



# MICROBIOLOGY

**ABRAHAM I. BRAUDE, M.D., Ph.D.**

Professor of Medicine and Pathology  
University of California, San Diego

*Associate Editors*

**CHARLES E. DAVIS, M.D.**

Professor of Pathology  
University of California, San Diego

**JOSHUA FIERER, M.D.**

Associate Professor of Medicine  
University of California, San Diego

**1982**

**W. B. SAUNDERS COMPANY** Philadelphia  
London  
Toronto  
Mexico City  
Sydney  
Tokyo

W. B. Saunders Company: West Washington Square  
Philadelphia, PA 19105  
1 St. Anne's Road  
Eastbourne, East Sussex BN21 3UN, England  
1 Goldthorne Avenue  
Toronto, Ontario M8Z 5T9, Canada  
Cedro 512  
Mexico 4, D.F. Mexico  
9 Waltham Street  
Artarmon, N.S.W. 2064, Australia  
Ichibancho, Central Bldg., 22-1  
Chiyoda-ku, Tokyo 102, Japan

Microbiology

ISBN 0-7216-1920-7

© 1982 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. Press of W. B. Saunders Company. Library of Congress catalog card number 81-40588.

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

# CONTRIBUTORS

**YOUSEF AL-DOORY, Ph.D.**

Associate Professor of Pathology, George Washington University School of Medicine; Chief, Sections of Mycology and Serology, Division of Laboratory Medicine, George Washington University Hospital, Washington, D.C.

DEMATIACEAE: AGENTS OF CHROMOMYCOSIS

**AARON D. ALEXANDER, Ph.D.**

Professor of Microbiology, Department of Microbiology, Chicago College of Osteopathic Medicine, Chicago, Illinois.

LEPTOSPIRA

**A. O. ANYA, Ph.D.**

Professor of Zoology and Director, School of Postgraduate Studies, University of Nigeria, Nsukka, Nigeria.

NEMATHELMINTHES

**HOWARD ROBERT ATTEBERY, D.D.S.**

Research Microbiologist, Veterans Administration Medical Center, San Diego, California.

FUSOBACTERIA; GRAM-POSITIVE COCCI: PEPTOCOCCUS, PEPTOSTREPTOCOCCUS, STREPTOCOCCUS (ANAEROBIC), AND SARCINIA; VEILLONELLA

**HERMAN BAER, M.D.**

Associate Professor of Pathology and Medical Microbiology; Director, Clinical Microbiology Laboratories, Shands Teaching Hospital and Clinics, Miller Health Center, University of Florida, College of Medicine, Gainesville, Florida.

CLASSIFICATION OF BACTERIA; MORAXELLA AND ACINETOBACTER

**LANE BARKSDALE, M.D.**

Professor of Microbiology, New York University School of Medicine and Medical Center, New York, New York.

DIPHTHERIA BACILLI AND OTHER CORYNEBACTERIA

**WILLIAM R. BEISEL, A.B., M.D., F.A.C.P.**

Deputy for Science, US Army Medical Research Institute of Infectious Diseases, Fort Dietrick, Maryland.

METABOLIC EFFECTS OF INFECTION

**ABRAHAM I. BRAUDE, M.D., Ph.D.**

Professor of Medicine and Pathology, University of California, San Diego, California.

THE ASPERGILLI; BACTERIAL ENDOTOXINS; CANDIDA TORULOPSIS; DESCRIPTION OF ANTIMICROBIAL DRUGS; MECHANISMS OF ACQUIRED RESISTANCE TO INFECTION; MECHANISMS OF ACTION OF ANTIMICROBIALS; MECHANISMS OF IMMUNOLOGIC INJURY IN INFECTIOUS DISEASES; MECHANISMS OF NATURAL RESISTANCE TO INFECTION; MISCELLANEOUS FUNGI: THE AGENTS OF MYCETOMA AND RHINOSPORIDIUM; POX-VIRUSES; RESISTANCE TO ANTIMICROBIAL DRUGS; SPOROTRICHOSIS; THE ZYGOMYCETES

**JOHN J. S. BURTON, Ph.D.**

University of California ICMR, Institute for Medical Research, Kuala Lumpur, Malaysia.

ARTHROPODS OF MEDICAL IMPORTANCE

**BARUN DEB CHATTERJEE, M.B.B.S., Ph.D.**

Professor and Head, Department of Bacteriology and Serology, School of Tropical Medicine, Calcutta, India.

VIBRIOS

**T. H. CHEN, M.D.**

Research Microbiologist, Department of Biomedical and Environmental Health Sciences, School of Public Health, University of California, Berkeley, California.

YERSINIA, PASTEURELLA, AND FRANCISELLA

**RICHARD W. COMPANS, Ph.D.**

Professor of Microbiology, University of Alabama Medical Center, Birmingham, Alabama.

MORPHOLOGY AND STRUCTURE OF VIRUSES



EUGENE H. COTA-ROBLES, Ph.D.

Professor of Biology, University of California,  
Santa Cruz, California.

THE STRUCTURE OF THE BACTERIAL CELL

MANUEL CUADRA, M.D.

Professor (Retired) of Infectious, Parasitic, and  
Tropical Diseases, Universidad Nacional Mayor  
de San Marcos, Facultad de Medicina, Lima,  
Peru; Staff Member, Robert Koch Institut, As-  
sociated with Virchow Krankenhaus, Berlin,  
West Germany.

BARTONELLA BACILLIFORMIS

CHARLES E. DAVIS, M.D.

Professor of Pathology, University of California,  
San Diego, School of Medicine; Associate Di-  
rector of Microbiology, University Hospital, San  
Diego, California.

CLASSIFICATION AND IDENTIFICATION OF BACTERIA;  
CRYPTOCOCCUS; ERYSIPELOTHRIX RHUSOPATHIAE

DENNIS M. DIXON, Ph.D.

