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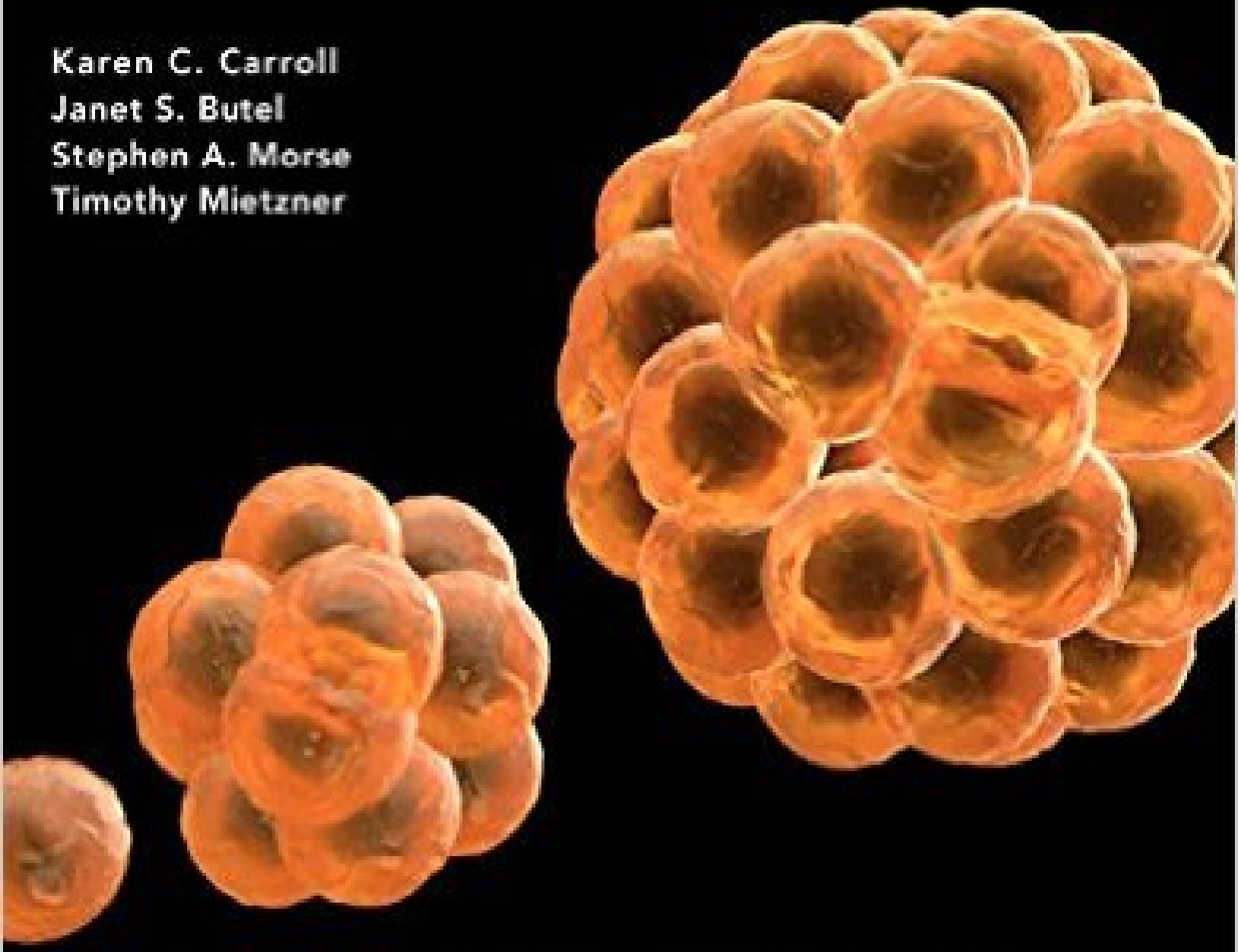

Jawetz, Melnick & Adelberg's

# MEDICAL MICROBIOLOGY

27th Edition

Mc Graw Hill Education
LANGE®

## SELECTED MEDICALLY IMPORTANT MICROORGANISMS

### *I. BACTERIA*

**AEROBIC AND FACULTATIVE BACTERIA**

**GRAM-POSITIVE COCCI**

**Catalase-Positive**

*Staphylococcus aureus*
*Staphylococcus epidermidis*
*Staphylococcus intermedius*
*Staphylococcus lugdunensis*
*Staphylococcus saprophyticus*
*Staphylococcus* species

