TEXTBOOK OF MEDICINE



WYNGAARDEN and SMITH

CECIL

TEXTBOOK OF MEDICINE

Edited by

JAMES B. WYNGAARDEN, M.D.

Director, National Institute Bethesda, Maryland

LLOYD H. SMIT

Professor of Medicine and Associate Dean, University of California, San Francisco, School of Medicine, San Francisco, California

1988

W. B. SAUNDERS COMPANY

Harcourt Brace Jóvanovich, Inc.

Philadelphia/London/Toronto/Montreal/Sydney/Tokyo

Philadelphia, PA 19105

Library of Congress Cataloging-in-Publication Data

Textbook of medicine.

Published simultaneously as 1 v. and as a 2 v. set.

Includes bibliographies and index.

 Internal medicine. I. Cecil, Russell L. (Russell La Fayette), 1881–1965. II. Wyngaarden, James B., 1924– . III. Smith, Lloyd H., 1924– . IV. Title: Cecil textbook of medicine. [DNLM: 1. Medicine. WB 100 T354]

RC46.T35 1988 616 86-27980

ISBN 0-7216-1848-0 (single v.) ISBN 0-7216-1851-0 (set) ISBN 0-7216-1849-9 (v. 1)

ISBN 0-7216-1850-2 (v. 2)

Acquisition Editor: John Dyson Designer: Lorraine B. Kilmer

Production Manager: Frank Polizzano Manuscript Editor: Donna Walker

Indexer: Nancy Guenther

ISBN 0-7216-1848-0 Single Volume

ISBN 0-7216-1849-9 Volume 1 ISBN 0-7216-1850-2 Volume 2 ISBN 0-7216-1851-0 Set

CECIL TEXTBOOK OF MEDICINE

© 1988 by W. B. Saunders Company. Copyright 1927, 1930, 1933, 1937, 1940, 1943, 1947, 1951, 1955, 1959, 1963, 1967, 1971, 1975, 1979, 1982, and 1985 by W. B. Saunders Company. Copyright under the Uniform Copyright Convention. Simultaneously published in Canada. All rights reserved. This book is protected by copyright. No part of it may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without written permission from the publisher. Made in the United States of America. Library of Congress catalog card number 86–27980.

Last digit is the print number: 9 8 7 6 5 4 3 2 1

DOSAGE NOTICE

Every effort has been made by the authors, the editors, and the publisher of this book to ensure that dosage recommendations are precise and in agreement with the standards of practice accepted at the time of publication.

However, dosage schedules are changed from time to time in the light of accumulating clinical experience and continuing laboratory studies. This is most likely to occur in the case of recently introduced products.

We urge, therefore, that you check the package information data for the manufacturer's recommended dosage to be certain that changes have not been made in the recommended dose or in the contraindications for administration. In addition, there are some quite serious situations in which drug therapy must be individualized and expert judgment advises the use of a higher dosage or administration by a different route than is included in the manufacturer's recommendations. Throughout the text examples of such instances are indicated by a footnote.

THE EDITORS

ALSO ASSOCIATED WITH THE CECIL TEXTBOOK OF MEDICINE

Review of General Internal Medicine: A Self-Assessment Manual 4th Edition, 1988

Editors: Lloyd H. Smith, Jr., M.D., James B. Wyngaarden, M.D.

The fourth edition of this self-assessment book contains approximately 1200 questions covering all the specialty areas of internal medicine. The answers are linked to the Cecil Textbook of Medicine and to other readily available sources.

Available from W. B. Saunders Company West Washington Square Philadelphia, Pa. 19105

PREFACE

Medicine is forever mutable. Although certain general principles remain, medical science moves on. Changes in medical practice follow—not in continuous flow, it is true, but nevertheless in rapid sequence. The pace has quickened as we approach the last decade of the twentieth century. New technologies have revolutionized molecular genetics, neurobiology, immunology, cell biology, and structural biology; the application of these disciplines to all branches of the traditional biomedical sciences proceeds apace. The structure of DNA was elucidated only a generation ago. Now it can be confidently predicted that the whole human genome of approximately three billion nucleotide base pairs (the information equivalent to a thousand large telephone books) will be sequenced within the next decade. The language of the new biology has already permeated medicine. Beyond these contributions from the biological sciences, new applications of the physical and mathematical sciences, especially in diagnostic imaging (CT, MRI, PET, sonography) and in the use of the computer, have radically altered medical practice. In such a climate of change medical competence itself is mutable. It must be constantly renewed or else it will erode.

In order to reflect the best in medical practice, a major textbook of medicine must also be constantly renewed. In that spirit this edition of the Cecil Textbook of Medicine has been thoroughly revised, the 18th such revision in a span of more than 60 years. Approximately one third of the book is "new" in that different authors have been selected, in this way assuring that their chapters have been completely recast. All other chapters have been revised and updated by their current authors, carefully chosen authorities in their respective subjects. A revised Cecil must reflect the problems of the day. As an example, nowhere is this more apparent than in its attention to the acquired immunodeficiency syndrome (AIDS), the most dramatic medical epidemic of our time. In the 17th edition of Cecil, this new and baffling syndrome was described in a single chapter of two pages in the section on Diseases of the Immune System. In this current edition are new chapters on "Retroviruses That Cause Human Disease" (R. C. Gallo), "Acquired Immunodeficiency Syndrome" (J. E. Groopman), "AIDS Dementia and Human Immunodeficiency Virus Brain Infection" (R. W. Price), "Cryptosporidiosis" (R. Soave), and "Giardiasis" (D. P. Stevens), as well as expanded descriptions of other disorders that accompany AIDS— Kaposi's sarcoma, pneumocystosis, Mycobacterium avium-intracellulare infections, etc. Examples of other chapters reflecting areas of medical progress include "Natriuretic Factors" (P. Needleman) and the expanded treatment of "Slow Virus Infections of the Nervous System." Lyme disease has been transferred from being listed as a form of infectious arthritis and now receives more extensive discussion as a systemic disorder in the section on Spirochetal Diseases. New chapters have been added on "Clinical Decision Making" (S. G. Pauker), "Control of Unintended Injuries and Those Due to Violence" (S. B. Hulley), and "The Health of the Physician" (L. H. Clever). All of these and many other changes throughout the 18th edition, including updated and annotated references, are designed to maintain the traditional theme of Cecil as providing "authoritative clinical guidance and a reasoned, scientific basis for the pursuit of medicine."

In this 18th edition the reader will note a major change in format, the first use of color in *Cecil* (other than that of color plates to illustrate specific entities). The introduction of this single additional color is designed to add clarity to headings and figures throughout the book. This innovation is part of a continuing program to make the book more attractive and easier to use.

Cecil not only stands alone; it is also the senior member of an extended family. Four current books are linked to the Cecil Textbook of Medicine by design, format, and editorial responsibility. Cecil Essentials of Medicine (edited by T. E. Andreoli, C. C. J. Carpenter, F. Plum, and L. H. Smith, Jr.) offers a more abbreviated description of the realm of internal medicine. Designed primarily for the medical student, for whom the authoritative compendium of Cecil may sometimes seem formidable, it does not attempt to be complete. Nevertheless it serves as a useful entry guide into the study of medicine. Review of General Internal Medicine (edited by the editors of Cecil) has appeared in a 4th edition in parallel with this 18th edition of Cecil. As before, its 1200 questions and answers are designed to be of general educational benefit as well as to reinforce the value of Cecil as a reference text. Pathophysiology: The Biological Principles of Disease (edited by L. H. Smith, Jr., and S. O. Thier) gives a more extensive description of the scientific basis of medical practice than can be contained within a book such as Cecil, which must devote most of its attention to the practicalities of clinical description, diagnosis, prognosis, and therapy. Medical Microbiology and Infectious Diseases (edited by the late A. I. Braude) gives a more extensive description of the world's experience with the infectious and parasitic diseases.

Editing a major textbook is a complex task, as one attempts to balance content, format, style, integration, and innovation. The editors have been privileged to work with an admirable group of colleagues in this shared responsibility. Fred Plum has continued in his role as Editor for Neurologic and Behavioral Diseases. We welcome Thomas W. Smith as our new Consulting Editor for Cardiovascular Diseases. He joins a seasoned team of fellow Consulting Editors: Thomas E. Andreoli (Renal Diseases), Charles C. J. Carpenter (Infectious Diseases), Robert J. Lefkowitz (Therapeutics), John F. Murray (Respiratory Diseases), David G. Nathan (Hematologic and Hematopoietic Diseases), William E. Paul (Immunology), and Marvin H. Sleisenger (Diseases of the Digestive System). The Consulting Editors continually review their respective sections of this complex book and bring us their ideas and expertise concerning modifications. Our special gratitude is extended to the 325 contributors who have written the 543 chapters that collectively comprise this 18th edition. The ultimate value and authenticity of Cecil lies not with the editors but with the scholarship and experience that these individual physicians and scientists have brought to this joint enterprise.

"Language is the armoury of the human mind; and at once contains the trophies of its past, and the weapons of its future conquests." The weaponry of language, in Coleridge's image above, does not always come fully burnished in submitted manuscripts. As in the 17th edition, we have been most fortunate to work with seasoned editorial assistants in Bethesda (Margaret Quinlan) and in San Francisco (Judith Serrell), without whose dedication and skill this large project could not have been completed. At W. B. Saunders Company, Lorraine Kilmer, Donna Walker, and Frank Polizzano carried out with experienced professionalism the intricate task of formatting, editing, and assembling the book, made more complex this time by the use of color. The overall editor at the W. B. Saunders Company for this 18th edition of Cecil was John Dyson, who has been an invaluable guide, colleague, and good friend. We are deeply indebted to him for his extensive contributions in bringing to completion this 18th edition of a venerable book.

> JAMES B. WYNGAARDEN, M.D. LLOYD H. SMITH, JR., M.D.

