as a basis for weighing known factors, along with the inevitable uncertainties, and then making a sound judgment; this synthesis of information is particularly important when a relevant evidence base is not available. Several quantitative tools may be invaluable in synthesizing the available information, including diagnostic tests, Bayes' theorem (the probability of an event predicated on prior knowledge of conditions possibly related to the event), and multivariate statistical models (Chap. 4). Diagnostic tests serve to reduce uncertainty about an individual's diagnosis or prognosis and help the physician decide how best to manage that individual's condition. The battery of diagnostic tests complements the history and physical examination. The accuracy of a particular test is ascertained by determining its sensitivity (true-positive rate) and specificity (true-negative rate), as well as the predictive value of a positive and a negative result. See Chap. 4 for a more thorough discussion of decision-making in clinical medicine.

Practice Guidelines Many professional organizations and government agencies have developed formal clinical-practice guidelines to aid physicians and other caregivers in making diagnostic and therapeutic decisions that are evidence-based, cost-effective, and most appropriate to a particular patient and clinical situation. As the evidence base of medicine increases, guidelines can provide a useful framework for managing patients with particular diagnoses or symptoms. Clinical guidelines can protect patients—particularly those with inadequate health care benefits—from receiving substandard care. These guidelines also can protect conscientious caregivers from inappropriate charges of malpractice and society from the excessive costs associated with the overuse of medical resources. There are, however, caveats associated with clinical-practice guidelines since they tend to oversimplify the complexities of medicine. Furthermore, groups with different perspectives may develop divergent recommendations regarding issues as basic as the need for screening of women by mammography or of men with serum prostate-specific antigen (PSA) measurements. Finally, guidelines, as the term implies, do not—and cannot be expected to—account for the uniqueness of each individual and his or her illness. The physician's challenge is to integrate into clinical practice the useful recommendations offered by experts without accepting them blindly or being inappropriately constrained by them.

Precision Medicine The concept of *precision* or *personalized medicine* reflects the growing recognition that diseases once lumped together can be further stratified on the basis of genetic, biomarker, phenotypic, and/or psychosocial characteristics that distinguish a given patient from other patients with similar clinical presentations. Inherent in this concept is the goal of targeting therapies in a more specific way to improve clinical outcomes for the individual patient and minimize unnecessary side effects for those less likely to respond to a particular treatment. In some respects, precision medicine represents the evolution of clinical practice guidelines, which are usually developed for populations of patients or a particular diagnosis (e.g., hypertension, thyroid nodule). As the pathobiology, prognosis, and treatment responses of subgroups within these diagnoses become better understood (i.e., through refined genomic analysis or enhanced deep phenotyping), the relevant clinical guidelines incorporate progressively more refined recommendations for individuals within these subgroups. The role of precision medicine is best illustrated for cancers in which genetic testing is able to predict responses (or the lack thereof) to

targeted therapies (Chap. 73). One can anticipate similar applications of precision medicine in pharmacogenomics, immunologic disorders, and diseases in which biomarkers can predict treatment responses. See Chap. 5 for a more thorough discussion of precision medicine.

Evaluation of Outcomes Clinicians generally use *objective* and readily measurable parameters to judge the outcome of a therapeutic intervention. These measures may oversimplify the complexity of a clinical condition as patients often present with a major clinical problem in the context of multiple complicating background illnesses. For example, a patient may present with chest pain and cardiac ischemia, but with a background of chronic obstructive pulmonary disease and renal insufficiency. For this reason, outcome measures, such as mortality, length of hospital stay, or readmission rates, are typically risk-adjusted. An important point to remember is that patients usually seek medical attention for *subjective* reasons; they wish to obtain relief from pain, to preserve or regain function, and to enjoy life. The components of a patient's health status or quality of life can include bodily comfort, capacity for physical activity, personal and professional function, sexual function, cognitive function, and overall perception of health. Each of these important domains can be assessed through structured interviews or specially designed questionnaires. Such assessments provide useful parameters by which a physician can judge patients' subjective views of their disabilities and responses to treatment, particularly in chronic illness. The practice of medicine requires consideration and integration of both objective and subjective outcomes.

Many health systems use survey and patient feedback data to assess qualitative features such as patient satisfaction, access to care, and communication with nurses and physicians. In the United States, HCAHPS (Hospital Consumer Assessment of Healthcare Providers and Systems) surveys are used by many systems and are publicly reported. Social media is also being used to assess feedback in real time as well as to share patient experiences with health care systems, potentially enriching the information available for use in medical decisions.