**Catalase-Negative**

*Aerococcus* species
*Enterococcus faecalis*
*Enterococcus faecium*
*Enterococcus* species
*Gemella* species
*Lactococcus* species
*Leuconostoc* species
*Pediococcus* species
*Streptococcus agalactiae* (Group B)
*Streptococcus canis* (Group G)
*Streptococcus gallolyticus* (Group D, formerly *S. bovis*)
*Streptococcus infantarius* (Group D, formerly *S. bovis*)
*Streptococcus pneumoniae*
*Streptococcus pyogenes* (Group A)
Viridans group streptococci
*Streptococcus anginosus*
*Streptococcus constellatus*
*Streptococcus intermedius*
*Streptococcus mitis*
*Streptococcus mutans*
*Streptococcus salivarius*
*Streptococcus sanguis*
*Abiotrophia* species (nutritionally variant streptococci)
*Granulicatella* species (nutritionally variant streptococci)

**GRAM-NEGATIVE COCCI**

*Moraxella catarrhalis*
*Neisseria gonorrhoeae*
*Neisseria meningitidis*
*Neisseria* species

**GRAM-POSITIVE BACILLI**

*Arcanobacterium* species
*Bacillus anthracis*
*Bacillus cereus*
*Corynebacterium diphtheriae*
*Corynebacterium jeikeium*
*Corynebacterium* species
*Corynebacterium urealyticum*
*Erysipelothrix rhusiopathiae*
*Gardnerella vaginalis*
*Gordonia* species
*Listeria monocytogenes*
*Mycobacterium abscessus*
*Mycobacterium avium*
*Mycobacterium bovis*
*Mycobacterium chelonae*
*Mycobacterium fortuitum*
*Mycobacterium intracellulare*
*Mycobacterium kansasii*
*Mycobacterium leprae*
*Mycobacterium marinum*
*Mycobacterium tuberculosis*
*Mycobacterium* species
*Nocardia asteroides*
*Rhodococcus equi*
*Tropheryma whippeli*
*Tsukamurella* species

**GRAM-NEGATIVE BACILLI**

**Enterobacteriaceae**

*Citrobacter freundii*
*Citrobacter koseri*
*Citrobacter* species
*Cronobacter sakazakii*
*Edwardsiella tarda*
*Enterobacter aerogenes*
*Enterobacter cloacae*
*Escherichia coli*
*Escherichia* species
*Klebsiella oxytoca*
*Klebsiella granulomatis*
*Klebsiella pneumoniae*
*Klebsiella pneumoniae subspecies rhinocscleromatis*
*Morganella morganii*
*Plesiomonas shigelloides*
*Proteus mirabilis*
*Proteus vulgaris*
*Providencia alcalifaciens*
*Providencia rettgeri*
*Providencia stuartti*
*Salmonella* Choleraesuis
*Salmonella* Paratyphi A
*Salmonella* Paratyphi B
*Salmonella* Typhi
*Salmonella* species
*Serratia liquefaciens*
*Serratia marcescens*
*Shigella boydii*
*Shigella dysenteriae*
*Shigella flexneri*
*Shigella sonnei*
*Yersinia enterocolitica*
*Yersinia pestis*
*Yersinia pseudotuberculosis*

**Nonenterobacteriaceae—Fermentative Bacilli**

*Aeromonas caviae*
*Aeromonas hydrophila*
*Aeromonas* species
*Aeromonas veronii biovar sobria*
*Pasteurella multocida*
*Vibrio cholerae*
*Vibrio parahaemolyticus*
*Vibrio* species
*Vibrio vulnificus*

**Nonenterobacteriaceae—Nonfermentative Bacilli**

*Acinetobacter* species
*Alcaligenes* species
*Brevundimonas* species
*Burkholderia cepacia*
*Burkholderia mallei*
*Burkholderia pseudomallei*
*Chryseobacterium* species
*Comamonas* species
*Eikenella corrodens*
*Moraxella* species
*Pseudomonas aeruginosa*
*Pseudomonas fluorescens*
*Pseudomonas* species
*Ralstonia pickettii*
*Roseomonas* species
*Shewanella putrefaciens*
*Sphingobacterium* species
*Sphingomonas* species
*Stenotrophomonas maltophilia*