CONTENTS

| P | ART I MEDICINE AS A LEARNED AND HUMANE PROFESSION | | 35 36 | | 158 16 |
|---|--|---------------------------------|--|---|--|
| 1 2 3 | 1,7 | 1 5 7 | 37 38 | | 169 171 |
| 4 5 | MEDICINE AS A VERY OLD PROFESSION, Lewis Thomas | 9 12 | P | ART VI CARDIOVASCULAR DISEASES | |
| PA | ART II HUMAN GROWTH, DEVELOPMEN | T, | | APPROACH TO THE PATIENT WITH CARDIOVASCULAR DISEASE, Thomas W. Smith | 175 |
| | AND AGING | | 40 | EPIDEMIOLOGY OF CARDIOVASCULAR DISEASE, William T. Friedewald | 179 |
| 6 | | 16 | 41 | CARDIAC FUNCTION AND CIRCULATORY CONTROL, John Ross, Jr | 184 |
| 7 | AGING AND GERIATRIC MEDICINE, John W. Rowe | 21 | 42 | | 191 |
| ٠ | T. Franklin Williams | 27 | | | 191 196 |
| 9 | | 31 | | 42.3 ECHOCARDIOGRAPHY, Richard L. Popp | 201 |
| D/ | ART III PERSONAL HEALTH CARE AND | | | 42.4 NUCLEAR CARDIOLOGY, Barry L. Zaret | 207 |
| r , | | | 40 | William H. Barry | 211 |
| | PREVENTIVE MEDICINE | | 43 44 | | 215 236 |
| 10 | PRINCIPLES OF PREVENTIVE MEDICINE, Stephen B. Hulley | 35 | 45 | | 250 |
| | TOBACCO AND HEALTH, David M. Burns | 36 | 46 | SUDDEN CARDIAC DEATH, James T. Willerson | 274 |
| 12 | Stephen B. Hulley | 40 | 47 48 | ARTERIAL HYPERTENSION, Suzanne Oparil | 276 |
| 13 | THE JUDICIOUS DIET, John P. Kane | 42 | | | 293 303 |
| | EXERCISE AND HEALTH, William L. Haskell | 45 | 50 | ATHEROSCLEROSIS, Russell Ross | 318 |
| 15 | ALCOHOL ABUSE AND ALCOHOL-RELATED ILLNESSES, Benjamin Kissin | 48 | 51 | DISORDERS OF CORONARY ARTERIES | 323 |
| 16 | DRUG ABUSE AND DEPENDENCE, Charles P. O'Brien | 52 | | | 323 |
| 17 | IMMUNIZATION, R. Gordon Douglas, Jr | 61 | | 51.3 SURGICAL TREATMENT OF CORONARY ARTERY DISEASE, | 329 |
| 18 | THE PREVENTIVE HEALTH EXAMINATION, Gary D. Friedman | 66 | | David C. Sabiston, Ir | 337 |
| | THE HEALTH OF THE PHYSICIAN, Linda Hawes Clever | 67 | 52 53 | DISEASES OF THE MYOCARDIUM, Joseph K. Perloff and | 340 |
| PA | ART IV PRINCIPLES OF DIAGNOSIS AND | | 54 | | 352 |
| | MANAGEMENT | | 55 | MISCELLANEOUS CONDITIONS OF THE HEART: TUMOR, TRAUMA, | 362 367 |
| | CLINICAL APPROACH TO THE PATIENT, William L. Morgan, Jr | 70 74 | 56 | DISEASES OF THE AORTA, Lawrence S. Cohen | 370 |
| | CLINICAL DECISION MAKING, Stephen G. Pauker THE USE AND INTERPRETATION OF LABORATORY-DERIVED DATA, | 74 | 57 | | 375 |
| 23 | James B. Wyngaarden OVERVIEW OF IMAGING TECHNIQUES AND PROJECTION FOR THE FUTURE, | 79 | | ART VII DECRIPATORY BIOTAGES | |
| 25 | Alexander R. Margulis | 82 | P | ART VII RESPIRATORY DISEASES | |
| | PRINCIPLES OF DRUG THERAPY, Alan S. Nies | 87 | 58 | | 390 |
| 25 26 | INTERACTIONS BETWEEN DRUGS, Alan S. Nies ADVERSE REACTIONS TO DRUGS, Alan S. Nies | 98 102 | 59 | RESPIRATORY STRUCTURE AND FUNCTION, John F. Murray 3 | 395 |
| 20 | PAIN AND ITS MANAGEMENT, Kathleen M. Foley and | 102 | 60 61 | | 403 410 |
| 21 | | | | DINORIO DIRTIDIO DIGENOLO, INCIMIN IL IVININI | |
| | Jerome B. Posner | 104 | 62 | ABNORMALITIES OF LUNG AERATION, Richard A. Matthay 4 | 419 |
| 28 | Jerome B. Posner ANTIMICROBIAL THERAPY, Lowell S. Young | 112 | 63 | ABNORMALITIES OF LUNG AERATION, Richard A. Matthay | 419 421 |
| 28 29 | Jerome B. Posner ANTIMICROBIAL THERAPY, Lowell S. Young ANTIVIRAL THERAPY, David W. Barry | 112 124 | 63 64 | ABNORMALITIES OF LUNG AERATION, Richard A. Matthay 4 INTERSTITIAL LUNG DISEASE, Ronald G. Crystal 4 LUNG ABSCESS, John G. Bartlett 4 | 421 435 |
| 28 29 30 | Jerome B. Posner ANTIMICROBIAL THERAPY, Lowell S. Young | 112 | 63 64 65 | ABNORMALITIES OF LUNG AERATION, Richard A. Matthay INTERSTITIAL LUNG DISEASE, Ronald G. Crystal LUNG ABSCESS, John G. Bartlett BRONCHIECTASIS, Christopher J. L. Newth | 421 435 438 |
| 28 29 30 31 | Jerome B. Posner ANTIMICROBIAL THERAPY, Lowell S. Young ANTIVIRAL THERAPY, David W. Barry GLUCOCORTICOSTEROID THERAPY, Anthony S. Fauci PHARMACOLOGIC PRINCIPLES RELATED TO THE AUTONOMIC NERVOUS SYSTEM, Robert J. Lefkowitz | 112 124 128 133 | 63 64 | ABNORMALITIES OF LUNG AERATION, Richard A. Matthay INTERSTITIAL LUNG DISEASE, Ronald G. Crystal LUNG ABSCESS, John G. Bartlett BRONCHIECTASIS, Christopher J. L. Newth CYSTIC FIBROSIS, Christopher J. L. Newth | 421 435 |
| 28 29 30 31 | Jerome B. Posner ANTIMICROBIAL THERAPY, Lowell S. Young ANTIVIRAL THERAPY, David W. Barry GLUCOCORTICOSTEROID THERAPY, Anthony S. Fauci PHARMACOLOGIC PRINCIPLES RELATED TO THE AUTONOMIC NERVOUS | 112 124 128 | 63 64 65 66 67 68 | ABNORMALITIES OF LUNG AERATION, Richard A. Matthay INTERSTITIAL LUNG DISEASE, Ronald G. Crystal LUNG ABSCESS, John G. Bartlett BRONCHIECTASIS, Christopher J. L. Newth CYSTIC FIBROSIS, Christopher J. L. Newth PULMONARY EMBOLISM, Robert M. Senior FAT EMBOLISM SYNDROME, Robert M. Senior 4 | 421 435 438 440 442 450 |
| 28 29 30 31 | Jerome B. Posner ANTIMICROBIAL THERAPY, Lowell S. Young ANTIVIRAL THERAPY, David W. Barry GLUCOCORTICOSTEROID THERAPY, Anthony S. Fauci PHARMACOLOGIC PRINCIPLES RELATED TO THE AUTONOMIC NERVOUS SYSTEM, Robert J. Lefkowitz COMMON POISONINGS, William O. Robertson | 112 124 128 133 140 | 63 64 65 66 67 68 69 | ABNORMALITIES OF LUNG AERATION, Richard A. Matthay INTERSTITIAL LUNG DISEASE, Ronald G. Crystal LUNG ABSCESS, John G. Bartlett BRONCHIECTASIS, Christopher J. L. Newth CYSTIC FIBROSIS, Christopher J. L. Newth PULMONARY EMBOLISM, Robert M. Senior FAT EMBOLISM SYNDROME, Robert M. Senior 4 SARCOIDOSIS, Barry L. Fanburg 4 | 421 435 438 440 442 450 451 |
| 28 29 30 31 | Jerome B. Posner ANTIMICROBIAL THERAPY, Lowell S. Young ANTIVIRAL THERAPY, David W. Barry GLUCOCORTICOSTEROID THERAPY, Anthony S. Fauci PHARMACOLOGIC PRINCIPLES RELATED TO THE AUTONOMIC NERVOUS SYSTEM, Robert J. Lefkowitz | 112 124 128 133 140 | 63 64 65 66 67 68 69 70 | ABNORMALITIES OF LUNG AERATION, Richard A. Matthay INTERSTITIAL LUNG DISEASE, Ronald G. Crystal LUNG ABSCESS, John G. Bartlett BRONCHIECTASIS, Christopher J. L. Newth 4 CYSTIC FIBROSIS, Christopher J. L. Newth 9 PULMONARY EMBOLISM, Robert M. Senior FAT EMBOLISM SYNDROME, Robert M. Senior SARGOIDOSIS, Barry L. Fanburg 9 PULMONARY NEOPLÄSMS, Charles H. Scoggin 4 | 421 435 438 440 442 450 |
| 28 29 30 31 32 PA 33 | Jerome B. Posner ANTIMICROBIAL THERAPY, Lowell S. Young ANTIVIRAL THERAPY, David W. Barry GLUCOCORTICOSTEROID THERAPY, Anthony S. Fauci PHARMACOLOGIC PRINCIPLES RELATED TO THE AUTONOMIC NERVOUS SYSTEM, Robert J. Lefkowitz COMMON POISONINGS, William O. Robertson RT V PRINCIPLES OF HUMAN GENETIC HUMAN HEREDITY, James B. Wyngaarden | 112 124 128 133 140 | 63 64 65 66 67 68 69 70 | ABNORMALITIES OF LUNG AERATION, Richard A. Matthay INTERSTITIAL LUNG DISEASE, Ronald G. Crystal LUNG ABSCESS, John G. Bartlett BRONCHIECTASIS, Christopher J. L. Newth CYSTIC FIBROSIS, Christopher J. L. Newth 4 PULMONARY EMBOLISM, Robert M. Senior FAT EMBOLISM SYNDROME, Robert M. Senior SARCOIDOSIS, Barry L. Fanburg PULMONARY NEOPLASMS, Charles H. Scoggin DISEASES OF THE PLEURA, MEDIASTINUM, DIAPHRAGM, AND CHEST WALL, Jerome S. Brody 4 | 421 435 438 440 442 450 451 |
| 28 29 30 31 32 PA 33 | Jerome B. Posner ANTIMICROBIAL THERAPY, Lowell S. Young ANTIVIRAL THERAPY, David W. Barry GLUCOCORTICOSTEROID THERAPY, Anthony S. Fauci PHARMACOLOGIC PRINCIPLES RELATED TO THE AUTONOMIC NERVOUS SYSTEM, Robert J. Lefkowitz COMMON POISONINGS, William O. Robertson RT V PRINCIPLES OF HUMAN GENETIC | 112 124 128 133 140 | 63 64 65 66 67 68 69 70 | ABNORMALITIES OF LUNG AERATION, Richard A. Matthay INTERSTITIAL LUNG DISEASE, Ronald G. Crystal LUNG ABSCESS, John G. Bartlett BRONCHIECTASIS, Christopher J. L. Newth CYSTIC FIBROSIS, Christopher J. L. Newth 4 CYSTIC FIBROSIS, Christopher J. L. Newth 9 PULMONARY EMBOLISM, Robert M. Senior FAT EMBOLISM SYNDROME, Robert M. Senior SARCOIDOSIS, Barry L. Fanburg 9 PULMONARY NEOPLASMS, Charles H. Scoggin DISEASES OF THE PLEURA, MEDIASTINUM, DIAPHRAGM, AND CHEST WALL, Jerome S. Brody 4 | 421 435 438 440 442 450 451 457 |