Errors in the Delivery of Health Care A series of reports from the Institute of Medicine (now the National Academy of Medicine [NAM]) called for an ambitious agenda to reduce medical error rates and improve patient safety by designing and implementing fundamental changes in health care systems (Chap. 8). It is the responsibility of hospitals and health care organizations to develop systems to reduce risk and ensure patient safety. Medication errors can be reduced through the use of ordering systems that rely on electronic processes or, when electronic options are not available, that eliminate misreading of handwriting. Whatever the clinical situation, it is the physician's responsibility to use powerful therapeutic measures wisely, with due regard for their beneficial actions, potential dangers, and cost. Implementation of infection control systems, enforcement of hand-washing protocols, and careful oversight of antibiotic use can minimize the complications of nosocomial infections. Central-line infection rates and catheter-associated urinary tract infections have been dramatically reduced at many centers by careful adherence of trained personnel to standardized protocols for introducing and maintaining central lines and urinary catheters, respectively. Rates of surgical infection and wrong-site surgery can likewise be reduced by the use of standardized protocols and checklists. Falls by patients can be minimized by judicious use of sedatives and appropriate assistance with bed-to-chair and bed-to-bathroom transitions. Taken together, these and other measures are saving thousands of lives each year.

Electronic Medical Records Both the growing reliance on computers and the strength of information technology now play central roles in medicine, including efforts to reduce medical errors. Laboratory data are accessed almost universally through computers. Many medical centers now have electronic medical records (EMRs), computerized order entry, and bar-coded tracking of medications. Some of these systems are interactive, sending reminders or warning of potential medical errors.

EMRs offer rapid access to information that is invaluable in enhancing health care quality and patient safety, including relevant data,

historical and clinical information, imaging studies, laboratory results, and medication records. These data can be used to monitor and reduce unnecessary variations in care and to provide real-time information about processes of care and clinical outcomes. Ideally, patient records are easily transferred across the health care system; however, technological limitations and concerns about privacy and cost continue to limit broad-based use of EMRs in many clinical settings.

For all of the advantages of EMRs, they can create distance between the physician and patient if care is not taken to preserve face-to-face contact. EMRs also require training and time for data entry. Many providers spend significant time entering information to generate structured data and to meet billing requirements. They may feel pressured to take short cuts, such as “cutting and pasting” parts of earlier notes into the daily record, thereby increasing the risk of errors. EMRs also structure information in a manner that disrupts the traditional narrative flow across time and among providers. These features, which may be frustrating for some providers, must be weighed against the advantages of ready access to past medical history, imaging, laboratory data, and consultant notes. Furthermore, the effort, time, and attention needed to maintain and utilize the EMR have led to a growing sense of dissatisfaction among physicians, lessening professional and personal well-being as a result. Clearly, this is an area of daily practice that requires improvement both for the delivery of safe and optimal care and physician wellness.

It is important to emphasize that information technology is merely a tool and can never replace the clinical decisions that are best made by the physician. Clinical knowledge and an understanding of a patient's needs, supplemented by quantitative tools, still represent the best approach to decision-making in the practice of medicine.

THE PATIENT-PHYSICIAN RELATIONSHIP

The significance of the intimate personal relationship between physician and patient cannot be too strongly emphasized, for in an extraordinarily large number of cases both the diagnosis and treatment are directly dependent on it. One of the essential qualities of the clinician is interest in humanity, for the secret of the care of the patient is in caring for the patient.

—Francis W. Peabody, October 21, 1925,
Lecture at Harvard Medical School

Physicians must never forget that patients are individuals with problems that all too often transcend their physical complaints. They are not “cases” or “admissions” or “diseases.” Patients do not fail treatments; treatments fail to benefit patients. This point is particularly important in this era of high technology in clinical medicine. Most patients are anxious and fearful. Physicians should instill confidence and offer reassurance, but they must never come across as arrogant, patronizing, impatient, or hurried. A professional attitude, coupled with warmth and openness, can do much to alleviate anxiety and to encourage patients to share all aspects of their medical history. Empathy and compassion are the essential features of a caring physician. The physician needs to consider the setting in which an illness occurs—in terms not only of patients themselves but also of their familial, social, and cultural backgrounds. The ideal patient-physician relationship is based on thorough knowledge of the patient, mutual trust, and the ability to communicate.

Informed Consent The fundamental principles of medical ethics require physicians to act in the patient's best interest and to respect the patient's autonomy. Both principles are reflected in the process of informed consent. Patients are required to sign consent forms for most diagnostic or therapeutic procedures. Many patients possess limited medical knowledge and must rely on their physicians for advice. Communicating in a clear and understandable manner, physicians must fully discuss the alternatives for care and explain the risks, benefits, and likely consequences of each alternative. The physician is responsible for ensuring that the patient thoroughly understands these risks and benefits; encouraging questions is an important part of this process. It may be necessary to go over certain issues with the patient more than once. This is the very definition of *informed consent*. Complete, clear

explanation and discussion of the proposed procedures and treatment can greatly mitigate the fear of the unknown that commonly accompanies hospitalization. Often the patient's understanding is enhanced by repeatedly discussing the issues in an unthreatening and supportive way, answering new questions that occur to the patient as they arise. Continuing efforts to educate the patient are essential. Patients are frequently inhibited from understanding by the fear of an uncertain future and potential impact of the illness on themselves and their families. Clear communication can also help alleviate misunderstandings in situations where complications of intervention occur. Special care should also be taken to ensure that a physician seeking a patient's informed consent has no real or apparent conflict of interest.