Assistant Professor, Department of Biology,  
Loyola College of Maryland, Baltimore, Mary-  
land.

BLASTOMYCES AND PARACOCOCCIDIODES

ALEXANDER L. DOHANY, Ph.D.,  
MAJ, MSC

Chief, Department of Acarology, US Army Med-  
ical Research Unit, Kuala Lumpur, Depart-  
ment of State, Washington, D.C.

ARTHROPODS OF MEDICAL IMPORTANCE

JEAN M. DOLBY, Ph.D.

Member of the Senior Scientific Staff of the  
Medical Research Council, Clinical Research  
Centre, Harrow, Middlesex, England.

BORDETELLA

SANFORD S. ELBERG, Ph.D.

Professor of Microbiology and Immunology,  
Department of Biomedical and Environmental  
Health Sciences, School of Public Health, Uni-  
versity of California, Berkeley, California.

YERSINIA, PASTEURELLA, AND FRANCISELLA

MAKOTO ENOMOTO, M.D.

Lecturer of Pathology, St. Marianna University,  
School of Medicine; Consulting Pathologist,  
Sagamihara Kyodo Hospital, Sagamihara,  
Japan.

FUNGAL TOXINS

VLADIMIR FARKAŠ, Ph.D.

Researcher, Institute of Chemistry, Depart-  
ment of Biochemistry of Saccharides, Slovak

Academy of Sciences, Bratislava, Czechoslo-  
vakia.

MORPHOLOGY AND STRUCTURE OF FUNGI

JOSHUA FIERER, M.D.

Associate Professor of Medicine, University of  
California, San Diego, School of Medicine;  
Chief, Microbiology Laboratory, Veterans Ad-  
ministration Medical Center; Attending Phy-  
sician, University Hospital, San Diego, Cali-  
fornia.

MONILIFORMIS

ROBERT G. GARRISON, Ph.D.

Associate Professor of Microbiology, Depart-  
ment of Microbiology, University of Kansas  
Medical Center; Research Microbiologist, Vet-  
erans Administration Medical Center, Kansas  
City, Missouri.

SPOROTHRIX SCHENKII

ISAAC GINSBURG, M.Sc., Ph.D.

Professor of Microbiology, The Hebrew Uni-  
versity Hadassah, Faculty of Dental Medicine  
Founded by the Alpha Omega Fraternity;  
Chairman, Department of Oral Biology, Fac-  
ulty of Dental Medicine, Hebrew University;  
Member, Institute for Microbiology, Faculty of  
Medicine, Hebrew University Hadassah Med-  
ical Center, Jerusalem, Israel.

STREPTOCOCCUS

RUTH E. GORDON, Ph.D.

Professor of Microbiology, Waksman Institute  
of Microbiology, Rutgers, The State University  
of New Jersey, Piscataway, New Jersey.

NOCARDIA AND STREPTOMYCES

NANCY K. HALL, Ph.D.

Assistant Professor of Pathology, Health Sci-  
ence Center, University of Oklahoma, Okla-  
homa City, Oklahoma.

HISTOPLASMA CAPSULATUM

HERBERT S. HEINEMAN, M.D.

Clinical Professor of Medicine, Jefferson Med-  
ical College of Thomas Jefferson University;  
Attending Physician and Consultant in Infec-  
tious Diseases, Mercy Catholic Medical Center;  
Director, Public Health Laboratory, Depart-  
ment of Public Health, Philadelphia, Pennsyl-  
vania.

SHOCK IN INFECTIOUS DISEASES

SHALOM Z. HIRSCHMAN, M.D.

Professor of Medicine and Director, Division of  
Infectious Diseases, The Mount Sinai School of  
Medicine of The University of New York; At-

## CONTRIBUTORS

tending Physician, The Mount Sinai Hospital,  
New York, New York.  
HEPATITIS VIRUSES

MONTO HO, M.D.

Professor of Medicine and Microbiology, University of Pittsburgh; Chief, Division of Infectious Diseases, Presbyterian-University Hospital, Pittsburgh, Pennsylvania.

INTERFERON AND INTERFERENCE

BETTY C. HOBBS, D.Sc., Ph.D., Dip. Bact.,  
F.R.C.Path., F.R.S.H.

Director (Retired), Food Hygiene Laboratory, Central Public Health Laboratory, London, England; Consultant Microbiologist, Christian Medical and Brown Memorial Hospital, Punjab, India.

THE CLOSTRIDIA

PATRICIA A. HOFFEE, Ph.D.

Professor of Microbiology, University of Pittsburgh, School of Medicine, Pittsburgh, Pennsylvania.

BACTERIAL GENETICS

TOR HOFSTAD, M.D.

Associate Professor of Microbiology, Faculty of Medicine, University of Bergen; Chief Physician, Department of Microbiology, Haukeland Hospital, Bergen, Norway.

BACTEROIDES

MARIAN C. HORZINEK, D.V.M., Ph.D.

Professor of Virology and Head, Department of Virology, Veterinary Faculty, State University, Utrecht, The Netherlands.

TOGAVIRUSES

GERALD T. KEUSCH, M.D.

Professor of Medicine, Tufts University School of Medicine; Attending Physician, New England Medical Center Hospitals, Boston, Massachusetts.

MALNUTRITION AND INFECTION

MOGENS KILIAN, D.D.S., Ph.D.

Associate Professor of Microbiology, Royal Dental College, Aarhus, Denmark.

HAEMOPHILUS

HOWARD W. LARSH, Ph.D.

Research Professor of Microbiology, University of Oklahoma, Norman, Oklahoma; Director of Research and Laboratories, Missouri State Chest Hospital, Mt. Vernon, Missouri.