| DAI | RT VIII CRITICAL CARE MEDICINE | | 118 | BILIRUBIN METABOLISM AND HYPERBILIRUBINEMIA, | |
|------------|--|------------------------|------------|---|------------|
| PAI | RT VIII CRITICAL CARE MEDICINE | | | Bruce F. Scharschmidt | 81 |
| 73 | CRITICAL CARE MEDICINE, Philip C. Hopewell | 482 | 119 | | 814 |
| | | | | APPROACHES TO THE DIAGNOSIS OF JAUNDICE, Robert K. Ockner | 817 |
| ΡΔ | RT IX RENAL DISEASES | | 121 | | 818 |
| | | | 123 | TOXIC AND DRUG-INDUCED LIVER DISEASE, Robert K. Ockner CHRONIC HEPATITIS, Robert K. Ockner | 826 830 |
| 74 | APPROACH TO THE PATIENT WITH RENAL DISEASE, | | 124 | | 030 |
| | Thomas E. Andreoli | 502 | | Bruce F. Scharschmidt | 834 |
| | STRUCTURE AND FUNCTION OF THE KIDNEYS, Saulo Klahr INVESTIGATIONS OF RENAL FUNCTION, Vincent W. Dennis | 508 520 | 125 | INHERITED, INFILTRATIVE, AND METABOLIC DISORDERS INVOLVING | |
| | DISORDERS OF FLUID VOLUME, ELECTROLYTES, AND ACID-BASE BALANCE, | 320 | | THE LIVER, Bruce F. Scharschmidt | 838 |
| •• | Thomas E. Andreoli | 528 | | CIRRHOSIS OF THE LIVER, Thomas D. Boyer | 842 |
| 78 | ACUTE RENAL FAILURE, Jared S. Grantham | 558 | | MAJOR SEQUELAE OF CIRRHOSIS, Thomas D. Boyer | 847 |
| 79 | CHRONIC RENAL FAILURÉ, Juha Kokko | 563 | 120 | ACUTE AND CHRONIC HEPATIC FAILURE AND HEPATIC TRANSPLANTATION, Bruce F. Scharschmidt | 852 |
| 80 | TREATMENT OF IRREVERSIBLE RENAL FAILURE | 573 | 129 | | 856 |
| | 80.1 DIALYSIS, Robert G. Luke | 573 577 | 130 | DISEASES OF THE GALLBLADDER AND BILE DUCTS, Peter F. Malet and | |
| 81 | at an annual transport to the state of the s | 582 | | Roger D. Soloway | 859 |
| 82 | TUBULOINTERSTITIAL DISEASES AND TOXIC NEPHROPATHIES, | 30 <u>L</u> | | | |
| - | T. Dwight McKinney | 602 | DΛ | RT XII HEMATOLOGIC DISEASES | |
| 83 | OBSTRUCTIVE NEPHROPATHY, Floyd C. Rector, Jr | 614 | FA | RT XII HEMATOLOGIC DISEASES | |
| 84 | | 617 | 131 | INTRODUCTION, David G. Nathan | 873 |
| 85 | | 624 | | INTRODUCTION TO THE ANEMIAS, Alan S. Keitt | 878 |
| 86 | URINARY TRACT INFECTIONS AND PYELONEPHRITIS, | 628 | | ANEMIA DUE TO BONE MARROW FAILURE, Alan S. Keitt | 884 |
| 87 | Vincent T. Andriole | 632 | | NORMOCHROMIC NORMOCYTIC ANEMIAS, James P. Kushner | 890 |
| 88 | RENAL DISEASE IN PREGNANCY, John P. Hayslett | 634 | | HYPOCHROMIC ANEMIAS, James P. Kushner | 892 |
| 89 | HEREDITARY CHRONIC NEPHROPATHIES, Wadi N. Suki | 637 | | MEGALOBLASTIC ANEMIAS, William S. Beck HEMOLYTIC DISORDERS: INTRODUCTION, Manuel E. Kaplan | 900 |
| 90 | RENAL CALCULI, Charles Y. C. Pak | 638 | 137 | HEREDITARY DEFECTS IN THE MEMBRANE OR METABOLISM | 907 |
| | | 644 | 100 | OF THE RED CELL, Samuel E. Lux | 909 |
| 92 | | 648 | 139 | ACQUIRED HEMOLYTIC DISORDERS, Manuel E. Kaplan | 917 |
| 93 | TUMORS OF THE KIDNEY, URETER, AND BLADDER, Richard D. Williams | 650 | | HEMOGLOBIN STRUCTURE AND FUNCTION, Alan N. Schechter | 925 |
| | Richard D. Williams | 030 | | HEMOGLOBIN SYNTHESIS, Arthur W. Nienhuis | 927 |
| D. A. | DT V OACTDOINTECTINAL DICEACEC | | 142 | THE THALASSEMIAS, Arthur W. Nienhuis | 930 |
| PA | RT X GASTROINTESTINAL DISEASES | | 143 | SICKLE CELL ANEMIA AND ASSOCIATED HEMOGLOBINOPATHIES, Bernard G. Forget | 936 |
| 94 | INTRODUCTION, Marvin H. Sleisenger | 656 | 144 | UNSTABLE HEMOGLOBINS, Ronald F. Rieder | 942 |
| 95 | DIAGNOSTIC IMAGING PROCEDURES IN GASTROENTEROLOGY, | | | ABNORMAL HEMOGLOBINS WITH ALTERED OXYGEN AFFINITY, | |
| | Susan D. Wall | 662 | | Ronald F. Rieder | 943 |
| | GASTROINTESTINAL ENDOSCOPY, Jack A. Vennes | 668 | 146 | ···-···-······························ | |
| | ORAL MEDICINE, Sol Silverman, Jr | 674 679 | | Ronald F. Rieder | 945 |
| | GASTRITIS, Charles T. Richardson | 689 | | BLOOD TRANSFUSION, Herbert A. Perkins | 947 |
| | PEPTIC ULCER | 692 | 140 | Bernard M. Babior | 951 |
| | 100.1 PATHOGENESIS, Charles T. Richardson | 692 | 149 | DISORDERS OF NEUTROPHIL FUNCTION, Bernard M. Babior | 957 |
| | 100.2 EPIDEMIOLOGY, CLINICAL MANIFESTATIONS, AND DIAGNOSIS, | | 150 | LEUKOPENIA, Grover C. Bagby, Ir | 961 |
| | Lawrence R. Schiller | 696 700 | 151 | LEUKOCYTOSIS AND LEUKEMOID REACTIONS, Grover C. Bagby, Jr | 967 |
| | 100.3 MEDICAL THERAPY, Walter L. Peterson | 700 703 | 152 | CLONAL DEVELOPMENT AND STEM CELL ORIGIN OF PROLIFERATIVE | 070 |
| | 100.5 COMPLICATIONS, Mark Feldman | 706 | 152 | DISORDERS, Philip J. Fialkow | 973 975 |
| | 100.6 ZOLLINGER-ELLISON SYNDROME, Charles T. Richardson | 708 | 153 154 | MYELOPROLIFERATIVE DISORDERS, Paul D. Berk | 984 |
| 101 | NEOPLASMS OF THE STOMACH, Sidney J. Winawer | 709 | 155 | THE CHRONIC LEUKEMIAS, Bayard Clarkson | 988 |
| 102 | DISORDERS OF GASTROINTESTINAL MOTILITY, Sidney Phillips | 714 | | | 1001 |
| 103 | DIARRHEA, Guenter J. Krejs | 725 | 157 | INTRODUCTION TO NEOPLASMS OF THE IMMUNE SYSTEM, | |
| 104 | MALABSORPTION, Phillip P. Toskes | 732 745 | | | 1007 |
| 105 | INFLAMMATORY BOWEL DISEASES | 745 745 | 158 | | 1009 |
| | 105.2 CROHN'S DISEASE, Irwin H. Rosenberg | 745 | 159 | | 1013 |
| | 105.3 ULCERATIVE COLITIS, Bernard Levin | 753 | 161 | LANGERHANS CELL (EOSINOPHILIC) GRANULOMATOSIS, | 1017 |
| 106 | VASCULAR DISEASES OF THE INTESTINE, James H. Grendell | 760 | , | Jerome E. Groopman | 1022 |
| 107 | NEOPLASMS OF THE LARGE AND SMALL INTESTINE, | 700 | 162 | EOSINOPHILIC SYNDROMES, David A. Bass | 1024 |
| 400 | Sidney J. Winawer | 766 774 | 163 | | 1026 |
| 108 | PANCREÄTITIS, Michael D. Levitt | 77 4 781 | 164 | | 1036 |
| 110 | FOOD POISONING, David F. Altman | 784 | 165 | BONE MARROW TRANSPLANTATION, Rainer Storb HEMORRHAGIC DISORDERS: ABNORMALITIES OF PLATELET AND VASCULAR | 1040 |
| 111 | | 787 | 100 | | 1042 |
| 112 | DISEASES OF THE PERITONEUM, Michael D. Bender | 790 | 167 | DISORDERS OF BLOOD COAGULATION, Deane F. Mosher | 1060 |
| 113 | DISEASES OF THE MESENTERY AND OMENTUM, Michael D. Bender | 795 | | • | |
| 114 | GASTROINTESTINAL HEMORRHAGE, Walter L. Peterson | 796 | D.A | DT VIII ONCOLOCY | |
| 115 | MISCELLANEOUS INFLAMMATORY DISEASES OF THE INTESTINE, | 800 | ra | RT XIII ONCOLOGY | |
| | Marvin H. Sleisenger | 000 | 168 | INTRODUCTION, John Laszlo | 1082 |
| | DT VI DIOPAGES OF THE LIVED | | 169 | ONCOGENES, J. Michael Bishop | 1089 |
| ۲A | RT XI DISEASES OF THE LIVER, | | 170 | EPIDEMIOLOGY OF CANCER, Joseph F. Fraumeni, Jr. | 1092 |
| | GALLBLADDER, AND BILE DUCTS | | 171 | PARANEOPLASTIC SYNDROMES, Paul A. Bunn, Jr. | |
| 110 | CLINICAL APPROACH TO LIVER DISEASE, Robert K. Ockner | 808 | 172 | TUMOR MARKERS, Paul A. Bunn, Jr | 1099 |
| 116 117 | HEPATIC METABOLISM IN LIVER DISEASE, Robert K. Ockner | 809 | 173 | PRODUCTION, William D. Odell | 1100 |
| | the state of the s | | | | |