**OTHER GRAM-NEGATIVE BACILLI AND COCCOBACILLI**

*Aggregatibacter (Actinobacillus) actinomycetemcomitans*
*Aggregatibacter (Haemophilus) aphrophilus*
*Arcobacter* species
*Bartonella bacilliformis*
*Bartonella henselae*
*Bartonella* species
*Bordetella bronchiseptica*
*Bordetella parapertussis*
*Bordetella pertussis*
*Bordetella* species
*Brucella melitensis*
*Brucella* species
*Campylobacter fetus*
*Campylobacter jejuni*
*Campylobacter* species
*Capnocytophaga* species
*Cardiobacterium hominis*
*Chlamydophila pneumoniae*
*Chlamydophila psittaci*
*Chlamydia trachomatis*
*Ehrlichia chaffeensis*
*Francisella tularensis*
*Haemophilus aegyptius*
*Haemophilus ducreyi*
*Haemophilus influenzae*
*Haemophilus parainfluenzae*
*Haemophilus* species
*Helicobacter pylori*
*Kingella kingae*
*Legionella micdadei*
*Legionella pneumophila*
*Legionella* species
*Orientia tsutsugamushi*
*Streptobacillus moniliformis*

**MYCOPLASMAS**

*Mycoplasma genitalium*
*Mycoplasma hominis*
*Mycoplasma pneumoniae*
*Mycoplasma* species
*Ureaplasma urealyticum*

**RICKETTSIA AND RELATED ORGANISMS**

**Anaplasma**

**Ehrlichia**

*Ehrlichia chaffeensis*
*Ehrlichia ewingii*

**Rickettsia**

*Rickettsia akari*
*Rickettsia conorii*
*Rickettsia mooseri*
*Rickettsia prowazekii*
*Rickettsia rickettsii*

**SPIRAL ORGANISMS**

*Borrelia burgdorferi*
*Borrelia recurrentis*
*Leptospira interrogans*
*Treponema pallidum*

**ANAEROBIC BACTERIA**

**GRAM-NEGATIVE BACILLI**

*Bacteroides fragilis* group
*Bacteroides ovatus*
*B distasonis*
*B thetaiotamicron*
*B vulgatus*
*Bacteroides* species
*Fusobacterium necrophorum*
*Fusobacterium nucleatum*
*Mobiluncus* species

(*Continued on inside back cover*)

a LANGE medical book

# Jawetz, Melnick, & Adelberg's Medical Microbiology

## Twenty-Seventh Edition


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# Contents

Preface **xii**

SECTION

## FUNDAMENTALS OF MICROBIOLOGY 1

*Stephen A. Morse, PhD and Timothy A. Meitzner, PhD*

1. **The Science of Microbiology 1**
   Introduction **1**
   Biologic Principles Illustrated by Microbiology **1**
   Viruses **2**
   Prions **3**
   Prokaryotes **4**
   Protists **7**
   Chapter Summary **9**
   Review Questions **9**
2. **Cell Structure 11**
   Optical Methods **11**
   Eukaryotic Cell Structure **13**
   Prokaryotic Cell Structure **15**
   Staining **38**
   Morphologic Changes During Growth **39**
   Chapter Summary **40**
   Review Questions **40**
3. **Classification of Bacteria 43**
   Taxonomy—The Vocabulary of Medical Microbiology **43**
   Criteria for Identification of Bacteria **43**
   Classification Systems **46**
   Description of the Major Categories and Groups of Bacteria **48**
   Nonculture Methods for the Identification of Pathogenic Microorganisms **52**
   Objectives **53**
   Review Questions **53**
4. **Growth, Survival, and Death of Microorganisms 55**
   Survival of Microorganisms in the Natural Environment **55**
   The Meaning of Growth **55**
   Exponential Growth **56**
   The Growth Curve in Batch Culture **57**
   Maintenance of Cells in the Exponential Phase **58**
   Growth in Biofilms **58**
   Definition and Measurement of Death **59**
   Environmental Control of Microbial Growth **59**
   Strategies to Control Bacteria at the Environmental Level **59**
   General Mechanisms of Biocide Action **60**
   Specific Actions of Selected Biocides **63**
   Relationship of Biocide Concentration and Time on Antimicrobial Killing **64**
   Summary **65**
   Key Concepts **65**
   Review Questions **66**
5. **Cultivation of Microorganisms 69**
   Requirements for Growth **69**
   Sources of Metabolic Energy **69**
   Nutrition **70**
   Environmental Factors Affecting Growth **71**
   Cultivation Methods **74**
   Chapter Summary **78**
   Review Questions **78**
6. **Microbial Metabolism 81**
   Role of Metabolism in Biosynthesis and Growth **81**
   Focal Metabolites and Their Interconversion **81**
   Assimilatory Pathways **84**
   Biosynthetic Pathways **92**
   Patterns of Microbial Energy-Yielding Metabolism **94**
   Regulation of Metabolic Pathways **101**
   Chapter Summary **103**
   Review Questions **103**
7. **Microbial Genetics 105**
   Nucleic Acids and Their Organization in Eukaryotic, Prokaryotic, and Viral Genomes **105**