HISTOPLASMA CAPSULATUM

D. L. LEE, B.Sc., Ph.D.

Professor of Agricultural Zoology and Head of

Department of Pure and Applied Zoology, University of Leeds, Leeds, England.

CLASSIFICATION AND ANATOMY OF PARASITES

FRITZ LEHMANN-GRUBE, M.D.

Professor of Virology, University of Hamburg, Hamburg, Germany.

ARENAVIRUSES

STANLEY M. LEMON, M.D.

Assistant Professor of Medicine, Department of Virus Diseases, Walter Reed Army Institute of Research, Walter Reed Army Medical Center; Staff Physician, Walter Reed General Hospital; Staff Physician, Walter Reed Army Medical Center, Washington, D.C.

THE HERPESVIRUSES

G. PHILIP MANIRE, Ph.D.

Kenan Professor of Bacteriology and Immunology, Vice Chancellor and Dean of Graduate School, University of North Carolina, Chapel Hill, North Carolina.

THE CHLAMYDIAE

FRANCOIS MARIAT, Dr. es Sciences (Paris)

Professor, Institut Pasteur, Paris, France.

SPOROTHRIX SCHENCKII

ZELL A. McGEE, M.D.

Professor of Medicine, Vanderbilt University, School of Medicine; Director, George Hunt Laboratory; Chief, Division of Infectious Diseases, Department of Medicine, Vanderbilt University Hospital, Vanderbilt, Tennessee.

CELL WALL-DEFECTIVE BACTERIA; MYCOPLASMAS

JOSEPH L. MELNICK, Ph.D.

Distinguished Service Professor and Chairman, Department of Virology & Epidemiology, Baylor College of Medicine, Houston, Texas.

CLASSIFICATION OF VIRUSES

JOSEPH H. MILLER, M.S., Ph.D.

Professor of Medical Parasitology, Louisiana State University Medical Center; Visiting Scientist, The Charity Hospital in New Orleans, New Orleans, Louisiana.

THE PROTOZOA

SAROJ K. MISHRA, Ph.D.

Chief, Serodiagnostic Division, Robert Koch Institute, Berlin, Germany.

NOCARDIA AND STREPTOMYCES

SUSUMU MITSUHASHI, Ph.D. Dr. Med. Sci.

Professor, Department of Microbiology, and Director, Laboratory of Bacterial Resistance,

Gunma University, School of Medicine, Maebashi City, Japan.

#### RESISTANCE TO ANTIMICROBIAL DRUGS

STEPHEN A. MORSE, Ph.D.

Associate Professor, Department of Microbiology and Immunology, University of Oregon Health Sciences Center, Portland, Oregon.

#### NEISSERIA

STEPHEN I. MORSE, M.D. (Deceased)

Professor and Chairman, Microbiology and Immunology, State University of New York, Downstate Medical Center, Brooklyn, New York.

#### STAPHYLOCOCCI

DANIEL M. MUSER, M.D.

Professor of Medicine, Professor of Microbiology and Immunology, Baylor College of Medicine; Chief, Infectious Disease Section, Veterans Administration Hospital, Houston, Texas.

#### SPIROCHETES: TREPONEMA AND BORRELLIA

HAROLD C. NEU

Professor of Medicine and Pharmacology, Columbia University, College of Physicians and Surgeons; Chief of Infectious Diseases Columbia-Presbyterian Medical Center, New York, New York.

#### PHARMACOLOGY AND TOXICOLOGY OF ANTIMICROBIAL AGENTS

FRITS ØRSKOV, M.D.

Collaborative Centre for Reference and Research on Escherichia (WHO), Statens Serum-institut, Copenhagen, Denmark.

#### ENTEROBACTERIACEAE

IDA ØRSKOV, M.D.

Collaborative Centre for Reference and Research on Escherichia (WHO), Statens Serum-institut, Copenhagen, Denmark.

#### ENTEROBACTERIACEAE

MICHAEL N. OXMAN, M.D.

Professor of Medicine and Pathology, University of California, San Diego, School of Medicine; Chief, Infectious Diseases and Clinical Virology Sections, Veterans Administration, Administration Medical Center, San Diego, California.

#### PAPOVAVIRUSES

JOSEPH S. PAGANO, M.D.

Director, Cancer Research Center, and Professor of Medicine and of Bacteriology and Immunology, University of North Carolina at Chapel Hill School of Medicine; Attending

Physician in Medicine and Infectious Disease, North Carolina Memorial Hospital, Chapel Hill, North Carolina.

#### THE HERPESVIRUSES

ZBIGNIEW S. PAWLOWSKI, M.D.,  
D.T.M.&H.

Professor of Medical Parasitology, Medical Faculty, Academy of Medicine, Poznan, Poland; Chief, Clinic of Parasitic and Tropical Diseases, Academy of Medicine, Poznan, Poland.

#### PLATYHELMINTHES

LENNART PHILIPSON, M.D., Dr. Med. Sci.

Professor of Microbiology, Uppsala University, Uppsala, Sweden.

#### ADENOVIRUS

M. J. PICKETT, Ph.D.

Professor of Microbiology, University of California, Los Angeles, California.

#### GENUS PSEUDOMONAS

LEO PINE, B.S., M.S., Ph.D.

Chief, Products Development Branch, Biological Products Division, Center for Disease Control, Atlanta, Georgia.

#### ACTINOMYCES AND MICROAEROPHILIC ACTINOMYCETES

BOSKO POSTIC, M.D.

Professor of Medicine, University of South Carolina, School of Medicine; Chief, Medical Service, William Jennings Bryan Dorn Veterans Hospital, Columbia, South Carolina.

#### RHABDOVIRUS

C. R. PRINGLE, B.Sc., Ph.D.

Honorary Lecturer, University of Glasgow; Member of the Medical Research Council, MRC Virology Unit, Glasgow, Scotland.