| 174 | NONETASTATIC EFFECTS OF CANCER ON THE NERVOUS SYSTEM, | | P | ART XV | /1 | ENDOCR | RINE AL | ND REPRO | DUCT | VF |
|----------------|--|--------------|------------------|------------------------------|---------------------------|---|-------------------------|-------------------------------|---------------------------------------|--------------|
| 175 | Jenne B. Posner CUTÆOUS MANIFESTATIONS OF INTERNAL MALIGNANCY, Frik Parker | | | | | DISEASI | ES | | | |
| 176 | PRINPLES OF CANCER THERAPY, Bruce A. Chabner | . 1113 | 221 222 | Z THE ENDOR | RPHIN | FAMILY OF OPE | OID PEPTIDE: | Baxter S: BIOCHEMISTRY, | ANATOMY. | |
| PΑ | RT(IV METABOLIC DISEASES | | 223 224 | I PROSTAGLI I NATRIURET | ANDIN TIC FAI | S AND RELATED CTORS, Philip | COMPOUND: Needlemar | S , Garret A. Fit. | zGerald . | 1271 |
| 177 | INTDUCTION, James B. Wyngaarden | 1120 | 225 | NEUROEND | JOCRIN | E REGULATION | AND ITS DISI | ORDERS. | | |
| | ords of Carbohydrate Metabolism | . 1100 | 226 | THE ANTER | RIOR PI | . Fronman ITUITARY. I aw | rence A F | rohman | • • • • • • • • | 1280 |
| | GALTOSEMIA, Stanton Segal | 1121 | 227 | THE POSTE | ERIOR I | PITUITARY, The | omas E. Ai | ndreoli | | 1305 |
| 179 180 | THRYCOGEN STORAGE DISEASES, R. Rodney Howell PEBSURIA (ESSENTIAL PENTOSURIA), R. Rodney Howell | . 1133 | 228 | THE PINEAL | IL, Sey DID, P. | mour Reichli Reed Larser | in 1 | | · · · · · · · · · · | 1313 |
| | ES#TIAL FRUCTOSURIA AND HEREDITARY FRUCTOSE INTOLERANCE, 1Rodney Howell | . 1135 | | 230.1 ST | TRUCTL | JRE AND DEVEL | OPMENT OF 1 | HE ADRENAL CORT | EX. | |
| | PRARY HYPEROXALURIA, Lloyd H. Smith, Jr. | 1136 | | 230.2 SÝ | YNTHES | SIS, CIRCULATION | DN, AND MET | ABOLISM OF ADREN | VAL | 1340 |
| | ords of Lipoprotein Metabolism | | | ST | FEROID: | S, John D. Bi | axter | | | 1341 |
| 184 | THYPERLIPOPROTEINEMIAS, John D. Brunzell FAY'S DISEASE (GLYCOSPHINGOLIPIDOSIS), nes B. Wyngaarden | | | J | John I | ION OF ADRENA D. Baxter OF ADDENAL ST | | RODUCTION, n D. Baxter | | 1344 |
| 185 | GHER'S DISEASE, Edwin H. Kolodny | 1145 | | 230.5 LA | BORAT | ORY EVALUATIO |)N OF ADREN | DCORTICAL FUNCTI | ON. | |
| | NANN-PICK DISEASE, Edwin H. Kolodny | 1147 | | 230.6 ADI | j. Biai I renoc | KE 1 <i>YTTELL</i> . ORTICAL HYPNI | | hn D. Baxter . | • • • • • • • | 1348 |
| | PRINTED OF AMINO ACID METABOLISM | | | 230./ (0: | ishing | 'S SYNDKOME. | I. Blake Tı | irrell | | 1353 |
| 187 | HERAMINOACIDURIA (WITH A CLASSIFICATION OF THE INBORN ADEVELOPMENTAL ERRORS OF AMINO ACID METABOLISM), | | 221 | 230.8 MIN | NERALI | UCORTICOID EX | CESS STATES | John D. Baxte | r | 1358 |
| | harles R. Scriver | 1149 | 231 232 | HANGI ACE | MIC DI | US, jerrold M ISORDERS F 1 | . Olefsky Iohn Samio | e | • • • • • • • • | 1360 |
| 188 | THYPERPHENYLALANINEMIAS, Lloyd H. Smith, Jr. | 1155 | 233 | PANUKEATIU | C ISLEI | I CELL TUMORS | i. Carl Gru | nfeld | | 1381 |
| 189 | APTONURIA, James B. Wyngaarden IIDINEMIA, Lloyd H. Smith, Jr. | 1157 | 234 | DIZOKDEKZ | UF SEX | KUAL DIFFEREN | TIATION, | | | |
| 191 | HYPERPROLINEMIAS AND HYDROXYPROLINEMIA, | 1157 | 235 | Julianne | Impe | erato-McGinl | ley | | · · · · · · · · · | 1390 |
| | 'oyd H. Smith, Jr | 1158 | 236 | DISEASES OF | F THE | n IVI. IVIAESUI PROSTATE. Pai | moto trick C W | ılsh | • • • • • • • • | 1404 |
| 192 | | 1158 | 237 | THE UVARIES | 5 , Rot | bert W. Reba | r | | | 1425 |
| 194 | NCHED-CHAIN AMINOACIDURIA, Lloyd H. Smith, Jr. IOCYSTINURIA, S. Harvey Mudd | 1159 | 238 | nikouliom, | , D. L | ynn Loriaux | | | | 1446 |
| | ors of Purine and Pyrimidine Metabolism | 1100 | 239 240 | RREAST CAN | IANI UI VCFR 7 | SEASES OF THE | BREAST, G | eorge Tolis | · · <i>·</i> · · · · · | 1449 |
| | I, James B. Wyngaarden | 4404 | 241 | POLYGLANDU | ULAR D | ISORDERS. Ich | n N. Loeb | | | 1452 1458 |
| 196 | ER DISORDERS OF PURINE METABOLISM, Edward W. Holmes | 1170 | 242 | THE AURENA | AL MED | ULLA AND THE | Sympatheti | C NERVOUS SYSTE | M. | |
| | JRDERS OF PYRIMIDINE METABOLISM, Lloyd H. Smith, Jr | 1173 | 243 | THE CARCING | OID SY | NDROME, Phili | ip E. Cryei | ` | | 1467 |
| 198 | | 1174 | | NT W | | | | | | |
| 199 200 | MARFAN SYNDROME, Peter H. Byers | 1177 1178 | PA | RT XVII | | | | ONE AND ABOLISM | BONE | |
| 201 | EOGENESIS IMPERFECTA, David W. Rowe | 1180 | 244 | MINERAL AND | | | | Arnaud | | 4.400 |
| | UDOXANTHOMA ELASTICUM, Jouni Uitto | 1181 | 240 | VIIAMIN U. L | Daniel | l D. Bikle | | | | 1177 |
| | ers of Porphyrins or Metals | | 240 | 09 I EUMALAU | HA ANL | J RICKETS. Dat | niel D. Bik | ·le | | 1479 |
| 203 | PHYRIA, D. Montgomery Bissell TALASIA, James B. Wyngaarden | 1182 | 247 | INE PAKAINY | ן עוטאז | GLANDS, HYPER | ICALCEMIA. / | IND HYPOCALCEMI | A . | |
| 205 | SON'S DISEASE, Andrew Deiss | 1188 | 248 | THE ULTIMOB | J. ZATY. Branch | MAL CELLS AND | CALCITONIN | , Claude D. Arı | · · · · · · · · | 1486 |
| 206 | NOCHROMATOSIS (IRON STORAGE DISEASE), Arno G. Motulsky | 1189 | 249 | KENAL USTEU | JUYSIR | OPHY, Eduard | to Slatonol: | sku | | 1507 |
| 207 | SPHORUS DEFICIENCY AND HYPOPHOSPHATEMIA, | | 230 | 02 FOLOKO21 | 15, B. | Lawrence Ri | QQS | | | 1510 |
| 208 | loyd H. Smith, Jr DRDERS OF MAGNESIUM METABOLISM, Lloyd H. Smith, Jr | 1193 | 251 | Frederick | R Si | F BONE (OSTEIT | IS DEFORMAI | VS), | | |
| Oth | ereditary Disorders | | 252 | 09 I Eの4をPがり2 | 313, US | I EUSCLEKUSIS | . AND OTHER | DISORDERS OF BO | NE. | |
| 209 I 210 : | ILIAL MEDITERRANEAN FEVER, Daniel G. Wright AMYLOID DISEASES, Joel N. Buxbaum | 1196 | 253 | BONE TUMORS | S , Her | iry J. Manki | n | | · · · · · · · · · · · · · · · · · · · | 1517 1521 |
| 211 (| DITARY SYNDROMES INVOLVING MULTIPLE ORGAN SYSTEMS. | | | | | | | | | |
| 1 | rno G. Motulsky | 1202 | PAR | RT XVIII | l i | NFECTION | DUS DI | SEASES | | |
| | | | Section | on 1 Introd | ductio | nn | | | | |
| PΓ | XV NUTRITIONAL DISEASES | | | | | | ISES. Charl | es C. J. Carpeni | for 1 | 523 |
| | | | 255 1 | HE FEBRILE P | PATIEN | I , Sheldon M | . Wolff | | 1 | 524 |
| 21211 213TI | RIENT REQUIREMENTS, Robert M. Russell RITIONAL ASSESSMENT, Robert M. Russell | 1204 | 256 P | PATHOGENESIS | S OF FE | VER, Charles | A. Dinare | llo | 1 | 525 |
| 21401 | EIN-CALORIE UNDERNUTRITION, Robert B. Baron | 1212 | 257 T 258 T | HE COMPROM | iaat Ki IISFN H | torunst, Cha: IOST. Richard | ries A. Dir K. Root | arello | 1 | 527 520 |
| 215E | EATING DISORDERS, Douglas A. Drossman | 1215 | 259 S | HOCK SYNDRO | OMES (| RELATED TO SEI | PSIS , Iohn 1 | V. Sheagren | 1 1 | 538 |
| ∠16E\$ 2170 | ITY, F. Xavier Pi-Sunyer RDERS OF VITAMIN METABOLISM: DEFICIENCIES, METABOLIC | 1219 | 260 P | REVENTION A | IND TR | EATMENT OF HO | ISPITAL-ACQU | JIRED INFECTIONS | | |
| :NC | RMALITIES, AND EXCESSES, Richard S. Rivlin JRBANCES OF TRACE MINERAL METABOLISM, | 1228 | 261 A | Richard P. DVICE TO TRA | . Wen WELER | s, Jeffrey A. | | | 1 1 | 541 549 |
| Cl | ifford Tasman-Iones | 1241 | Sectio | n 2 Bacter | | | | | | |
| ZIMI Do | ÍPLES OF NUTRITIONAL SUPPORT: ENTERAL NUTRITIONAL THERAPY, wid H. Alpers | 1243 | Pneun | | 70 | PINAMA | | | | |
| 22IRE | NTERAL NUTRITION, Ray E. Clouse | 1243 | 262 IN 263 Pi | I I RUDUCTION Neumococcai | TO PN LL PNEL | EUMONIA, Wai UMONIA, David | ldemar G. d T. Durac | Johanson, Jr k | | 551 554 |