Replication **110**
Transfer of DNA **111**
Mutation and Gene Rearrangement **114**
Gene Expression **115**
Genetic Engineering **117**
Characterization of Cloned DNA **120**
Site-Directed Mutagenesis **123**
Analysis With Cloned DNA: Hybridization Probes **124**
Manipulation of Cloned DNA **124**
Objectives **125**
Review Questions **125**

SECTION II

**IMMUNOLOGY 127**

*Barbara Detrick, PhD*

**8. Immunology 127**
Overview **127**
Innate Immunity **127**
Adaptive Immunity **130**
Complement **141**
Cytokines **143**
Hypersensitivity **145**
Deficiencies of the Immune Response **146**
Clinical Immunology Laboratory (Diagnostic Testing) **147**
Chapter Summary **149**
Review Questions **149**

SECTION III

**BACTERIOLOGY 153**

*Karen C. Carroll, MD and Jeffery A. Hobden, PhD*

**9. Pathogenesis of Bacterial Infection 153**
Identifying Bacteria That Cause Disease **154**
Transmission of Infection **155**
The Infectious Process **156**
Genomics and Bacterial Pathogenicity **156**
Regulation of Bacterial Virulence Factors **157**
Bacterial Virulence Factors **158**
Chapter Summary **165**
Review Questions **165**

**10. Normal Human Microbiota 169**
Human Microbiome Project **169**
Role of the Resident Microbiota **169**
Normal Microbiota of the Skin **171**
Normal Microbiota of the Mouth and Upper Respiratory Tract **171**
Normal Microbiota of the Urethra **176**
Normal Microbiota of the Vagina **176**
Normal Microbiota of the Conjunctiva **176**
Chapter Summary **177**
Review Questions **177**

**11. Spore-Forming Gram-Positive Bacilli: *Bacillus* and *Clostridium* Species 179**
*Bacillus* Species **179**
*Bacillus anthracis* **179**
*Bacillus cereus* **182**
*Clostridium* Species **182**
*Clostridium botulinum* **183**
*Clostridium tetani* **184**
Clostridia That Produce Invasive Infections **186**
*Clostridium difficile* and Diarrheal Disease **187**
Review Questions **188**

**12. Aerobic Non–Spore-Forming Gram-Positive Bacilli: *Corynebacterium, Listeria, Erysipelothrix, Nocardia,* and Related Pathogens 191**
*Corynebacterium diphtheriae* **192**
Other Coryneform Bacteria **195**
*Listeria monocytogenes* **196**
*Erysipelothrix rhusiopathiae* **198**
Complex Aerobic Actinomycetes **198**
Nocardiosis **199**
Actinomycetoma **200**
Review Questions **200**

**13. The Staphylococci 203**
Chapter Summary **210**
Review Questions **210**

**14. The Streptococci, Enterococci, and Related Genera 213**
Classification of Streptococci **213**
**Streptococci of Particular Medical Interest 215**
*Streptococcus pyogenes* **215**
*Streptococcus agalactiae* **220**
Groups C and G **220**
Group D Streptococci **221**
*Streptococcus anginosus Group* **221**
Groups E, F, G, H, and K–U Streptococci **221**
Viridans Streptococci **221**
Nutritionally Variant Streptococci **222**
Peptostreptococcus and Related Genera **222**
*Streptococcus pneumoniae* **222**
Enterococci **226**
Other Catalase-Negative Gram-Positive Cocci **227**
Review Questions **228**