#### THE GENETICS OF VIRUSES

T. RAMAKRISHNAN, M.Sc., Ph.D.

Professor, Microbiology and Cell Biology Laboratory, Indian Institute of Science, Bangalore, India.

#### BACTERIAL PHYSIOLOGY

G. RAMANANDA RAO, M. Pharm., Ph.D.

Assistant Professor, Microbiology and Cell Biology Laboratory, Indian Institute of Science, Bangalore, India.

#### BACTERIAL PHYSIOLOGY

GARRISON RAPMUND, M.D.

Brigadier General, MC, US Army; Assistant Surgeon General (Research and Development), Department of the Army, Washington, D.C.

#### RICKETTSIA

**DOUGLAS D. RICHMAN, M.D.**

Assistant Professor of Pathology and Medicine,  
University of California, San Diego, School of  
Medicine; Attending Physician, Veterans Ad-  
ministration Medical Center, San Diego, Cali-  
fornia.

**ORTHOMYXOVIRUSES AND PARAMYXOVIRUSES****DAVID L. RINGO, Ph.D.**

Assistant Research Biologist, University of  
California, Santa Cruz, California.

**THE STRUCTURE OF THE BACTERIAL CELL****HOWARD J. SAZ, Ph.D.**

Professor of Biology, University of Notre Dame,  
Notre Dame, Indiana.

**BIOCHEMISTRY OF PARASITES: HELMINTHS****H. P. R. SEELIGER, M.D.**

Full Professor of Hygiene and Microbiology  
and Director of Institute of Hygiene, Bayer-  
ische Julius-Maximilians-Universität, Wuerz-  
burg, Federal Republic of Germany.

**LISTERIA MONOCYTOGENES****SMITH SHADOMY, Ph.D.**

Professor of Medicine and Microbiology, Med-  
ical College of Virginia, Virginia Common-  
wealth University, Richmond, Virginia.

**BLASTOMYCES AND PARACOCIDIOMYCES****RUDOLF SIEGERT, M.D.**

Professor of Medical Microbiology, Institute of  
Hygiene, Philipps-Universität, Marburg, Fed-  
eral Republic of Germany.

**MARBURG VIRUS AND EBOLA VIRUS****SAMUEL C. SILVERSTEIN, M.D.**

Associate Professor and Physician, Laboratory  
of Cellular Physiology and Immunology, Rocke-  
feller University; Physician, Rockefeller Uni-  
versity Hospital, New York, New York.

**VIRAL REPLICATION****IRVING J. SLOTNICK, Ph.D.**

Chief Microbiologist, Cedars Sinai Medical  
Center, Los Angeles, California.

**ACTINOBACILLUS AND CARDIOBACTERIUM****DONALD W. SMITH, Ph.D.**

Professor of Medical Microbiology, University  
of Wisconsin, Madison, Wisconsin.

**MYCOBACTERIA****STEPHEN A. SPECTOR, M.D.**

Assistant Professor of Pediatrics, University of  
California, San Diego, School of Medicine; As-  
sistant Professor of Pediatrics, Division of In-  
fectious Diseases, University of California,

San Diego, University Hospital, San Diego,  
California.

**IMMUNOPROPHYLAXIS AND IMMUNOTHERAPY****WESLEY W. SPINK, A.B., M.D.**

Emeritus Regents' Professor of Medicine and  
Comparative Medicine, University of Minne-  
sota Medical School; Staff Member, University  
of Minnesota Hospitals, Minneapolis, Minne-  
sota.

**BRUCELLA****NEVILLE F. STANLEY, B.Sc., D.Sc.,**

F.R.A.C.P.(Hon.), M.A.S.M.

Professor and Chairman, Department of Micro-  
biology, University of Western Australia; Di-  
rector, Clinical Microbiology Services, Queen  
Elizabeth II Medical Centre, Perth, Western  
Australia.

**REOVIRIDAE PATHOGENIC FOR MAN****WILLARD ALLEN TABER**

Professor, Department of Biology, Texas A & M  
University, College of Sciences, College Sta-  
tion, Texas.

**CLASSIFICATION OF FUNGI****DAVID TAYLOR-ROBINSON, M.D.**

Division of Communicable Diseases, M.R.C.  
Clinical Research Centre; Hon. Consultant Mi-  
crobiologist, Northwick Park Hospital, Harrow,  
Middlesex, England.

**MYCOPLASMAS****D. A. J. TYRRELL, C.B.E., M.D., D.Sc.,**

F.R.C.P., F.R.C.Path., F.R.S.

Head, Division of Communicable Diseases,  
Clinical Research Centre; Consultant Physi-  
cian, Northwick Park Hospital, Harrow,  
Middlesex, London, England.

**CORONAVIRUS****WILLIAM EDWARD VAN HEYNINGEN, Ph.D.,**

Sc.D., D.Sc.  
Emeritus Reader in Bacterial Chemistry, Sir  
William Dunn School of Pathology, University  
of Oxford, Oxford, England.

**BACTERIAL EXOTOXINS****HENRY A. WALCH, Ph.D.**

Professor of Microbiology, San Diego State Uni-  
versity, San Diego, California.

**COCCIDIOMYCES IMMITIS****TADEUSZ J. WIKTOR, D.V.M.**

Member, The Wistar Institute, Philadelphia,  
Pennsylvania.

**RHABDOVIRUS**



**ROBERT P. WILLIAMS**

Professor of Microbiology and Immunology,  
Baylor College of Medicine, Houston, Texas.  
**BACILLUS ANTHRACIS AND OTHER AEROBIC  
SPORE-FORMING BACILLI**

**SHELDON M. WOLFF, M.D.**

Endicott Professor and Chairman, Department  
of Medicine, Tufts University School of Medi-  
cine; Physician-in-Chief, New England Medical  
Center Hospital, Boston Massachusetts.