| 264 | MYCOPLASMAL INFECTIONS, Stephen G. BaumPNEUMONIA CAUSED BY AEROBIC GRAM-NEGATIVE BACILLI, | 1561 | 314 RAT-BITE FEVERS, J. Bruce McClain 172 315 LEPTOSPIROSIS, J. Bruce McClain 173 |
|------------|---|--------------|---|
| | Waldemar G. Johanson, Ir. | 1565 | Diseases Caused by Chlamydiae, Walter E. Stamm |
| 266 | RECURRENT ASPIRATION PNEUMONIA, Waldemar G. Johanson, Jr | 1568 | 316 INTRODUCTION 173 |
| 267 | LEGIONELLOSIS, David W. Fraser | 1570 | 317 TRACHOMA 173 |
| Stre | otococcal Diseases | | 318 NFONATAL CHLAMYDIAL INFECTIONS |
| 268 | STREPTOCOCCAL DISEASES, Richard M. Krause | 1572 1580 | 319 PSITTACOSIS AND RELATED INFECTIONS |
| | | | 320 INTRODUCTION, Richard B. Hornick |
| :nac | ocarditis INFECTIVE ENDOCARDITIS, David T. Durack | 1586 | 321 THE TYPHUS GROUP, Richard B. Hornick |
| | | ,000 | 322 ROCKY MOUNTAIN SPOTTED FEVER, Richard B. Hornick 174 |
| | hylococcal Infections | 4500 | 323 OTHER TICK-BORNE RICKETTSIOSES, Richard B. Hornick 174 |
| | STAPHYLOCOCCAL INFECTIONS, John N. Sheagren | 1596 | 324 RICKETTSIALPOX, Richard B. Hornick 174 325 SCRUB TYPHUS, Richard B. Hornick 174 |
| Bact | erial Meningitis, Morton N. Swartz | | 325 SCRUB TYPHUS, Richard B. Hornick |
| 272 | BACTERIAL MENINGITIS | 1604 | 327 Q FEVER, Theodore C. Eickhoff |
| 273 | MENINGOCOCCAL DISEASE | 1611 | |
| | INFECTIONS CAUSED BY HEMOPHILUS SPECIES | 1017 | Section 3 Viral Diseases |
| Oste | omyelitis | | 328 INTRODUCTION TO VIRAL DISEASES, R. Gordon Douglas, Jr 1750 |
| 275 | OSTEOMYELITIS, Francis A. Waldvogel | 1622 | Viral Infections of the Respiratory Tract |
| Who | oping Cough | | 329 THE COMMON COLD. Albert Z. Kapikian |
| 276 | WHOOPING COUGH (PERTUSSIS), Samuel L. Katz | 1624 | 330 VIRAL PHARYNGITIS, LARYNGITIS, CROUP, AND BRONCHITIS, |
| | ntheria | | Maurice A. Mufson |
| 977 977 | DIPHTHERIA, Erik L. Hewlett | 1626 | 331 RESPIRATORY SYNCYTIAL VIRUS, Robert M. Chanock |
| | | | 332 PARAINFLUENZA VIRAL DISEASES, Robert M. Chanock 1760 333 INFLUENZA, R. Gordon Douglas, Jr. 1762 |
| | tridial Diseases, John G. Bartlett CLOSTRIDIAL MYONECROSIS AND OTHER CLOSTRIDIAL DISEASES | 1629 | 334 ADENOVIRUS DISEASES, Stephen G. Baum |
| 2/8 270 | PSEUDOMEMBRANOUS COLITIS | 1632 | Viral Disease of the Gastrointestinal Tract |
| 280 | BOTULISM | 1633 | 335 VIRAL GASTROENTERITIS, Albert Z. Kapikian |
| 281 | TETANUS | 1634 | |
| Ana | erobic Bacteria | | Viral Infections Caused by Cutaneous Lesions |
| | DISEASES CAUSED BY NON-SPORE-FORMING ANAEROBIC BACTERIA, | | 336 MEASLES (MORBILLI, RUBEOLA), Samuel L. Katz |
| | Sherwood L. Gorbach | 1637 | 338 FOOT AND MOUTH DISFASE. Catherine M. Wilfert |
| Ente | eric Infections | | 339 MUMPS, Catherine M. Wilfert |
| | TYPHOID FEVER, Thomas Butler | 1641 | Diseases Characterized by Herpes-Type Viruses |
| 284 | SALMONFILA INFECTIONS OTHER THAN TYPHOID FEVER. | | 340 HERPES SIMPLEX VIRUS INFECTIONS, R. Gordon Douglas, Jr 1780 |
| | Richard B. Hornick | 1643 | 341 CYTOMEGALOVIRUS INFECTION. David I. Lang 1784 |
| 285 | SHIGELLOSIS, Thomas Butler | 1648 | 342 INFECTIOUS MONONUCLEOSIS: EPSTEIN-BARR VIRUS INFECTION, |
| 286 | CAMPYLOBACTER ENTERITIS, Richard L. Guerrant CHOLERA (ASIATIC CHOLERA), Nathaniel F. Pierce | 1651 | Elliott Kieff |
| 288 | ENTERIC <i>ESCHERICHIA COLI</i> INFECTIONS. | | 343 VARICELLA, Philip A. Brunell |
| | Richard L. Guerrant | 1653 | |
| 289 | THE DIARRHEA OF TRAVELERS, R. Bradley Sack | 1656 | Diseases Caused by Retroviruses |
| | er Bacterial Infections | | 345 RETROVIRUSES THAT CAUSE HUMAN DISEASE, Robert C. Gallo 1794 346 THE ACQUIRED IMMUNODEFICIENCY SYNDROME, |
| 290 | EXTRAINTESTINAL INFECTIONS CAUSED BY ENTERIC BACTERIA, | | Jerome E. Groopman1799 |
| | Elizabeth I. Ziegler | 1658 | Enteroviral Diseases, Raphael Dolin |
| 291 | YERSINIA INFECTIONS, Thomas Butler TULAREMIA, Richard B. Hornick | 1661 1664 | 347 INTRODUCTION |
| 292 | ANTHRAX, Philip S. Brachman | 1667 | 240 EDIDEMIC PLEIDODVNIA |
| 293 294 | DISFASES CAUSED BY PSEUDOMONADS, Michael Barza | 1669 | 349 MYGCARDITIS AND PERICARDITIS CAUSED BY ENTEROVIRUSES 1811 |
| 295 | IISTERIOSIS Michael Barza | 16/0 | 250 MILCOCUTANFOLIS INFECTIONS CAUSED BY ENTEROVIRUSES1813 |
| 296 | FRYSIPFI DID. Michael Barza | 16/3 | 351 ACUTE HEMORRHAGIC CONJUNCTIVITIS |
| 297 | ACTINOMYCOSIS, David J. Drutz | 1675 | Arthropod-Borne Viral Fevers |
| 298 299 | | 1676 | 352 INTRODUCTION, Robert E. Shope |
| 300 | CAT SCRATCH DISFASE, Andrew M. Margileth | 1679 | Undifferentiated Fevers |
| 301 | BARTONELLOSIS, Theodore C. Eickhoff | 1681 | 353 DENGUE, Robert B. Tesh |
| Dis | eases Due to Mycobacteria | | 354 WEST NILE FEVER, Robert B. Tesh |
| 302 | TURFRCUI OSIS. Emanuel Wolinsky | 1682 | 355 PHLEBOTOMUS FEVER, Robert B. Tesh |
| 303 | OTHER MYCOBACTERIOSES. Emanuel Wolinsky | 1693 | 356 RIFT VALLEY FEVER, Robert B. Tesh |
| 304 | | 1696 | MAYARO, ROSS RIVER, AND OCKELBO, Robert B. Tesh1819 |
| Sex | ually Transmitted Diseases, P. Frederick Sparling | | 358 COLORADO TICK FEVER, Theodore C. Eickhoff |
| 305 | INTRODUCTION AND COMMON SYNDROMES | 1701 | Encephalitides |
| 306 | CONDCOCCAL INFECTIONS | 1706 | 359 ARTHROPOD-BORNE VIRAL ENCEPHALITIDES, Thomas P. Monath 821 |
| 307 | | 1710 | Viral Hemorrhagic Fevers, Robert E. Shope |
| 308 309 | CHANCROID | 1/12 | |
| 310 | SYPHILIS | 1713 | 360 INTRODUCTION |
| | rochetal Diseases Other Than Syphilis | | 362 HEMORRHAGIC FEVER CAUSED BY DENGUE VIRUSES |
| 311 | NONSYPHILITIC TREPONEMATOSES, Thomas Butler | 1723 | 363 TICK-BORNE FLAVIVIRUS DISEASES: KYASANUR FOREST DISEASE AND |
| 312 | RELAPSING FEVER, Thomas Butler | . 1/24 | OMSK HEMORRHAGIC FEVER833 |
| 212 | IVME DICEACE Stonbon F. Malarnista | 1726 | 364 CRIMEAN-CONGO HEMORRHAGIC FEVER |