**15. Enteric Gram-Negative Rods (Enterobacteriaceae) 231**
Classification **231**
Diseases Caused By Enterobacteriaceae Other Than *Salmonella* and *Shigella* **234**
The Shigellae **237**
The Salmonellae **239**
Chapter Summary **242**
Review Questions **243**

**16. Pseudomonads and *Acinetobacter* 245**
The Pseudomonad Group **245**
*Pseudomonas aeruginosa* **245**
*Burkholderia pseudomallei* **248**
*Burkholderia cepacia* Complex **248**
*Stenotrophomonas maltophilia* **249**
*Acinetobacter* **249**
Chapter Summary **249**
Review Questions **249**

**17. *Vibrio, Campylobacter, and Helicobacter* 253**
The Vibrios **253**
*Vibrio cholerae* **253**
*Vibrio parahaemolyticus* and *Vibrio vulnificus* **256**
*Campylobacter* **256**
*Campylobacter jejuni* **256**
*Helicobacter pylori* **258**
Review Questions **259**

**18. *Haemophilus, Bordetella, Brucella*, and *Francisella* 263**
The *Haemophilus* Species **263**
*Haemophilus influenzae* **263**
*Haemophilus aegyptius* **265**
*Aggregatibacter aphrophilus* **266**
*Haemophilus ducreyi* **266**
Other *Haemophilus* Species **266**
The Bordetellae **266**
*Bordetella pertussis* **266**
*Bordetella parapertussis* **268**
*Bordetella bronchiseptica* **268**
The Brucellae **269**
*Francisella tularensis* and Tularemia **271**
Review Questions **273**

**19. *Yersinia* and *Pasteurella* 275**
*Yersinia pestis* and Plague **275**
*Yersinia enterocolitica* **277**
*Pasteurella multocida* **278**
Review Questions **278**

**20. The Neisseriae 281**
*Neisseria gonorrhoeae* **281**
*Neisseria meningitidis* **287**
Other Neisseriae **288**
Chapter Summary **289**
Review Questions **289**

**21. Infections Caused by Anaerobic Bacteria 293**
**Physiology and Growth Conditions for Anaerobes 293**
Anaerobic Bacteria Found in Human Infections **294**
**Bacteria That Cause Vaginosis 295**
*Gardnerella vaginalis* **295**
Pathogenesis of Anaerobic Infections **296**
The Polymicrobial Nature of Anaerobic Infections **297**
Diagnosis of Anaerobic Infections **297**
Treatment of Anaerobic Infections **298**
Chapter Summary **298**
Review Questions **298**

**22. *Legionella, Bartonella*, and Unusual Bacterial Pathogens 301**
*Legionella pneumophila* and Other Legionellae **301**
*Bartonella* **304**
*Streptobacillus moniliformis* **306**
Whipple Disease **306**
Review Questions **307**

**23. Mycobacteria 309**
*Mycobacterium tuberculosis* **309**
Other Mycobacteria **317**
*Mycobacterium leprae* **319**
Review Questions **320**

**24. Spirochetes and Other Spiral Microorganisms 323**
*Treponema pallidum* and Syphilis **323**
***Borrelia* 327**
*Borrelia* Species and Relapsing Fever **327**
*Borrelia burgdorferi* and Lyme Disease **328**
***Leptospira* and Leptospirosis 330**
Review Questions **332**

**25. Mycoplasmas and Cell Wall–Defective Bacteria 335**
Mycoplasmas **335**
*Mycoplasma pneumoniae* and Atypical Pneumonias **337**
*Mycoplasma hominis* **338**
*Ureaplasma urealyticum* **338**
*Mycoplasma genitalium* **338**
Chapter Summary **338**
Review Questions **339**

**26. Rickettsia and Related Genera 341**
General **341**
*Rickettsia* and *Orientia* **341**
*Ehrlichia* and *Anaplasma* **345**
*Coxiella burnetii* **346**
Review Questions **348**