**FEVER**

**NATHANIEL A. YOUNG, M.D. (Deceased)**

Head, Viral Oncology and Molecular Pathology  
Sections, Laboratory of Pathology, National  
Institutes of Health; Senior Attending Physi-  
cian in Infectious Diseases, Clinical Center,  
National Institutes of Health, Bethesda, Mary-  
land.

**PICORNAVIRUSES**

**JULIUS S. YOUNGNER, Sc.D.**

Professor and Chairman, Department of Micro-  
biology, University of Pittsburgh, School of  
Medicine, Pittsburgh, Pennsylvania.

**PERSISTENT VIRAL INFECTIONS**

# PREFACE

Soon after we set out to prepare a comprehensive textbook of microbiology we realized that the subject matter was too vast for a few authors to handle. We decided instead to call upon leading experts throughout the world to write individual chapters on subjects that belong to their areas of acknowledged authority. This international approach allowed us to go beyond the limitations imposed by the usual institutional, regional, or even national boundaries that most textbooks must observe in their authorship and to produce the first multi-authored international textbook of microbiology. Seventy-one authors have contributed 88 chapters to this new systematic textbook.

In addition to striving for authenticity, we have tried to give students a cohesive account of all aspects of microbiology. This was done by presenting the information in three sections that would give a logical progression from general principles to specific information. Because the contributors are both scientists and teachers, they have presented their material in a way that lets even the beginning student understand this complicated subject. Students concerned primarily with the basic aspects of microbiology will find complete presentations of microbial genetics, biochemistry, morphogenesis, physiology, latency, and taxonomy. These fundamental topics are covered not only with respect to bacteria and viruses but to mycology and parasitology as well. Students with a special interest in fungi or parasites should

find this textbook valuable because it satisfies their need for information in their own fields and also allows them to refer to closely related information dealing with the other microbial agents. It should be noted that the parasitology in this book is not restricted to invasive agents but presents extensive coverage of ectoparasites and other arthropods important to entomologists.

The chapters on specific microbial agents will meet the needs of the special areas of microbiology. For the medical technologist there are complete diagnostic data on every organism of medical importance; for the experimental pathologist and immunologist there is an extensive analysis of the pathogenic properties and immune reactions for each pathogenic agent; for the pharmacist and pharmacologist there are the essentials of antimicrobial chemotherapy; and for the epidemiologist there are sections in each chapter dealing with the prevalence, mode of spread, and protection against each specific microbial agent.

This textbook plus a larger section on specific infectious diseases is also published under the title of *Medical Microbiology and Infectious Diseases* by the same publisher.

For all this we thank our many distinguished authors who gave generously of their time, expert knowledge, and teaching skills. We hope this book will justify their valuable efforts by helping students learn microbiology throughout the world.

# CONTENTS

## I. MICROBIOLOGY

### A. General Microbiology

#### Bacteriology

1. The Structure of the Bacterial Cell ..... 1  
*Eugene H. Cota-Robles, Ph.D., and David L. Ringo, Ph.D.*
2. Classification and Identification of Bacteria ..... 9  
*Herman Baer, M.D., and Charles E. Davis, M.D.*
3. Bacterial Physiology ..... 21  
*T. Ramakrishnan, M.Sc., Ph.D., and  
G. Ramananda Rao, M. Pharm., Ph.D.*
4. Bacterial Genetics ..... 36  
*Patricia A. Hoffee, Ph.D.*
5. Bacterial Exotoxins ..... 51  
*William Edward van Heyningen, Ph.D., Sc.D.*
6. Bacterial Endotoxins ..... 63  
*Abraham I. Braude, M.D.*

#### Virology

7. Morphology and Structure of Viruses ..... 75  
*Richard W. Compans, Ph.D.*
8. Classification of Viruses ..... 83  
*Joseph L. Melnick, Ph.D.*
9. Viral Replication ..... 94  
*Samuel C. Silverstein, M.D.*
10. The Genetics of Viruses ..... 110  
*C. R. Pringle, B.Sc., Ph.D.*
11. Persistent Viral Infections ..... 121  
*Julius S. Youngner, Sc.D.*
12. Interferon and Interference ..... 128  
*Monto Ho, M.D.*

**Mycology**

13. Morphology and Structure of Fungi..... 134  
Vladimir Farkaš, Ph.D.
14. Classification of Fungi..... 147  
Willard A. Taber, Ph.D.
15. Fungal Toxins..... 156  
Makoto Enomoto, M.D.

**Parasitology**

16. Classification and Anatomy of Parasites..... 162  
D. L. Lee, B.Sc., Ph.D.
17. Biochemistry of Parasites: Helminths..... 184  
Howard J. Saz, Ph.D.
18. Arthropods of Medical Importance ..... 196  
A. L. Dohany, Ph.D., and John J. S. Burton, Ph.D.

**Principles of Antimicrobial Chemotherapy of Infections**

19. Description of Antimicrobial Drugs..... 210  
Abraham I. Braude, M.D., Ph.D.
20. Mechanisms of Action of Antimicrobial Drugs..... 234  
Abraham I. Braude, M.D., Ph.D.
21. Resistance to Antimicrobial Drugs..... 247  
Susumu Mitsuhashi, Ph.D., Dr. Med. Sci., and  
Abraham I. Braude, M.D., Ph.D.
22. The Pharmacology and Toxicology of Antimicrobial Agents ..... 257  
Harold C. Neu, M.D.

**B. Specific Microbial Agents of Disease****1. AEROBIC BACTERIA OR FACULTATIVELY ANAEROBIC BACTERIA****Gram-Positive Cocci**

23. Staphylococci..... 275  
Stephen I. Morse, M.D.
24. Streptococcus..... 281  
Isaac Ginsburg, M.Sc., Ph.D.

**Gram-Positive Rods**

25. Diphtheria Bacilli and Other Corynebacteria ..... 295  
Lane Barksdale, Ph.D.
26. *Listeria Monocytogenes* ..... 306  
H. P. R. Seeliger, M.D.
27. *Erysipelothrix Rhusiopathiae* ..... 310  
Charles E. Davis, M.D.