| 458 | , | 2077 | Section 14 Injury to the Head and Spine, Donald P. Becker |
|--------------------|---|------|---|
| 459 | | | 496 HEAD INJURIES 2239 |
| 400 | Antonio R. Damasio | 2080 | 497 INJURIES TO THE SPINE 2244 |
| 460 | FOCAL DISTURBANCES OF HIGHER FUNCTION, Antonio R. Damasio | 2002 | Section 15 Mechanical Lesions of the Spine and Related |
| 461 | | 2003 | Structures, Jerome B. Posner |
| | PSYCHIATRIC DISORDERS IN MEDICAL PRACTICE, Gary J. Tucker | 2091 | 498 ANATOMY, PHYSIOLOGY, AND DIFFERENTIAL DIAGNOSIS 2247 |
| | ction 3 Pathophysiology and Management of Major | | 499 INTERVERTEBRAL DISC DISEASE |
| 300 | Neurologic Symptoms | | 500 NEOPLASMS OF THE SPINAL CANAL |
| 463 | | 2102 | 501 INFLAMMATORY DISEASES OF THE SPINAL CANAL |
| 464 | | | 502 VASCULAR DISORDERS OF THE SPINAL CANAL |
| 465 | | | 503 CONGENITAL ANOMALIES OF THE CRANIOVERTEBRAL JUNCTION, SPINE, |
| | 465.1 ASTHENIA, FATIGUE, AND WEAKNESS, Fred Plum | | AND SPINAL CORD 2257 |
| | 465.2 ATAXIA AND RELATED GAIT DISORDERS, Fred Plum | | Section 16 Diseases of the Peripheral Nervous System, |
| | 465.3 EPISODIC LOSS OF MOTOR FUNCTION, Jerome B. Posner | 2127 | Herbert H. Schaumburg |
| 466 | DISORDERS OF SENSATION, Jerome B. Posner | 2128 | 504 INTRODUCTION AND BASIC TERMINOLOGY |
| Sec | tion 4 Alcohol and Nutritional Complications | | 505 ANATOMIC CLASSIFICATION OF NEUROPATHY |
| 467 | NUTRITIONAL DISORDERS OF THE NERVOUS SYSTEM, Ivan Diamond | 2137 | 506 INFLAMMATORY POLYNEUROPATHY (GUILLAIN-BARRE SYNDROME AND RELATED DISORDERS) |
| Sec | tion 5 The Extrapyramidal Disorders, Stanley Fahn | | 507 NEUROPATHY ASSOCIATED WITH ENDOCRINE DISEASES |
| | PARKINSONISM | 2142 | 508 HEREDITARY NEUROPATHIES |
| 469 | ESSENTIAL TREMOR (FAMILIAL OR SENILE TREMOR) | 2143 | 509 TOXIC NEUROPATHIES |
| | THE CHOREAS | | 510 MISCELLANEOUS DISEASE-SPECIFIC NEUROPATHIES 2266 |
| 471 | THE DYSTONIAS | 2149 | 511 ACUTE PHYSICAL INJURY AND CHRONIC COMPRESSION-ENTRAPIENT |
| 472 | OTHER EXTRAPYRAMIDAL DISORDERS | 2151 | NEUROPATHIES 2267 |
| Sec | tion 6 Degenerative Diseases of the Nervous System, | | Section 17 Diseases of Muscle (Myopathies) and |
| • | Robert B. Layzer | | Neuromuscular Junction, Andrew G. Engel |
| 473 | HEREDITARY CEREBELLAR ATAXIAS AND RELATED DISORDERS | 2152 | 512 GENERAL APPROACH TO MUSCLE DISEASES |
| | HEREDITARY SPASTIC PARAPLEGIAS | | 513 MUSCULAR DYSTROPHIES 2272 |
| 475 | HEREDITARY AND ACQUIRED INTRINSIC MOTOR NEURON DISEASES | 2154 | 514 MORPHOLOGICALLY DISTINCT CONGENITAL MYOPATHIES 2275 |
| | SYRINGOMYELIA | | 515 INFLAMMATORY MYOPATHIES |
| 477 | THE PHAKOMATOSES | 2158 | 516 METABOLIC MYOPATHIES |
| Sec | tion 7 Cerebrovascular Diseases | | 518 DISORDERS OF NEUROMUSCULAR TRANSMISSION |
| 478 | INTRODUCTION, H. J. M. Barnett and Irene Meissner | 2159 | |
| 479 | | 2162 | PART XXIII EYE DISEASES, John W. Gittger, Jr. |
| | SPONTANEOUS INTRACRANIAL HEMORRHAGÉ, H. J. M. Barnett | 2173 | 519 TRANSIENT VISUAL LOSS |
| Sec | tion 8 Infectious and Inflammatory Disorders | | 520 CATARACT 2289 |
| | of the Nervous System | | 521 GLAUCOMA 2290 |
| | PARAMENINGEAL INFECTIONS, Donald H. Harter | 2181 | 522 DISC SWELLING AND OPTIC ATROPHY |
| 482 | SYPHILITIC INFECTIONS OF THE CENTRAL NERVOUS SYSTEM, | | 523 UVEITIS 2293 |
| | Kenneth P. Johnson | 2187 | 524 OCULAR INFECTIONS |
| Sec | tion 9 Viral Infections of the Nervous System | | 525 ORBITAL DISEASE AND TUMORS |
| | INTRODUCTION, Richard W. Price | | 527 EPISCLERITIS, SCLERITIS, AND THE DRY EYE |
| | ACUTE VIRAL MENINGITIS AND ENCEPHALITIS, Richard W. Price | 2192 | 528 OCULAR VASCULAR DISEASE |
| 485 | HERPES VIRUS INFECTIONS OF THE NERVOUS SYSTEM, | 0405 | 529 THE EYE AND MEDICATIONS |
| 400 | Richard W. Price | 2195 | |
| 100 187 | RABIES, Daniel B. Fishbein and George M. Baer | 2200 | PART XXIV SKIN DISEASES, Frank Parker |
| 488 | SLOW VIRUS INFECTIONS OF THE NERVOUS SYSTEM | 2203 | 530 INTRODUCTION 2300 |
| | 488.1 INTRODUCTION, Richard W. Price | | 531 THE STRUCTURE AND FUNCTION OF SKIN 2300 |
| | 488.2 AIDS DEMENTIA AND HUMAN IMMUNODEFICIENCY VIRUS | | 532 EXAMINATION OF THE SKIN AND AN APPROACH TO DIAGNOSING |
| | BRAIN INFECTION, Richard W. Price | | SKIN DISEASES 2306 |
| | 488.3 CREUTZFELDT-JAKOB DISEASE, Paul E. Bendheim | 2205 | 533 PRINCIPLES OF THERAPY 2314 |
| | 488.4 SUBACUTE SCLEROSING PANENCEPHALITIS, Ierry S. Wolinsky | 220E | 534 SKIN DISEASES OF GENERAL IMPORTANCE |
| | 488.5 PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY, | 4400 | PART XXV OCCUPATIONAL AND |
| | Richard W. Price | 2207 | |
| Sect | tion 10 Neurologic Disorders Associated with Altered | | ENVIRONMENTAL MEDICINI |
| | Immunity or Unexplained Host-Parasite | | 535 PRINCIPLES OF OCCUPATIONAL MEDICINE, Charles E. Becker 2354 |
| | Alterations, Jerry S. Wolinsky | | 536 OCCUPATIONAL PULMONARY DISORDERS, Dean Sheppard 2356 |
| 189 | CENTRAL NERVOUS SYSTEM COMPLICATIONS OF VIRAL INFECTIONS | | 537 PHYSICAL, CHEMICAL, AND ASPIRATION INJURIES OF THE LUNG, |
| | AND VACCINES | 2208 | James D. Crapo |
| | REYE SYNDROME | 2209 | 538 OCCUPATIONAL DISEASES OF THE SKIN, Edward A. Emmett 2373 539 RADIATION INJURY, Theodore L. Phillips |
| 491 | NEUROLOGIC COMPLICATIONS IN THE IMMUNOLOGICALLY | | 539 RADIATION INJURY, Theodore L. Phillips |
| | COMPROMISED HOST | 2210 | 541 DISORDERS DUE TO HEAT AND COLD, James P. Knochel |
| Sect | ion 11 The Demyelinating Diseases | | 542 TRACE METAL POISONING, Donald B. Louria |
| 192 | THE DEMYELINATING DISEASES, Donald H. Silberberg | 2211 | |
| | ion 12 The Epilepsies | | PART XXVI LABORATORY REFERENCE |
| | THE EPILEPSIES, Jerome Engel, Jr. | 2217 | RANGE VALUES OF CLINICA |
| | ion 13 Intracranial Tumors and States of Altered | 11 | IMPORTANCE |
| , , ,,, | Intracranial Pressure | | |
| 194 | INTRACRANIAL TUMORS, William R. Shapiro | 2220 | 543 REFERENCE INTERVALS AND LABORATORY VALUES OF CLINICAL IMPORTANCE, Ronald J. Elin2394 |
| 95 | DISORDERS OF INTRACRANIAL PRESSURE, David A. Rottenberg | 2235 | ини октанов, <i>колици ј. Ешт</i> .2394 |
| | 2 | | |

PART I

MEDICINE AS A LEARNED AND HUMANE PROFESSION

The Cecil Textbook of Medicine is addressed to medical students, residents, fellows, and practitioners of all ages. It deals with the body of knowledge of human disease. In contrast, these introductory essays are presented mainly for those now entering the profession, for students deserve a broader perspective of medicine than is offered by its subject matter alone.

MEDICINE AS AN ART

Lloyd H. Smith, Jr.

What is medicine? "Medicine is not a science but a learned profession, deeply rooted in a number of sciences and charged with the obligation to apply them for man's benefit." In this eloquent statement from an earlier edition of this book, Walsh McDermott defined medicine as a human activity undertaken for the benefit of others whether in the area of public health, "statistical compassion," or in the care of the individual patient.

Medicine can also be defined in other terms. It is a mutable body of knowledge, skills, and traditions applicable to the preservation of health, the cure of disease, and the amelioration of suffering. The boundaries of medicine blend into psychology, sociology, economics, and even into cultural heritage. Disease may be encoded in the genome; disease may also be encoded by the deprivations of poverty and ignorance. Medicine must therefore be concerned not only with an abnormal molecule but also with an abnormal childhood. As such it is open ended in a way that is both humbling and exhilarating to those who pursue it as a career.

Medicine is continually changing. The honored verities of one generation become the shopworn shibboleths of the next. Much of what we now so confidently espouse, including that compressed within this edition, will amuse our successors as being remarkably bizarre in its naiveté. Medical competence is based on the continuing pursuit of ever changing concepts. It must be renewed as the substance of medicine itself is transformed.

The practice of medicine is far more than the application of scientific principles to a particular biologic aberration. Its focus is on the patient whose welfare is its continuing purpose. That purpose of medicine is self evident in theory, but more difficult to sustain under the pressures of medical practice. For example, it is tragically easy for the patient to become merely the repository in which a disease or a syndrome has chosen to manifest its particular silhouette. During the training years every physician has subconsciously participated in what might be termed the personification of disease. A case of meningitis is admitted through the emergency room; a

pheochromocytoma will be discussed at Grand Rounds. It is perhaps inevitable that a disease becomes symbolically an entity to the physician who must become familiar with all of its manifestations and guises. In the art of medicine the physician must be the advocate of the patient as well as the adversary of disease. It is the patient who is personified rather than the disease.

THE PATIENT. The description of a patient is simply that of a fellow human being in need of help. The patient comes seeking help because of a problem relating to his or her health. This subjective judgment carries with it disquieting concerns, although these may be unexpressed. Anxiety is present even in the most stoical of patients; this fact must never be forgotten or disregarded by the physician. The patient's anxiety may be specific—for example, in a fear of cancer with all that implies in the public mind concerning pain, degradation, and inexorable death. More often the anxiety is amorphous: fear of loss of independence or employment; fear of failure to meet obligations to one's family or to retain the regard of a loved one; or fear of an inability to maintain a life of dignity and significance. In the rush to crystallize a chief complaint and present illness the physician too often brushes aside these considerations.

The patient presents to the physician on alien and unfamiliar ground-in the structured and artificial setting of an office, a clinic, or a hospital bed. This form of health care of the individual, as opposed to health care in the aggregate, is often described by the unfelicitous phrase "the personal encounter system." Unfortunately it often seems distressingly like confrontation to the patient, who comes after all for comfort, not for encounter. Each human being is unique within a life that is enormously complex—in heredity, early experiences, cultural and psychologic environment, education, opportunities, successes, failures, fantasies, emotional commitments, motivations, and in the adjustments and compromises that serve to cripple or to mature. Living, therefore, is the ultimate personal encounter system. With an extensive and diverse experience the patient comes to the physician with "a problem." A chief complaint is requested. Defenses must be lowered and the emotions that spill out may be distressing. The patient's response must be selective and brief; as a result it is not infrequently distorted, perhaps even

What does the patient want when coming to see a physician? There are certain common hopes and expectations. Patients want to be listened to, so that their fears and concerns can be fully expressed and the burden shared. They want physicians to be interested in them as fellow human beings in a compassionate but nonjudgmental fashion. They expect professional competence incorporating the best in medical science and technology. They want to be reasonably informed as to the probable cause of their concerns and what the future is likely to hold. They want not to be abandoned. To each patient these desires and expectations vary in relative impor-

tance. It is notable that not all patients expect to be cured. These expectations will be further discussed in the light of how the physician should endeavor to meet them.

TRADITIONAL EXPECTATIONS OF PATIENTS. Patients want to be listened to and understood. This has been well expressed by Wilfred Trotter, a great English neurosurgeon:

"... As long as medicine is an art, its chief and characteristic instrument must be human faculty. We come therefore to the very practical question of what aspects of human faculty it is necessary for the good doctor to cultivate. . . . The first to be named must always be the power of attention, of giving one's whole mind to the patient without the interposition of oneself. It sounds simple but only the very greatest doctors ever fully attain it. It is an active process and not either mere resigned listening or even politely waiting until you can interrupt. Disease often tells its secrets in a casual parenthesis. . . ."

Eventually the medical record must be organized in a logical and consistent fashion. But a history rarely unfolds that way. Patients do not divulge their fears in neat paragraphs or in direct responses to a cascade of queries. It is important to let patients tell their own stories. The manner of formulation and expression of symptoms and anxieties may be as informative as the medical data transmitted. The good physician is an attentive listener, with an ear for Trotter's "casual parenthesis."