Approach to Grave Prognoses and Death No circumstance is more distressing than the diagnosis of an incurable disease, particularly when premature death is inevitable. What should the patient and family be told? What measures should be taken to maintain life? What can be done to optimize quality of life?

Transparency of information, delivered in an appropriate manner, is essential in the face of a terminal illness. Even patients who seem unaware of their medical circumstances, or whose family members have protected them from diagnoses or prognoses, often have keen insights into their condition. They may also have misunderstandings that can lead to additional anxiety. The patient must be given an opportunity to speak with the physician and ask questions. A wise and insightful physician uses such open communication as the basis for assessing what the patient wants to know and when he or she wants to know it. On the basis of the patient's responses, the physician can assess the most appropriate time and pace for sharing information. Ultimately, the patient must understand the expected course of the disease so that appropriate plans and preparations can be made. The patient should participate in decision-making with an understanding of the goal of treatment (palliation) and its likely effects. The patient's religious beliefs should be taken into consideration. Some patients may find it easier to share their feelings about death with their physician, nurses, or members of the clergy than with family members or friends.

The physician should provide or arrange for emotional, physical, and spiritual support, and must be compassionate, unhurried, and open. In many instances, there is much to be gained by the laying on of hands. Pain should be controlled adequately, human dignity maintained, and isolation from family and close friends avoided. These aspects of care tend to be overlooked in hospitals, where the intrusion of life-sustaining equipment can detract from attention to the individual person and encourage concentration instead on the life-threatening disease, against which the battle ultimately will be lost in any case. In the face of terminal illness, the goal of medicine must shift from *cure* to *care* in the broadest sense of the term. *Primum succurrere*, first to help, is a guiding principle. In offering care to a dying patient, a physician should be prepared to provide information to family members and deal with their grief and sometimes their feelings of guilt or even anger. It is important for the physician to assure the family that everything reasonable is being done. A substantial challenge in these discussions is that the physician often does not know exactly how to gauge the prognosis. In addition, various members of the health care team may offer different opinions. Good communication among providers is essential so that consistent information is provided to patients. This is especially important when the best path forward is uncertain. Advice from experts in palliative and terminal care should be sought whenever appropriate to ensure that clinicians are not providing patients with unrealistic expectations. **For a more complete discussion of end-of-life care, see Chap. 12.**

Maintaining Humanism and Professionalism Many trends in the delivery of health care tend to make medical care impersonal. These trends, some of which have been mentioned already, include (1) vigorous efforts to reduce the escalating costs of health care; (2) the growing number of managed-care programs, which are intended to reduce costs but where the patient may have little choice in selecting a physician; (3) increasing reliance on technological advances and

computerization; and (4) the need for numerous physicians and other health professionals to be involved in the care of most patients who are seriously ill.

In light of these changes in the medical care system, it is a major challenge for physicians to maintain the *humane* aspects of medical care. The American Board of Internal Medicine, working together with the American College of Physicians–American Society of Internal Medicine and the European Federation of Internal Medicine, has published a *Charter on Medical Professionalism* that underscores three main principles in physicians’ contract with society: (1) the primacy of patient welfare, (2) patient autonomy, and (3) social justice. While medical schools appropriately place substantial emphasis on professionalism, a physician’s personal attributes, including integrity, respect, and compassion, also are extremely important. In the United States, the Gold Humanism Society recognizes individuals who are exemplars of humanistic patient care and serve as role models for medical education and training.

Availability to the patient, expression of sincere concern, willingness to take the time to explain all aspects of the illness, and a nonjudgmental attitude when dealing with patients whose cultures, lifestyles, attitudes, and values differ from those of the physician are just a few of the characteristics of a humane physician. Every physician will, at times, be challenged by patients who evoke strongly negative or positive emotional responses. Physicians should be alert to their own reactions to such situations and should consciously monitor and control their behavior so that the patient’s best interest remains the principal motivation for their actions at all times.

Another important aspect of patient care involves an appreciation of the patient’s “quality of life,” a subjective assessment of what each patient values most. This assessment requires detailed, sometimes intimate knowledge of the patient, which usually can be obtained only through deliberate, unhurried, and often repeated conversations. Time pressures will always threaten these interactions, but they should not diminish the importance of understanding and seeking to fulfill the priorities of the patient.