**27. *Chlamydia* spp. 351**
*Chlamydia trachomatis* Ocular, Genital, and Respiratory Infections **354**
Trachoma **354**
*Chlamydia trachomatis* Genital Infections and Inclusion Conjunctivitis **355**
*Chlamydia trachomatis* and Neonatal Pneumonia **356**
Lymphogranuloma Venereum **356**
*Chlamydia pneumoniae* and Respiratory Infections **357**
*Chlamydia psittaci* and Psittacosis **358**
Chapter Summary **360**
Review Questions **360**

**28. Antimicrobial Chemotherapy 363**
**Mechanisms of Action of Antimicrobial Drugs 363**
Selective Toxicity **363**
Inhibition of Cell Wall Synthesis **363**
Inhibition/Alteration of Cell Membrane Function **365**
Inhibition of Protein Synthesis **366**
Inhibition of Nucleic Acid Synthesis **367**
**Resistance to Antimicrobial Drugs 368**
Origin of Drug Resistance **368**
Cross-Resistance **369**
Limitation of Drug Resistance **369**
Clinical Implications of Drug Resistance **369**
**Antimicrobial Activity in Vitro 370**
Factors Affecting Antimicrobial Activity **370**
Measurement of Antimicrobial Activity **371**
**Antimicrobial Activity in Vivo 372**
Drug–Pathogen Relationships **372**
Host–Pathogen Relationships **373**
**Clinical Use of Antibiotics 373**
Selection of Antibiotics **373**
Dangers of Indiscriminate Use **374**
Antimicrobial Drugs Used in Combination **374**
Antimicrobial Chemoprophylaxis **375**
**Antimicrobial Drugs for Systemic Administration 377**
Penicillins **377**
Cephalosporins **383**
Other β-Lactam Drugs **385**
Tetracyclines **385**
Glycylcyclines **386**
Chloramphenicol **386**
Macrolides **387**
Clindamycin and Lincomycin **387**
Glycopeptides, Lipopeptides, Lipoglycopeptides **388**
Streptogramins **388**
Oxazolidinones **389**
Bacitracin **389**
Polymyxins **389**
Aminoglycosides **389**
Quinolones **391**
Sulfonamides and Trimethoprim **392**
Other Drugs with Specialized Uses **392**
Drugs Used Primarily To Treat Mycobacterial Infections **393**
Review Questions **394**

SECTION IV
**VIROLOGY 397**

*Steve Miller, MD, PhD*

**29. General Properties of Viruses 397**
Terms and Definitions in Virology **397**
Evolutionary Origin of Viruses **398**
Classification of Viruses **398**
Principles of Virus Structure **404**
Chemical Composition of Viruses **405**
Cultivation and Detection of Viruses **407**
Purification and Identification of Viruses **408**
Laboratory Safety **409**
Reaction to Physical and Chemical Agents **409**
Replication of Viruses: an Overview **410**
Genetics of Animal Viruses **414**
Natural History (Ecology) and Modes of Transmission of Viruses **416**
Chapter Summary **418**
Review Questions **418**

**30. Pathogenesis and Control of Viral Diseases 421**
Principles of Viral Diseases **421**
Pathogenesis of Viral Diseases **421**
Prevention and Treatment of Viral Infections **433**
Chapter Summary **438**
Review Questions **438**

**31. Parvoviruses 441**
Properties of Parvoviruses **441**
Parvovirus Infections in Humans **441**
Chapter Summary **445**
Review Questions **445**

**32. Adenoviruses 447**
Properties of Adenoviruses **447**
Adenovirus Infections in Humans **451**
Chapter Summary **454**
Review Questions **454**

**33. Herpesviruses 457**
Properties of Herpesviruses **457**
**Herpesvirus Infections in Humans 460**
Herpes Simplex Viruses **460**
Varicella-Zoster Virus **466**
Cytomegalovirus **470**
Epstein-Barr Virus **474**
Human Herpesvirus 6 **477**
Human Herpesvirus 7 **478**
Human Herpesvirus 8 **478**
Herpes B Virus **478**
Chapter Summary **479**
Review Questions **479**

**34. Poxviruses 483**
Properties of Poxviruses **483**
Poxvirus Infections in Humans: Vaccinia and Variola **486**
Monkeypox Infections **490**
Cowpox Infections **490**
Buffalopox Infections **490**
Orf Virus Infections **490**
Molluscum Contagiosum **490**
Tanapox and Yaba Monkey Tumor Poxvirus Infections **492**
Chapter Summary **493**
Review Questions **493**