Patients want physicians to be interested in them as fellow human beings. This interest cannot be that of the unusual "case" of the carcinoid syndrome or of hairy cell leukemia; the center of interest must be the patient as a person. It is difficult for the physician to feign such an interest, for patients are very perceptive, especially during the vulnerability that illness induces. In the practice of medicine the physician will encounter all of the virtues and vices to which mankind is heir. The physician need not be morally neutral in personal judgments, but these must be stringently excluded from professional activities. The response of the physician to human frailty and fallibility should be that of compassion rather than cynicism, of interest in the infinite variety of human experience rather than of repulsion from its aberrations.

Patients expect professional competence in medical science and technology. The physician must be a scholar both to attain professional competence and to sustain it during times of revolutionary changes in science and technology. All of the other attributes of the good physician will be of little avail in the absence of sound scholarship. Compassion is no substitute for knowing what should be done. The education of the physician and the role of the physician as a scientist will be discussed more fully below.

Patients want to be kept reasonably informed. The physician must listen to and communicate with the patient. Time must be set aside for this. Failure to do so is a serious error, for silence is a form of communication that is usually adverse. The physician should voluntarily answer questions of concern to the patient. The physician must also inform the patient concerning the illness and what it implies. A number of books have been developed to assist in patient education and are often quite effective in translating medical terminology into lay terms. Furthermore, clubs for mutual support and education have been formed by patients who share their common experiences with such chronic disabilities as ileostomies or amputations. Admirable and important as these are, they do not obviate the need for patients to learn from their own physicians about their particular illnesses and what they may mean in and for their future lives. This need extends beyond the legal confines of informed consent, which is now an important issue in medical practice.

Patients want not to be abandoned. Death comes to everyone. There are finite limits to what can be accomplished by medical science and technology in the alleviation of suffering and the prolongation of life. This fact is well known to both patients and physicians. When that limit is reached, the physician

often feels powerless and even guilty that no more can be done. As a consequence there is a tendency to withdraw attention and direct it elsewhere. Nothing could be a greater mistake. It is at the margins of medical science that the role of the physician is enhanced. It is here that the art of medicine comes to the forefront in the care of the patient, whether it be by emotional support, relief of pain, small adjustments in medicines or diet, daily conversation and examination, or other methods to show that the patient is still someone of dignity and worth in whom interest has not been lost and for whom hope has not been abandoned. And when no more can be done for the patient it is time to care for the family. It is this caring role rather than the curing role of the physician that is so well described in Ch. 4 by Lewis Thomas. At this stage, as Walsh McDermott has written, "it is up to each of us to follow to the fullest measure the charge laid down long ago for the physician to become himself the treatment.'

THE PHYSICIAN. The physician has both chosen and been chosen to enter an arduous and demanding profession, the origins of which stretch back to antiquity. Part priest, part shaman, part mystic, part alchemist, the physician of the past reflected the beliefs and expectations of the time and met a perceived need of fellow men. The history of medicine is part of the heritage of every physician and reflects the cultural history of each society.

The physician enters a profession with established values and traditions of ethical conduct and responsibilities. But each physician, as each patient, is unique. The physician is not a disembodied instrument that can be passively shaped by the profession, but rather a human being with innate strengths and weaknesses that must be recognized in order to meet the expectations of patients and of the profession, not least of which are those standards established for oneself. The qualities of the ideal physician are easy to state but difficult to attain: compassion, sincere interest in one's fellow man, knowledge of human nature, tact, equanimity, sustained scholarship, curiosity, and high ethical standards. Physical and mental vigor might be added to those traits, for the life of the physician is not for the languid or the disengaged. No one has been endowed with or ever fully achieves excellence in all of these qualities. One must first know oneself and judge how one can most closely approach those ideals in one's professional life.

THE EDUCATION OF THE PHYSICIAN. Barriers are encountered at the very beginning in the initial selection for medical school as many seek entry for few positions. Undergraduate education is sometimes distorted and breadth of personal experience curtailed in a grim and often distasteful race for competitive acceptance. This inadvertent feedback inhibition not infrequently results from erroneous conceptions of what may or may not impress admission committees of medical schools. Nevertheless, the phenomenon remains as a concern to all who are interested in the future of our profession. Admission committees of medical schools too often exercise allosteric control over the higher education of those destined to enter our profession.

The Basic Science Years. In the standard curriculum of medical school in the United States two years are largely devoted to the sciences basic to medicine and two years to clinical training. Fortunately there are a number of interesting variations on this thematic progression which diminish its rigidity and permit the student to re-explore basic science after an introductory clinical experience.

In the United States students usually arrive at medical school after an intensive four-year experience at a college or a university. They anticipate a scholarly atmosphere of a graduate school which will prepare them to enter the practice of a profession for which they hold idealistic expectations. Instead they are immediately assailed with a formidable array of "basic sciences" linked to the structure and function of the human organ systems. New facts constitute not so much an

intellectual feast as an engorgement. Each discipline is attended by devotees who are passionately persuaded of the seminal role of their segment of science in the future of the profession. This commitment is translated into the basic academic commodity, curricular time, in which these cluttered wares are exhibited. Awed by the dimensionless task, students struggle with uneven success to assimilate and survive, conscious always that their receptor mechanisms are overloaded and of a continuing sense of high output failure. They look forward in hope that subsequent years will reward their endurance in the more congenial atmosphere of the clinic.

This is patently a caricature, as all will recognize. It can be said, as Mark Twain said of Wagner's music, "it is not as bad as it sounds." The quality of basic science in medical schools is often superb; the substance of modern science has a certain grandeur; many faculty members are gifted in imparting a sense of intellectual adventure to their students; finally, many students now arrive at medical school with a mature understanding of one or more of the fundamental disciplines of biology. Nevertheless this caricature contains elements of truth as seen from the perspective of medical students. The central question is not whether basic science is necessary for medical research, since few would deny its importance there, but whether it is relevant in the education of every physician to the degree to which it is currently emphasized. In the real world of patient care, public health, and medical economics, should the student have to struggle with the intricacies of post-transcriptional modifications of messenger RNA, or is this merely a rite of passage prescribed by a science-obsessed faculty? This is a reasonable question and calls for a response other than a simple reference to flexnerian orthodoxy.

A knowledge of the scientific underpinnings of medicine is clearly necessary in order to marshal the basic information required to understand a patient's illness and to be able to reason logically about the problems of diagnosis and therapy. If there were any doubt on that point, it would be quickly dispelled by random perusal of this book. Much of the basic science which seems abstruse and irrelevant today will find its way into clinical practice in the not too distant future. Medical research is only one step removed from patient care.

Beyond the assimilation of scientific information, there is an even more important consideration. Many of you will have most of your professional experience in the twenty-first century. The changes in medical science and technology will be enormous and largely unpredictable. Only the scientific method will remain unaltered as an invaluable instrument with which fallible man can acquire new knowledge and, equally important, debride that which proves fallacious. It is imperative that students learn the scientific method as part of their education if they are to participate critically and effectively in a changing profession. How can this be done? Perhaps the best method is to participate personally, even for a relatively brief period of time, in a research project so that learning comes from first hand experience. If that does not prove practical, one can pursue some scientific topic in depth and write a critical analysis of it. It is important to learn one area of inquiry in great detail, even though it may have to be a limited area, in order to penetrate to its frontier. It is only there that science can be understood as a process rather than as a repository.

The Clinical Years. In his perceptive essay "On Becoming a Clinician," in an earlier edition of this textbook, Paul B. Beeson described many of the disquieting stresses to which the student is subjected on entry into the clinical years. Every medical student will benefit from reading those thoughts from one of America's most distinguished physicians. Most students enter the clinical years with a sense of relief, but it is relief linked with anxieties. Some of these anxieties cluster around the following questions:

How can I cope with the uncertainties of clinical medicine?

What are the boundaries of clinical medicine? How much and what am I supposed to learn?

How will I function in my interactions with patients?

How will I measure up to the expectations of my colleagues? How will I be able to maintain my own identity as an individual in a profession that so obsessively dominates my time and energy?

Other questions could be formulated. Each student possesses a unique idiotype of anxieties that cannot be purged by platitudes. Each will arrive at personal answers, or more likely at personal accommodations, through experience.

THE UNCERTAINTY PRINCIPLE OF CLINICAL MEDICINE. There is an "uncertainty principle" in medicine as there is in physics. The practice of medicine is inexact and will remain so. If it were not, it would be a science or a technology rather than an art. The measuring instrument is personal and unique. Subjective mensuration defies precision. Who can quantify nausea or the severity of pain? Symptoms may be forgotten, suppressed, or amplified when filtered through the grid of personality. Available data are often indirect, incomplete, or even contradictory. Patients respond in varying fashions to treatment across the range from simple reassurance (which is rarely simple) to surgical or pharmaceutical interventions. Clinical medicine is often based on experience and judgment—which are largely euphemisms for a knowledge of probabilities.

The process of formulating a diagnosis or selecting a therapy is not as arbitrary as it first seems. There are rational means for narrowing the range of diagnostic possibilities: a precise description of symptoms; an accurate and thorough characterization of physical findings; selective laboratory studies to evaluate the functions of organ systems; a synthesis of information to define syndromic patterns; a marshaling of information on etiology and pathogenesis. All of this requires attention to detail, consistency of work habits, and good intellect.

Hypotheses are formed and algorithms branch away from various entry points as new data are obtained which support or fail to support a working diagnosis. This process of clinical reasoning is often best displayed in the Clinicopathologic Conference (CPC). In the absence of certainty, best guesses must be utilized and in making informed guesses, generally dignified as judgments, the clinician actually relies upon subliminal statistics.

Medical decisions based on probabilities are necessary but also perilous. Even the most astute physician will occasionally be wrong. The wise physician will often recognize that a decision is erroneous and discard or modify the hypothesis on which it is based. The best decision may be approached only by successive approximations. Action may have to be taken despite lack of confirmation of a hypothesis (working diagnosis). Chester M. Jones, a noted clinical teacher, used to say: "If you cannot make a diagnosis, make a decision." Despite the remarkable contributions of science and technology, clinical medicine is frequently inexactitude in action. The student entering the clinical years will quickly realize the dangers to the welfare of the patient of dogmatism in clinical practice. The ambiguities and errors that you will encounter in your own experience and observe in the work of others should be an antidote to arrogance. Some errors are inevitable and should not humiliate you, but they should teach humility.

CLINICAL MEDICINE AS A DISCIPLINE WITHOUT BOUNDARIES. The basic sciences are demanding but, as taught in medical schools, they have reasonably defined margins. It is true that these margins are somewhat artificial, since the disciplines of modern biology merge almost imperceptibly into one another. Nevertheless, the educational responsibilities of the medical student can often be designated within the subject material of a lecture course, syllabus, and textbook. Not so in clinical medicine. The student emerges into an open-ended system

of bewildering complexity in which science is blurred by sociology; psychology interacts with economics; and traditions and ethical concepts are buffeted by new imperatives. Within this complicated system, the practice of clinical medicine goes forward. The student does not encounter a theoretical discipline to be observed and analyzed in tranquility, but is abruptly thrown into the structured workings of the second largest industry in the United States where the health and even the survival of many people are at stake on a daily basis.