28. <i>Bacillus Anthracis and Other Aerobic Spore-Forming Bacilli</i> .....	315
<i>Robert P. Williams, Ph.D.</i>	
<i>Gram-Negative Cocci and Coccobacilli</i>	
29. <i>Neisseria</i> .....	326
<i>Stephen A. Morse, Ph.D.</i>	
30. <i>Moraxella and Acinetobacter</i> .....	334
<i>Herman Baer, M.D.</i>	
<i>Gram-Negative Rods</i>	
31. <i>Enterobacteriaceae</i> .....	340
<i>Frits Ørksø, M.D., and Ida Ørksø, M.D.</i>	
32. <i>Vibrios</i> .....	353
<i>Barun Deb Chatterjee, M.B.B.S., Ph.D.</i>	
33. <i>Genus Pseudomonas</i> .....	365
<i>M. J. Pickett, Ph.D.</i>	
34. <i>Brucella</i> .....	374
<i>Wesley W. Spink, A.B., M.D.</i>	
35. <i>Bordetella</i> .....	379
<i>Jean M. Dolby, Ph.D.</i>	
36. <i>Haemophilus</i> .....	387
<i>Mogens Kilian, D.D.S., Ph.D.</i>	
37. <i>Yersinia, Pasteurella, and Francisella</i> .....	393
<i>T. H. Chen, M.D., and Sanford S. Elberg, Ph.D.</i>	
38. <i>Streptobacillus Moniliformis</i> .....	408
<i>Joshua Fierer, M.D.</i>	
39. <i>Actinobacillus and Cardiobacterium</i> .....	410
<i>Irving J. Slotnick, Ph.D.</i>	
<i>Acid-Fast Rods</i>	
40. <i>Mycobacteria</i> .....	416
<i>Donald W. Smith, Ph.D.</i>	
41. <i>Nocardia and Streptomyces</i> .....	425
<i>Saroj K. Mishra, Ph.D., and Ruth E. Gordon, Ph.D.</i>	
<i>Spirochetes</i>	
42. <i>Leptospira</i> .....	437
<i>A. D. Alexander, Ph.D.</i>	
2. ANAEROBIC BACTERIA	
43. <i>Gram-Positive Cocci: Peptococcus, Peptostreptococcus, Streptococcus (Anaerobic), and Sarcina</i> .....	443
<i>Howard Robert Attebery, D.D.S.</i>	



44.	Actinomyces and Microaerophilic Actinomycetes .....	449
	<i>Leo Pine, Ph.D.</i>	
45.	The Clostridia .....	467
	<i>Betty C. Hobbs, Ph.D., D.Sc., F.R.C.Path., Dip.Bact.</i>	
46.	Bacteroides .....	480
	<i>Tor Hofstad, M.D.</i>	
47.	Fusobacteria .....	485
	<i>Howard Robert Attebery, D.D.S.</i>	
48.	Veillonella .....	488
	<i>Howard Robert Attebery, D.D.S.</i>	
49.	Spirochetes: Treponema and Borrelia .....	490
	<i>Daniel M. Musher, M.D.</i>	
3.	UNIQUE INTRACELLULAR GRAM-NEGATIVE BACTERIA	
50.	Rickettsia .....	495
	<i>Garrison Rapmund, M.D.</i>	
51.	Bartonella Bacilliformis.....	510
	<i>Manuel Cuadra, M.D.</i>	
52.	The Chlamydiae .....	516
	<i>G. Philip Manire, Ph.D.</i>	
4.	MYCOPLASMAS AND L-FORMS	
53.	Mycoplasmas.....	522
	<i>Zell A. McGee, M.D., and David Taylor-Robinson, M.D.</i>	
54.	Cell Wall-Defective Bacteria.....	529
	<i>Zell A. McGee, M.D.</i>	
5.	VIRUSES	
	DNA Viruses	
55.	Adenovirus .....	533
	<i>Lennart Philipson, M.D., Dr. Med. Sci.</i>	
56.	The Herpesviruses .....	541
	<i>Joseph S. Pagano, M.D., and Stanley M. Lemon, M.D.</i>	
57.	Poxviruses .....	549
	<i>Abraham I. Braude, M.D., Ph.D.</i>	
58.	Papovaviruses .....	556
	<i>Michael N. Oxman, M.D.</i>	
	RNA Viruses	
59.	Orthomyxoviruses and Paramyxoviruses .....	569
	<i>Douglas D. Richman, M.D.</i>	
60.	Picornaviruses.....	585
	<i>Nathaniel A. Young, M.D.</i>	