**35. Hepatitis Viruses 495**
Properties of Hepatitis Viruses **495**
Hepatitis Virus Infections in Humans **500**
Chapter Summary **512**
Review Questions **512**

**36. Picornaviruses (Enterovirus and Rhinovirus Groups) 515**
Properties of Picornaviruses **515**
**Enterovirus Group 516**
Polioviruses **516**
Coxsackieviruses **522**
Other Enteroviruses **524**
Enteroviruses in the Environment **525**
Rhinoviruses **526**
Parechovirus Group **527**
Foot-and-Mouth Disease (Aphthovirus of Cattle) **528**
Chapter Summary **528**
Review Questions **528**

**37. Reoviruses, Rotaviruses, and Caliciviruses 531**
Reoviruses and Rotaviruses **531**
Rotaviruses **532**
Reoviruses **536**
Orbiviruses and Coltiviruses **536**
Caliciviruses **536**
Astroviruses **539**
Chapter Summary **539**
Review Questions **539**

**38. Arthropod-Borne and Rodent-Borne Viral Diseases 541**
**Human Arbovirus Infections 541**
Togavirus and Flavivirus Encephalitis **543**
Yellow Fever Virus **550**
Dengue Virus **552**
Bunyavirus Encephalitis Viruses **554**
Sandfly Fever Virus **554**
Rift Valley Fever Virus **554**
Severe Fever with Thrombocytopenia Syndrome Virus **555**
Heartland Virus **555**
Colorado Tick Fever Virus **555**
Rodent-Borne Hemorrhagic Fevers **555**
Bunyavirus Diseases **555**
Arenavirus Diseases **557**
Filovirus Diseases **559**
Chapter Summary **561**
Review Questions **561**

**39. Orthomyxoviruses (Influenza Viruses) 565**
Properties of Orthomyxoviruses **565**
Influenza Virus Infections in Humans **570**
Chapter Summary **576**
Review Questions **576**

**40. Paramyxoviruses and Rubella Virus 579**
Properties of Paramyxoviruses **579**
Parainfluenza Virus Infections **583**
Respiratory Syncytial Virus Infections **586**
Human Metapneumovirus Infections **588**
Mumps Virus Infections **589**
Measles (Rubeola) Virus Infections **591**
Hendra Virus and Nipah Virus Infections **594**
**Rubella (German Measles) Virus Infections 595**

Postnatal Rubella **595**
Congenital Rubella Syndrome **596**
Chapter Summary **597**
Review Questions **598**

**41. Coronaviruses 601**
Properties of Coronaviruses **601**
Coronavirus Infections in Humans **602**
Chapter Summary **605**
Review Questions **605**

**42. Rabies, Slow Virus Infections, and Prion Diseases 607**
Rabies **607**
Borna Disease **613**
Slow Virus Infections and Prion Diseases **613**
Chapter Summary **616**
Review Questions **616**

**43. Human Cancer Viruses 619**
General Features of Viral Carcinogenesis **619**
Molecular Mechanisms of Carcinogensis **620**
Interactions of Tumor Viruses with Their Hosts **621**
RNA Tumor Viruses **622**
Hepatitis C Virus **622**
Retroviruses **622**
**DNA Tumor Viruses 628**
Polyomaviruses **628**
Papillomaviruses **630**
Adenoviruses **633**
Herpesviruses **633**
Poxviruses **634**
Hepatitis B Virus **634**
**How to Prove That a Virus Causes Human Cancer 635**
Chapter Summary **635**
Review Questions **635**

**44. Aids and Lentiviruses 639**
Properties of Lentiviruses **639**
Hiv Infections in Humans **643**
Chapter Summary **653**
Review Questions **653**