■ EXPANDING FRONTIERS IN MEDICAL PRACTICE

The Era of “Omics” In the spring of 2003, announcement of the complete sequencing of the human genome officially ushered in the genomic era. However, even before that landmark accomplishment, the practice of medicine had been evolving as a result of insights into both the human genome and the genomes of a wide variety of microbes. The clinical implications of these insights are illustrated by the complete genome sequencing of H1N1 influenza virus in 2009 and even faster sequencing of COVID-19 in early 2020, leading to the swift development and dissemination of effective vaccines. Today, gene expression profiles are being used to guide therapy and inform prognosis for a number of diseases, and genotyping is providing a new means to assess the risk of certain diseases as well as variations in response to a number of drugs. Despite these advances, the use of complex genomics in the diagnosis, prevention, and treatment of disease is still in its early stages. The task of physicians is complicated by the fact that phenotypes generally are determined not by genes alone but by the complex interactions among genes and gene products, and by the interplay of genetic and environmental factors.

Rapid progress is also being made in other areas of molecular medicine. *Epigenetics* is the study of alterations in chromatin and histone proteins and methylation of DNA sequences that influence gene expression (**Chap. 483**). Every cell of the body has identical DNA sequences; the diverse phenotypes a person’s cells manifest are, in part, the result of epigenetic regulation of gene expression. Epigenetic alterations are associated with a number of cancers and other diseases. *Proteomics*, the study of the entire library of proteins made in a cell or organ and the complex relationship of these proteins to disease, is enhancing the repertoire of the 23,000 genes in the human genome through alternate splicing, posttranslational processing, and posttranslational modifications that often have unique functional consequences. The presence or absence of particular proteins in the circulation or in cells is being explored for many diagnostic and disease-screening

applications. *Microbiomics* is the study of the resident microbes in humans and other mammals, which together compose the microbiome. The human haploid genome has ~23,000 genes, whereas the microbes residing on and in the human body encompass more than 3–4 million genes; these resident microbes are likely to be of great significance with regard to health status. Ongoing research is demonstrating that the microbes inhabiting human mucosal and skin surfaces play a critical role in maturation of the immune system, in metabolic balance, in brain function, and in disease susceptibility. A variety of environmental factors, including the use and overuse of antibiotics, have been tied experimentally to substantial increases in disorders such as obesity, metabolic syndrome, atherosclerosis, and immune-mediated diseases in both adults and children. *Metagenomics*, of which microbiomics is a part, is the genomic study of environmental species that have the potential to influence human biology directly or indirectly. An example is the study of exposures to microorganisms in farm environments that may be responsible for the lower incidence of asthma among children raised on farms. *Metabolomics* is the study of the range of metabolites in cells or organs and the ways they are altered in disease states. The aging process itself may leave telltale metabolic footprints that allow the prediction (and possibly the prevention) of organ dysfunction and disease. It seems likely that disease-associated patterns will be found in lipids, carbohydrates, membranes, mitochondria and mitochondrial function, and other vital components of cells and tissues. *Exposomics* is the study of the exposome—i.e., the environmental exposures such as smoking, sunlight, diet, exercise, education, and violence that together have an enormous impact on health. All of this new information represents a challenge to the traditional reductionist approach to medical thinking. The variability of results in different patients, together with the large number of variables that can be assessed, creates challenges in identifying preclinical disease and defining disease states unequivocally. Accordingly, the tools of *systems biology* and *network medicine* are being applied to the enormous body of information (“big data”) now obtainable for every patient and may eventually provide new approaches to classifying disease. **For a more complete discussion of a complex systems and network science approach to human disease, see Chap. 486.**

The rapidity of these advances may seem overwhelming to practicing physicians; however, physicians have an important role to play in ensuring that these powerful technologies and sources of new information are applied judiciously to patient care. Since omics are evolving so rapidly, physicians and other health care professionals must engage in continuous learning so that they can apply this new knowledge to the benefit of their patients’ health and well-being. Genetic testing requires wise counsel based on an understanding of the value and limitations of the tests as well as the implications of their results for specific individuals. **For a more complete discussion of genetic testing, see Chap. 467.**

The Globalization of Medicine Physicians should be cognizant of diseases and health care services beyond local boundaries. Global travel has critical implications for disease spread, and it is not uncommon for diseases endemic to certain regions to be seen in other regions after a patient has traveled to and returned from those regions. The outbreak of Zika virus infections in the Americas is a cogent example of this phenomenon. In addition, factors such as wars, the migration of refugees, and increasing climate extremes are contributing to changing disease profiles worldwide. Patients have broader access to unique expertise or clinical trials at distant medical centers, even those in other countries, and the cost of travel may be offset by the quality of care at those distant locations. As much as any other factor influencing global aspects of medicine, the Internet has transformed the transfer of medical information throughout the world. This change has been accompanied by the transfer of technological skills through telemedicine and international consultation—for example, interpretation of radiologic images and pathologic specimens. **For a complete discussion of global issues, see Chap. 472.**