61. Togaviruses.....	592
<i>Marian C. Horzinek, D.V.M., Ph.D.</i>	
62. Arenaviruses.....	602
<i>Fritz Lehmann-Grube, M.D.</i>	
63. Reoviridae Pathogenic for Man.....	610
<i>Neville F. Stanley, D.Sc.</i>	
64. Rhabdovirus.....	616
<i>Bosko Postic, M.D., and Tadeusz J. Wiktor, D.V.M.</i>	
65. Coronavirus.....	619
<i>D. A. J. Tyrrell</i>	
66. Marburg Virus and Ebola Virus.....	621
<i>Rudolf Siegert, M.D.</i>	
<b>Unclassified Viruses</b>	
67. Hepatitis Viruses.....	627
<i>Shalom Z. Hirschman, M.D.</i>	
<b>6. FUNGI</b>	
68. Cryptococcus.....	634
<i>Charles E. Davis, M.D.</i>	
69. Candida and Torulopsis.....	643
<i>Abraham I. Braude, M.D., Ph.D.</i>	
70. Sporothrix Schenckii.....	650
<i>F. Mariat, Dr. es Sciences, and R. G. Garrison, Ph.D.</i>	
71. Histoplasma Capsulatum.....	654
<i>Howard W. Larsh, Ph.D., and Nancy K. Hall, Ph.D.</i>	
72. Coccidioides Immitis.....	658
<i>Henry A. Walch, Ph.D.</i>	
73. Blastomyces and Paracoccidioides.....	665
<i>Smith Shadomy, Ph.D., and Dennis M. Dixon, Ph.D.</i>	
74. The Aspergilli.....	669
<i>Abraham I. Braude, M.D., Ph.D.</i>	
75. The Zygomycetes.....	675
<i>Abraham I. Braude, M.D., Ph.D.</i>	
76. Dematiaceae: Agents of Chromomycosis.....	680
<i>Yousef Al-Doory, Ph.D.</i>	
77. Miscellaneous Fungi: The Agents of Mycetoma and Rhinosporidium.....	684
<i>Abraham I. Braude, M.D., Ph.D.</i>	
<b>7. PARASITES</b>	
78. The Protozoa.....	688
<i>Joseph H. Miller, M.S., Ph.D.</i>	

79. *Nemathelminthes* (Roundworms) ..... 704  
*A. O. Anya, Ph.D.*
80. *Platyhelminthes* ..... 726  
*Zbigniew S. Pawlowski, M.D.*

### C. General Response to Infection

#### Immunologic

81. Mechanisms of Natural Resistance to Infection ..... 739  
*Abraham I. Braude, M.D., Ph.D.*
82. Mechanisms of Acquired Resistance to Infection ..... 757  
*Abraham I. Braude, M.D., Ph.D.*
83. Mechanisms of Immunologic Injury in Infectious Diseases ..... 764  
*Abraham I. Braude, M.D., Ph.D.*
84. Immunoprophylaxis and Immunotherapy ..... 770  
*Stephen A. Spector, M.D.*

#### Metabolic

85. Fever ..... 794  
*Sheldon M. Wolff, M.D.*
86. Shock in Infectious Diseases ..... 796  
*Herbert S. Heineman, M.D.*
87. Metabolic Effects of Infection ..... 803  
*William R. Beisel, M.D.*
88. Malnutrition and Infection ..... 808  
*Gerald T. Keusch, M.D.*

## II. CLINICAL INFECTIOUS DISEASES

### A. Upper Respiratory and Oral Infections

89. Pharyngitis and Tonsillitis ..... 813  
*Hans A. Valkenburg, M.D., Ph.D.*
90. Diphtheria ..... 817  
*Richard V. McCloskey, M.S., M.D.*
91. Vincent's Infection ..... 823  
*Howard Robert Attebery, D.D.S.*
92. Sinusitis ..... 825  
*Paul B. van Cauwenberge, M.D.*
93. Otitis Media and Otitis Externa ..... 834  
*Burt R. Meyers, M.D., and William Lawson, M.D., D.D.S.*
94. Epiglottitis and Pseudocroup ..... 841  
*Paula Branefors, M.D., Ph.D.*

# I Microbiology

## A. GENERAL MICROBIOLOGY

### Bacteriology

## THE STRUCTURE OF THE BACTERIAL CELL

1

Eugene H. Cota-Robles, Ph.D.  
and David L. Ringo, Ph.D.

The structure of bacteria can be best understood by contrasting their cellular organization to that of the higher biologic forms — animals, plants, protozoa, algae, and fungi. In these life forms the cells are divided into internal compartments by membrane systems. These compartments (cellular *organelles*) have specific activities for the maintenance of the life functions of the cell. The nuclear compartment (*nucleus*) contains the cell's hereditary material, *deoxyribonucleic acid* (DNA). The nucleus is separated by a nuclear membrane from the rest of the cell, the *cytoplasm*. The DNA of higher cells is organized in two or more chromosomes.

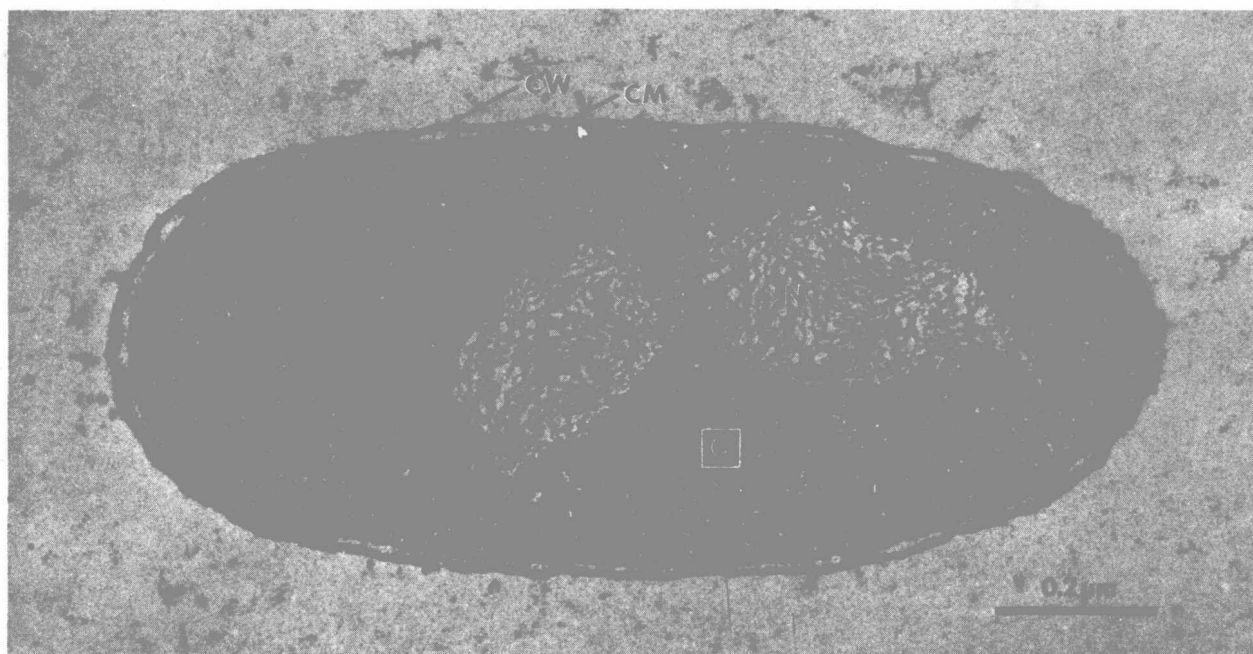
Bacterial cells are not compartmentalized and therefore are considered to lack organelles. The hereditary material of bacteria consists of a single chromosome. This bacterial *nucleoid* is a single, tightly bundled, long strand of DNA that lies within the cytoplasm not surrounded by a nuclear membrane. For this reason bacteria are referred to as *prokaryotic*, that is, having a primitive nuclear structure; and higher cells are designated as *eukaryotic*, literally, having a true nucleus. All bacteria (as well as the blue-green algae) possess the prokaryotic form of organization.