Based on previous educational experiences, students often ask, "How much am I expected to learn in this course?" No one can supply a satisfactory answer. The student stands on the threshold of a learning experience in clinical medicine that will extend over the remainder of an active career as a physician. Learning must have that stretch if the student is to meet the responsibilities of a physician. The course is merely a contrived entry point into that longitudinal experience. More advanced faculty members, medical residents, or even senior students in other rotations in medicine seem remarkably well informed. Yet no single individual has a balanced knowledge in all aspects of medicine. The specialist will often be adept only within a defined subset of medicine, and even the generalist will be uneven in many areas of information. Within this confusing and sometimes overwhelming setting the student must become an independent scholar in medicine-independent in the sense that never again will others outline or circumscribe the subject material.

Most students adapt themselves remarkably quickly to the changed environment of clinical medicine. The new language of the hospital, including its acronymic barbarisms (SOB, PERLA, COPD, etc.), no longer jar the ear, and the concepts of pathophysiology being applied at the bedside awaken latent memories. The student learns that there are habits of thought and clusters of associations so that the physician does not laboriously go back to first principles to meet each new clinical problem. These thought patterns are efficient and useful if they do not gel into medicine by reflex and aphorism. The student learns by listening, participating, observing, arguing, reading, and reflecting. As earlier generations of students have discovered, the intensity of the experience and the special chemistry of confronting the clinical problem of a specific patient serve to fix the information received in one's memory with a vividness far beyond that obtained from even the most brilliant lecture.

Beyond the required participation in clinical rotations, how should the student approach the study of medicine? It would be presumptuous to give a doctrinaire answer. Medical students have usually been seasoned by five or six years of higher education before they begin the study of clinical medicine and during those years have developed their own best methods of learning. In approaching internal medicine, in contrast perhaps to some more circumscribed specialties, it will usually prove most valuable to study in depth the specific problems presented by one's own patients rather than beginning with a systematic approach to cover all of the discipline. In this way one can exploit the intense immediacy of those experiences which, supplemented by conferences, rounds, seminars, conversations, and all of the other ways of learning on the fly, will usually converge to give a broad familiarity with the subject. A share in the responsibility of caring for a patient is a powerful stimulus to learning.

What is the role of the Cecil Textbook of Medicine in the learning process? This book attempts to provide the student or the physician with succinct but authoritative summaries about diseases or groups of diseases. Essays written by more than 250 acknowledged experts in their respective fields represent collectively a systematic approach to internal medicine. The chapters are designed to give a basic, lucid, and up-to-date consensus concerning the state of the art in our understanding of specific diseases, but they cannot be all inclusive. Many of the topics discussed within a few pages

have received more extended treatment elsewhere as separate monographs. Each of the subspecialty areas (cardiology, gastroenterology, endocrinology, etc.) is the subject of textbooks similar in size to this one. The student should therefore cultivate the habit of consulting at least some of the carefully selected references that extend the information supplied in this basic text.

In general it is also wise for students to begin reading medical journals early in their study of clinical medicine. In this way a start can be made toward the regular study of current medical literature and also the foundations of one's own medical library can be laid. Each student may have a personal preference. The most frequently read medical journal by students and practitioners is the *New England Journal of Medicine*. It is particularly useful for the student with its CPC, surveys of medical progress, editorial comments on current topics, original articles, and lively correspondence. In this manner the student establishes an early acquaintance with the frontiers of medicine and with its issues, uncertainties, and controversies.

THE STUDENT AND THE PATIENT. One of the student's earliest concerns on entering clinical medicine is how to interact with patients and how to assume the traditional role of a physician. The student is concerned that personal insecurities will impair effective communication with patients in whose care he or she is now called upon to participate. Rarely does this turn out in practice to be a serious problem. The expectations of most patients in the physician-patient interaction, discussed above, are realistic ones. Patients are usually aware of the progression of assigned responsibilities in the student-house staff-faculty team and do not expect omniscience or authoritarianism from the student. Not infrequently the patient forms a special attachment to the student, especially if the student has been perceptive enough to listen in the sense described above by Wilfred Trotter. If the student respects the personal dignity of the patient as a fellow human being, and listens in a sensitive manner, the patient responds with gratitude and returns that respect. Even when patients are initially perceived as hostile or belligerent, the student must maintain equanimity and try to understand the sources of these reactions. Do not allow yourself to be drawn into the flippant cynicism that sometimes passes for sophistication in the subculture of student and house staff training. Francis Peabody's sentient summary is still most apt, "for the secret of the care of the patient is in caring for the patient.'

STUDENTS AND THEIR COLLEAGUES. Beginning in the clinical years the relationships of students with their colleagues in medicine undergo a subtle change. No longer are they merely the passive recipients of data and concepts supplied by the faculty through lectures, conferences, syllabi, or laboratories. They are participating with graduated responsibilities in the practice of medicine. A point in the medical history or a question asked by the student may prove decisive in arriving at the solution of a clinical problem. Frequently the most effective teachers of students are the house staff or more advanced students. Students will find many residents to be splendid teachers who not only make them feel at home on the service but also take the extra time to include them in all of the discussions. On most teaching services there is a certain amount of badinage or gamesmanship which enlivens interactions. If this is recognized as such, and not taken too seriously, it can serve to enhance rather than demean the learning experience. As a student you must not hesitate to ask questions or bring up new points of view and must not be intimidated by your current position in this shifting hierarchy. Even the chief medical resident faced similar qualms only a few years ago. But above all, remember that it is the patient's welfare, and not your own ego, that is paramount.

THE PHYSICIAN AS A NONPHYSICIAN. Beginning in the basic science years but exacerbated in the clinical years, students often become concerned about the level of commitment de-

manded of them. How much of a life that is finite in time and energy must be devoted to medicine? What is the boundary between dedication and obsession? After all one does not really become a physician; one remains a human being who has acquired certain knowledge and skills that allow one to function as a physician during specific periods of time. What should those times be? How and when does one shift roles from being a physician to being a "nonphysician"? This is, of course, a generic question that is as applicable to science, art, business, or any other human activity as it is to medicine.

The student will not readily find an all-embracing answer to this question. Each student will most likely evolve a personal answer and it will be an operational one representing the integral of microcompromises and adjustments made throughout one's subsequent career. The "complete physician," narrowly construed, would be a very poor physician if he were merely an observer rather than a participant in the pageantry of his time. Physicians owe it to themselves, to their families, to society, and to their patients not to become simply skilled but detached automatons. On the other hand, the practice of medicine is not a job but a profession that cannot be sealed off into convenient hours for earning one's living. To attempt to do so smacks of dilettantism. Between these extremes one must decide for oneself where the compromises will be made along the varying border between personal and professional life. Tensions will remain, but properly channeled they can be creative and rewarding.

2 MEDICINE AS A SCIENCE

James B. Wyngaarden

The practice of medicine rests firmly upon a foundation of biologic and behavioral sciences, which in turn trace their evolution to chemistry, physics, mathematics, psychology, anthropology, and epidemiology. During college and medical school years, the physician acquires both an extensive knowledge base in science and a comfortable familiarity with the ways of science. But scientific knowledge is not static. It undergoes continuous remodeling as new discoveries are made and erroneous interpretations are discarded. As a consequence, preservation of professional competence throughout a working lifetime is a daunting challenge. It requires a continuing growth of knowledge, a critical assessment of new hypotheses and scientific advances, and a selective incorporation of the most useful of these into one's own practice.

Advances in biologic science and accompanying technologic developments underlie most of the medical progress of the past half century, which has so remarkably advanced the ability of the physician to intervene in illness. Much of this progress has been in fundamental or "basic" science, conducted in the pursuit of understanding for its own sake. Significant progress has also resulted from research conducted by physician-scientists with a specified clinical goal in mind for example, the elucidation of a disease mechanism or the critical evaluation of a therapeutic practice. Advances in medicine also continue to occur through serendipity or by astute clinical observations concerning patients or groups of patients and their illnesses. Nevertheless, the only rational approach to finding new methods for prevention or treatment is based on scientific explanations of the causes and mechanisms of disease.

Some years ago, Comroe and Dripps* traced the origins of

ten major clinical innovations in cardiovascular and pulmonary medicine in an effort to identify the antecedents of these advances. Over 60 per cent of the enabling discoveries were in the category of basic science; over 40 per cent were the result of research carried out without any particular clinical application in mind. These observations are probably representative of medical progress in general.

The ability to control infections with antibiotics, hypertension with antihypertensive agents, and inflammatory reactions with glucocorticoids represents remarkable advances that have contributed to a lengthening of life expectancy. But the agenda is far from being fulfilled. The major health care problems of our time lie in the continued existence of diseases for which we can as yet do little. Even if the best of contemporary medicine were universally available, cancer would continue to kill, rheumatoid arthritis would continue to cripple, and schizophrenia would continue to render insane. We have no definitive answers for these diseases and for many more the descriptions of which constitute the substance of this book-or else we have what Lewis Thomas has called a "halfway technology," measures capable of modifying and ameliorating illness but not of prevention or cure. Medicine as a science is incomplete. It will remain so, for science itself is by its nature incomplete.

The present bioscientific character of medical practice is a relatively recent development. Throughout most of recorded history, medicine was anything but scientific, being dominated by empiricism and shackled by dogma. Diagnoses were inexact, causes of diseases poorly understood, and therapies frivolous and haphazard. Interventions by physicians consisted of bleeding, purging, cupping, administration of infusions of every known plant and of solutions of every known metal, and prescription of every possible diet—with no scientific foundation for these practices. Nor could there be such a foundation, for the scientific base did not yet exist.

Harbingers of change emerged slowly in the early nineteenth century, as new principles of physics and chemistry were applied to medicine. Physiologists stressed functions of organs and tissues. Its exemplars, especially Claude Bernard (1813-1878), emphasized the experimental method in establishing biologic knowledge and the necessity of basing medical practice in such knowledge. Pathologists, led by Virchow (1821-1902), stressed the critical study of normal and abnormal tissues and the correlation of features of disease with precise anatomic observations. Bacteriologists, with Pasteur (1822-1895) and Koch (1843-1910) in the vanguard, began to identify the microorganisms and to implicate specific organisms in specific diseases—the anthrax bacillus in anthrax, the tubercle bacillus in consumption, the pneumococcus in lobar pneumonia, the streptococcus in puerperal fever. The groundwork for future therapies was being laid by these great Western European scientists, but there was relatively little that physicians could do about most illnesses at the time. Their major contributions were diagnostic, prognostic, and supportive. By correct diagnosis they could advise concerning outcome. By common-sense supportive measures they could provide comfort and maximize opportunities for recovery. But interventions were as likely as not to make things worse. The first edition of Osler's Textbook of Medicine in 1892 was revolutionary for its skepticism and its therapeutic nihilism, as this outstanding physician and teacher condemned the majority of nostrums and remedies as useless, even harmful.

Slowly, specific therapies—insulin for diabetes, liver extract for pernicious anemia—or specific immunizations—diphtheria antitoxin, pneumococcic antisera—appeared. But it was not until the decade of 1935 to 1945 that the entry of sulfonamides and penicillin into clinical medicine made curable a large number of previously lethal and untreatable diseases. It is customary to date the beginnings of modern medicine from these relatively recent events.

The language of contemporary biologic science has become

^{*}Comroe JH, Dripps RD: The top ten clinical advances in cardiovascularpulmonary medicine and surgery between 1945 and 1975: How they came about. Bethesda, Md., Public Inquiries and Reports Branch, National Heart, Lung, and Blood Institute, National Institutes of Health, 1977.