Medicine on the Internet On the whole, the Internet has had a positive effect on the practice of medicine; through personal computers, a wide range of information is available to physicians and patients

almost instantaneously at any time and from anywhere in the world. This medium holds enormous potential for the delivery of current information, practice guidelines, state-of-the-art conferences, journal content, textbooks (including this text), and direct communications with other physicians and specialists, expanding the depth and breadth of information available to the physician regarding the diagnosis and care of patients. Medical journals are now accessible online, providing rapid sources of new information. By bringing them into direct and timely contact with the latest developments in medical care, this medium also serves to lessen the information gap that has hampered physicians and health care providers in remote areas.

Patients, too, are turning to the Internet in increasing numbers to acquire information about their illnesses and therapies and to join Internet-based support groups. Patients often arrive at a clinic visit with sophisticated information about their illnesses. In this regard, physicians are challenged in a positive way to keep abreast of the latest relevant information while serving as an “editor” as patients navigate this seemingly endless source of information, the accuracy and validity of which are not uniform.

A critically important caveat is that virtually anything can be published on the Internet, with easy circumvention of the peer-review process that is an essential feature of academic publications. Both physicians and patients who search the Internet for medical information must be aware of this danger. Notwithstanding this limitation, appropriate use of the Internet is revolutionizing information access for physicians and patients, and in this regard represents a remarkable resource that was not available to practitioners a generation ago.

Public Expectations and Accountability The general public’s level of knowledge and sophistication regarding health issues has grown rapidly over the past few decades. As a result, expectations of the health care system in general and of physicians in particular have risen. Physicians are expected to master rapidly advancing fields (the *science* of medicine) while considering their patients’ unique needs (the *art* of medicine). Thus, physicians are held accountable not only for the technical aspects of the care they provide but also for their patients’ satisfaction with the delivery and costs of care.

In many parts of the world, physicians increasingly are expected to account for the way in which they practice medicine by meeting certain standards prescribed by federal and local governments. The hospitalization of patients whose health care costs are reimbursed by the government and other third parties is subjected to utilization review. Thus, a physician must defend the cause for and duration of a patient’s hospitalization if it falls outside certain “average” standards. Authorization for reimbursement increasingly is based on documentation of the nature and complexity of an illness, as reflected by recorded elements of the history and physical examination. A growing “pay-for-performance” movement seeks to link reimbursement to quality of care. The goal of this movement is to improve standards of health care and contain spiraling health care costs. In many parts of the United States, managed (capitated) care contracts with insurers have replaced traditional fee-for-service care, placing the onus of managing the cost of all care directly on the providers and increasing the emphasis on preventive strategies. In addition, physicians are expected to give evidence of their current competence through mandatory continuing education, patient record audits, maintenance of certification, and relicensing.

Medical Ethics and New Technologies The rapid pace of technological advances has profound implications for medical applications that go far beyond the traditional goals of disease prevention, treatment, and cure. Cloning, genetic engineering, gene therapy, human-computer interfaces, nanotechnology, and use of targeted therapies have the potential to modify inherited predispositions to disease, select desired characteristics in embryos, augment “normal” human performance, replace failing tissues, and substantially prolong life span. Given their unique training, physicians have a responsibility to help shape the debate on the appropriate uses of and limits placed on these new technologies and to consider carefully the ethical issues associated with the implementation of such interventions. As medicine becomes more complex, shared decision-making is increasingly important, not

only in areas such as genetic counseling and end-of-life care, but also in diagnostic and treatment options.

Learning Medicine More than a century has passed since the publication of the Flexner Report, a seminal study that transformed medical education and emphasized the scientific foundations of medicine as well as the acquisition of clinical skills. In an era of burgeoning information and access to medical simulation and informatics, many schools are implementing new curricula that emphasize lifelong learning and the acquisition of competencies in teamwork, communication skills, system-based practice, and professionalism. The tools of medicine also change continuously, necessitating formal training in the use of EMRs, large datasets, ultrasound, robotics, and new imaging techniques. These and other features of the medical school curriculum provide the foundation for many of the themes highlighted in this chapter and are expected to allow physicians to progress, with experience and learning over time, from competency to proficiency to mastery.