In a broad sense, all types of cells function in the same manner. The information stored in the DNA is transcribed as *messenger ribonucleic acid* (mRNA), which moves from the nucleus into the cytoplasm. Here the messenger RNA attaches to

ribosomes, where the genetic information is translated into specific proteins by the polymerization of amino acids. The synthesis of proteins is one of the most basic of cell processes, since virtually every metabolic activity of the cell is mediated by enzymes, the proteins that catalyze specific chemical reactions.

The basic function of a bacterial cell is to assimilate chemicals from its environment in order to grow and divide. Some bacteria perform these functions by using the simplest inorganic chemicals (carbon dioxide and minerals), and are termed *autotrophs*. Certain members of this group, photosynthetic bacteria and blue-green algae, rely on light as a source of energy and thus resemble plants in their photoautotrophic metabolism. Another and larger group of bacteria, the *heterotrophs*, use simple organic molecules from their environment as a source of energy and as building blocks for cellular material. Many of this latter group have adapted to growth within the animal body. Some are harmless symbionts, such as *Escherichia coli*, which normally inhabits the mammalian gut. Others are harmful and may cause human disease. These bacteria are termed *pathogens*, and their infection of body tissues results in a characteristic illness. Many of the features of bacterial cell structure are related, in one way or another, to their role as disease organisms and to the ways in which these diseases are treated and controlled.





**FIGURE 1.** This electron micrograph outlines the organization that is common to all bacterial cells. The nucleoid (N) occupies the central area of the cell; the cytoplasm (C) contains many ribosomes (individual dark granules); a cytoplasmic membrane (CM) and cell wall (CW) surround the cell. This bacterium, *Alteromonas espejiana*, is a marine pseudomonad that possesses a very simple wall structure.

The generalized structure of a typical bacterial cell is shown in Figure 1. The prokaryotic cell consists of a cell wall, a cytoplasmic membrane surrounding a cytoplasm packed with ribosomes, and a more or less central nucleoid. The figure is an example of the image produced by the electron microscope of a very thin section cut through a chemically preserved (fixed) bacterium. It is possible to determine the overall shape and size of such a bacterial cell with the light microscope, but details that are smaller than about  $0.2\ \mu\text{m}$  cannot be resolved (Table 1). Thus, the internal structure of the bacterium can be deduced only through the use of the higher resolving power of the electron microscope, and all such detailed knowledge has been obtained only within the past 25 years.

**TABLE 1.** Units Used to Describe Bacteria and their Structures, and the Useful Limits of Resolution of the Human Eye, the Light Microscope, and the Electron Microscope

**Units:**

- $1\ \text{m} \times 10^{-3} = 1\ \text{mm}$  (millimeter)
- $1\ \text{mm} \times 10^{-3} = 1\ \mu\text{m}$  (micrometer or micron)
- $1\ \mu\text{m} \times 10^{-3} = 1\ \text{nm}$  (nanometer)

**Limits of Resolving Power:**

- Unaided human eye:  $0.2\ \text{mm}$
- Compound light microscope:  $0.2\ \mu\text{m}$
- Transmission electron microscope:  $2\ \text{nm}$  to  $0.2\ \text{nm}$

### NUCLEOID

Embedded in the ribosome-rich cytoplasm is the bacterial genetic apparatus, the nucleoid. No boundary separates it from the rest of the cytoplasm; the nucleoid's physical segregation is maintained by the very nature of the DNA that is its make up. The DNA consists of one very long and narrow molecule — a double helix — which if stretched to its full length would measure more than  $1.0\ \text{mm}$  long and only  $0.000002\ \text{mm}$  ( $2\ \text{nm}$ ) wide. Genetic analysis has shown that most of the bacterial genes are linked to one another in an orderly fashion, and, moreover, that the linkage is continuous and circular. We therefore describe the bacterial nucleoid as a single, circular chromosome. Physical studies also demonstrate that the DNA strand of the chromosome is a circle that is tightly coiled into a bundle to produce the nucleoid image shown with the electron microscope. The chromosome replicates in the growing cell in preparation for cell division. Bacterial cells divide by binary fission into two daughter cells, each of which retains a copy of the chromosome. A small percentage of the cell's genetic information is present as much smaller DNA molecules, *plasmids*, which may be present in many copies and replicate independently. Bacterial plasmids often carry the genes involved in resistance to chemotherapeutic drugs. Plasmids cannot be observed