At a time when the amount of information that must be mastered to practice medicine continues to expand, increasing pressures both within and outside of medicine have led to the implementation of restrictions on the amount of time a physician-in-training can spend in the hospital and in clinics. Because the benefits associated with continuity of medical care and observation of a patient’s progress over time were thought to be outstripped by the stresses imposed on trainees by long hours and by fatigue-related errors, strict limits were set on the number of patients that trainees could be responsible for at one time, the number of new patients they could evaluate in a day on call, and the number of hours they could spend in the hospital. In 1980, residents in medicine worked in the hospital more than 90 hours per week on average. In 1989, their hours were restricted to no more than 80 per week. Resident physicians’ hours further decreased by ~10% between 1996 and 2008, and in 2010, the Accreditation Council for Graduate Medical Education further restricted (i.e., to 16 hours per shift) consecutive in-hospital duty hours for first-year residents. The impact of these changes is still being assessed, but the evidence that medical errors have decreased as a consequence is sparse. An unavoidable by-product of fewer hours at the bedside is an increase in the number of “handoffs” of patient responsibility from one physician to another. These transfers often involve a transition from a physician who knows the patient well, having evaluated that individual on admission, to a physician who knows the patient less well. It is imperative that these transitions of responsibility be handled with care and thoroughness, with all relevant information exchanged and acknowledged. These issues highlight the challenge our profession has in establishing a reliable measure of physician effectiveness.

The Physician as Perpetual Student From the time physicians graduate from medical school, it becomes all too apparent that this milestone is symbolic and that they must embrace the role of a “perpetual student.” This realization is at the same time exhilarating and anxiety-provoking. It is exhilarating because physicians can apply constantly expanding knowledge to the treatment of their patients; it is anxiety-provoking because physicians realize that they will never know as much as they want or need to know. Ideally, physicians will translate the latter feeling into energy through which they can continue to improve and reach their potential. It is the physician’s responsibility to pursue new knowledge continually by reading, attending conferences and courses, and consulting colleagues and the Internet. This is often a difficult task for a busy practitioner; however, a commitment to continued learning is an integral part of being a physician and must be given the highest priority.

The Physician as Citizen Being a physician is a privilege. The capacity to apply one’s skills for the benefit of fellow human beings is a noble calling. The physician-patient relationship is inherently unbalanced in the distribution of power. In light of their influence, physicians must always be aware of the potential impact of what they do and say, and must always strive to strip away individual biases and preferences to find what is best for their patients. To the extent possible, physicians should also act within their communities to promote health

and alleviate suffering. Meeting these goals begins by setting a healthy example and continues in taking action to deliver needed care even when personal financial compensation may not be available.

Research, Teaching, and the Practice of Medicine The word *doctor* is derived from the Latin *docere*, “to teach.” As teachers, physicians should share information and medical knowledge with colleagues, students of medicine and related professions, and their patients. The practice of medicine is dependent on the sum total of medical knowledge, which in turn is based on an unending chain of scientific discovery, clinical observation, analysis, and interpretation. Advances in medicine depend on the acquisition of new information through research, and improved medical care requires the transmission of that information. As part of their broader societal responsibilities, physicians should encourage patients to participate in ethical and properly approved clinical investigations if these studies do not impose undue hazard, discomfort, or inconvenience. Physicians engaged in clinical research must be alert to potential conflicts of interest between their research goals and their obligations to individual patients. The best interests of the patient must always take priority.

To wrest from nature the secrets which have perplexed philosophers in all ages, to track to their sources the causes of disease, to correlate the vast stores of knowledge, that they may be quickly available for the prevention and cure of disease—these are our ambitions.

—William Osler, 1849–1919

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2

Promoting Good Health

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GOALS AND APPROACHES TO PREVENTION

Prevention of acute and chronic diseases before their onset has been recognized as one of the hallmarks of excellent medical practice for centuries and is now used as a metric for highly functioning health care systems. The ultimate goal of preventive strategies is to avoid premature death. However, as longevity has increased dramatically

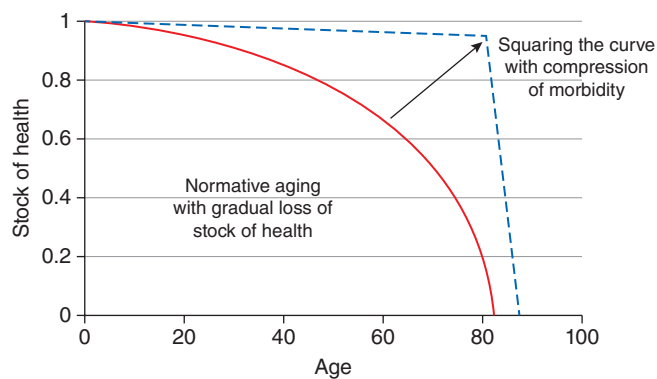


FIGURE 2-1 Loss of health with aging. Representation of normative aging with loss of the full stock of health with which individuals are born (indicating gain of morbidity), contrasted with a squared curve with greater longevity and fuller stock of health (less morbidity) until shortly before death. The “squared curve” represents the likely ideal situation for most patients.

worldwide over the last century (largely as a result of public health practices), increasing emphasis is placed on prevention for the purpose of preserving quality of life and extending the health span, not just the life span. Given that all patients will eventually die, the goal of prevention ultimately becomes compression of morbidity toward the end of the life span; that is, reduction of the amount of burden and time spent with disease prior to dying. As shown in **Fig. 2-1**, normative aging tends to involve a steady decline in the stock of health, with accelerating decline over time. Successful prevention offers the opportunity both to extend life and to extend healthy life, thus “squaring the curve” of health loss during aging.

Prevention strategies have been characterized as tertiary, secondary, primary, and primordial. *Tertiary prevention* requires rapid action to prevent imminent death in the setting of acute illness, such as through percutaneous coronary intervention in the setting of ST-segment elevation myocardial infarction. *Secondary prevention* strategies focus on avoiding the recurrence of disease and death in an individual who is already affected. For example, tamoxifen is recommended for women with surgically treated early-stage, estrogen receptor–positive breast cancer, because it reduces the risk of recurrent breast cancer (including in the contralateral breast) and death. *Primary prevention* attempts to reduce the risk of incident disease among individuals with one or more risk factors. Treatment of elevated blood pressure in individuals who have not yet experienced cardiovascular disease represents one example of primary prevention that has proven effective in reducing the incidence of stroke, heart failure, and coronary heart disease.

Primordial prevention is a more recent concept (first introduced in 1979) that focuses on prevention of the development of *risk factors* for disease, not just prevention of disease. Primordial prevention strategies emphasize upstream determinants of risk for chronic diseases, such as eating patterns, physical activity, and environmental and social determinants of health. It therefore encompasses medical treatment strategies for some individuals as well as a strong reliance on public health and social policy. It is increasingly clear that primordial prevention represents the ultimate means for reducing the burden of chronic diseases of aging. Once risk factors develop, it is difficult to restore risk to the low level of someone who never developed the risk factor. The time spent with adverse levels of the risk factor often causes irreversible damage that precludes complete restoration of low risk. For example, individuals with hypertension who are treated back to optimal levels (<120/<80 mmHg) do have a lower risk compared with untreated patients with hypertension, but they still have twice the risk of cardiovascular events as those who maintained optimal blood pressure without medications. Patients with elevated blood pressure that is subsequently treated have greater left ventricular mass index, worse renal function, and more evidence of atherosclerosis and other target organ damage as a result of the time spent with elevated blood pressure; such damage cannot be fully reversed despite efficacious therapy with antihypertensive medications. Conversely, as described below in greater detail, individuals who maintain optimal levels of all major

cardiovascular risk factors into middle age through primordial prevention essentially abolish their lifetime risk of developing cardiovascular disease while also living substantially longer and having a lower burden and later onset of other comorbid illnesses (compression of morbidity).

Prevention strategies should be distinguished from disease screening strategies. Screening attempts to detect evidence of disease at its earliest stages, when treatment is likely to be more efficacious than for advanced disease (Chap. 6). Screening can be performed in service of prevention, especially if it aids in identifying preclinical markers, such as dyslipidemia or hyperglycemia, associated with elevated disease risk.

■ HEALTH PROMOTION

In recent decades, medical practice has increasingly focused on clinical and public health approaches to promote health, and not just prevent disease. Prevention of disease is a worthy individual and societal goal in and of itself, but it does not necessarily guarantee health. Health is a broader construct encompassing more than just absence of disease. It includes biologic, physiologic, and psychological domains (among others) in a continuum, rather than occurring as a dichotomous trait. Health is therefore somewhat subjective, but attempts have been made to use more objective criteria to define health in order to raise awareness, prevent disease, and promote healthy longevity.

For example, in 2010, the American Heart Association (AHA) defined a new construct of “cardiovascular health” based on evidence of associations with longevity, disease avoidance, healthy longevity, and quality of life. The definition of cardiovascular health is based on seven health behaviors and health factors (eating pattern, physical activity, smoking status, body mass index [BMI], and levels of blood pressure, blood cholesterol, and blood glucose) and includes a spectrum from poor to ideal. Individuals with optimal levels of all seven metrics simultaneously are considered to have ideal cardiovascular health. The state of cardiovascular health for an individual or a population can be assessed with simple scoring by counting the number of ideal metrics (out of seven) or applying 0 points for each poor metric, 1 point for each intermediate metric, and 2 points for each ideal metric, thus creating a composite cardiovascular health score ranging from 0 to 14 points. Higher cardiovascular health scores in younger and middle ages have been associated with greater longevity, lower incidence of cardiovascular disease, lower incidence of other chronic diseases of aging (including dementia, cancer, and more), compression of morbidity, greater quality of life, and lower health care costs, achieving both individual and societal goals for healthy aging and further establishing the critical importance of primordial prevention and cardiovascular health promotion.

Focusing on health promotion, rather than just disease prevention, may also provide greater motivation for patients to pursue lifestyle changes or adhere to clinician recommendations. Extensive literature suggests that providing patients solely with information regarding disease risk, or risk reduction with treatment, is unlikely to motivate desired behavior change. Empowering patients with strategies to achieve positive health goals after discussing risks can provide more effective adherence and better long-term outcomes. In the case of smoking cessation, enumerating only the risks of smoking can lead to patient inertia and therapeutic nihilism and has proven to be an ineffective approach, whereas strategies that incorporate positive health messaging, support, and feedback, with appropriate use of evidence-based therapies, have proven far more effective.

■ PRIORITIZING PREVENTION STRATEGIES

In secondary prevention, the patient already has manifest clinical disease and is therefore at high risk for progression. The approach should be to work with the patient to implement all evidence-based strategies that will help to prevent recurrence or progression. This will typically include drug therapy as well as therapeutic lifestyle changes to control ongoing risk factors that may have caused disease in the first place. Juggling priorities can be difficult, and barriers to implementation are many, including costs, time, patient health literacy, and patient and caregiver capacity to organize the regimen. Addressing these potential barriers with the patient can help to forge a therapeutic bond and

may improve adherence; ignoring them will likely lead to therapeutic failure. Numerous studies demonstrate that, even in high-functioning health systems, only ~50% of patients are taking recommended, evidence-based secondary prevention medications, such as statins, by 1 year after a myocardial infarction.

In patients who are eligible for primary prevention strategies, it is important to frame the discussion around the overall evidence base as well as an individual patient’s likelihood of benefit from a given preventive intervention. A first step is to understand the patient’s estimated absolute risk for disease in the foreseeable future or during their remaining life span. However, absolute risk estimation and presentation of those risks are generally insufficient to motivate behavior change. It is critical to assess the patient’s understanding and tolerance of the risk, their readiness to implement lifestyle changes or adhere to drug therapy, and their overall preferences regarding use of drug therapy to prevent an event (e.g., cancer, myocardial infarction, stroke). The clinician can help the patient by informing them of the risks for disease and potential for absolute benefits (and harms) from the available evidence-based choices. This may take more than one conversation, but given that diseases, such as cancer and cardiovascular disease, are the leading causes of premature death and disability, the time is well spent.

Partnering with the patient through motivational interviewing may assist in the process of selecting initial approaches to prevention. Selecting an area that the patient feels they are ready to change can lead to better adherence and greater achievement of success in the short and longer term. If the patient is uncertain what course to choose, prudence would dictate focusing on control of risk factors that may lead to the most rapid reduction in risk for acute events. For example, blood pressure is both a chronic risk factor and an acute trigger for cardiovascular events. Thus, if a patient has both significant elevations in blood pressure and dyslipidemia, it would be appropriate to focus initial efforts on blood pressure control. Likewise, a focus on smoking cessation can lead to more rapid reductions in risk for acute events than some other lifestyle interventions.

■ PREVENTION AND HEALTH PROMOTION ACROSS THE LIFE COURSE

Periodic Health Evaluations The “routine annual physical” has in many ways become an expected part of the patient-physician relationship in primary care practice. However, evidence for the efficacy of the periodic health evaluation in asymptomatic adults unselected for risk factors or disease is mixed and depends on the outcome. Systematic reviews and meta-analyses of published trials have consistently observed lack of benefit (and also lack of harm) in terms of total mortality in association with periodic health evaluations. Data are more heterogeneous but overall suggest no benefit for cancer- or cardiovascular-specific mortality, with the potential for either benefit or harm depending on number of evaluations and patient-level factors. Well-designed studies on nonfatal clinical events and morbidity have been sparsely reported, but there appear to be no large effects.

Periodic health evaluations do appear to lead to greater diagnosis of certain conditions such as hypertension and dyslipidemia, as expected. Likewise, periodic health examinations also improve the delivery of recommended preventive services, such as gynecologic examinations and Papanicolaou smears, fecal occult blood testing, and cholesterol screening. The benefits and risks associated with screening tests are discussed in detail in Chap. 6. Risks of routine evaluations include inappropriate testing or overtesting or false-positive findings that require follow-up and induce patients to worry. Periodic health examinations appear to be associated with less patient worry. On balance, given the lack of convincing evidence of harm and the potential for better delivery of appropriate screening, counseling, and preventive services, periodic health evaluations appear reasonable for general populations at average risk for chronic conditions.

It is important to note that routine annual comprehensive physical examinations of asymptomatic adult patients have very low yield and may take an inordinate amount of time in a wellness visit. Such time