SECTION V
**MYCOLOGY 657**

*Thomas G. Mitchell, PhD*

**45. Medical Mycology 657**
General Properties, Virulence, and Classification of Pathogenic Fungi **658**
Laboratory Diagnosis of Mycoses **663**
Superficial Mycoses **665**
Cutaneous Mycoses **665**
Key Concepts: Superficial and Cutaneous Mycoses **669**
Subcutaneous Mycoses **669**
Sporotrichosis **670**
Chromoblastomycosis **671**
Phaeohyphomycosis **672**
Mycetoma **673**
Key Concepts: Subcutaneous Mycoses **674**
Endemic Mycoses **674**
Coccidioidomycosis **675**
Histoplasmosis **678**
Blastomycosis **681**
Paracoccidioidomycosis **682**
Key Concepts: Endemic Mycoses **683**
Opportunistic Mycoses **683**
Candidiasis **684**
Cryptococcosis **687**
Aspergillosis **690**
Mucormycosis **691**
*Pneumocystis* Pneumonia **691**
Penicilliosis **692**
Other Opportunistic Mycoses **693**
Key Concepts: Opportunistic Mycoses **693**
Antifungal Prophylaxis **693**
Hypersensitivity to Fungi **694**
Mycotoxins **694**
Antifungal Chemotherapy **694**
Topical Antifungal Agents **700**
Key Concepts: Antifungal Chemotherapy **700**
Review Questions **700**

SECTION VI
**PARASITOLOGY 705**

*Judy A. Sakanari, PhD and James H. McKerrow, MD, PhD*

**46. Medical Parasitology 705**
**Classification of Parasites 705**
**Intestinal Protozoan Infections 709**
*Giardia lamblia* (Intestinal Flagellate) **709**
*Entamoeba histolytica* (Intestinal and Tissue Ameba) **710**
Other Intestinal Amebae **712**
*Cryptosporidium* (Intestinal Sporozoa) **712**
*Cyclospora* (Intestinal Sporozoa) **713**
**Sexually Transmitted Protozoan Infection 713**
*Trichomonas vaginalis* (Genitourinary Flagellate) **713**

**Blood and Tissue Protozoan Infections 713**
Blood Flagellates **713**
*Trypanosoma brucei rhodesiense* and *Trypanosoma brucei gambiense* (Blood Flagellates) **714**
*Trypanosoma cruzi* (Blood Flagellate) **715**
*Leishmania* Species (Blood Flagellates) **715**
*Entamoeba histolytica* (Tissue Ameba)—See Intestinal Protozoan Infections Section **717**
*Naegleria fowleri*, *Acanthamoeba castellanii*, and *Balamuthia mandrillaris* (Free-Living Amebae) **717**
*Plasmodium* Species (Blood Sporozoa) **717**
*Babesia microti* (Blood Sporozoa) **721**
*Toxoplasma gondii* (Tissue Sporozoa) **722**
Microsporidia **722**
**Intestinal Helminthic Infections 723**
*Enterobius vermicularis* (Pinworm—Intestinal Nematode) **723**
*Trichuris trichiura* (Whipworm—Intestinal Nematode) **724**
*Ascaris lumbricoides* (Human Roundworm—Intestinal Nematode) **724**
*Ancylostoma duodenale* and *Necator americanus* (Human Hookworms—Intestinal Nematode) **728**
*Strongyloides stercoralis* (Human Threadworm—Intestinal and Tissue Nematode) **729**
*Trichinella spiralis* (Intestinal and Tissue Nematode) **730**
*Fasciolopsis buski* (Giant Intestinal Fluke—Intestinal Trematode) **730**
*Taenia saginata* (Beef Tapeworm—Intestinal Cestode) and *Taenia solium* (Pork Tapeworm—Intestinal and Tissue Cestode) **731**
*Diphyllobothrium latum* (Broad Fish Tapeworm—Intestinal Cestode) **731**
*Hymenolepis nana* (Dwarf Tapeworm—Intestinal Cestode) **732**
*Dipylidium caninum* (Dog Tapeworm—Intestinal Cestode) **732**
**Blood and Tissue Helminthic Infections 732**
*Wuchereria bancrofti*, *brugia malayi*, and *Brugia timori* (Lymphatic Filariasis—Tissue Nematodes) **732**
*Onchocerca volvulus* (River Blindness—Tissue Nematode) **733**
*Dracunculus medinensis* (Guinea Worm—Tissue Nematode) **734**
Larva Migrans (Zoonotic Larval Nematode Infections) **734**
*Clonorchis sinensis* (Chinese Liver Fluke), *Fasciola hepatica* (Sheep Liver Fluke), and *Paragonimus westermani* (Lung Fluke)—Tissue Trematodes **734**
*Schistosoma mansoni*, *Schistosoma japonicum*, and *Schistosoma haematobium* (Blood Flukes) **735**
**Tissue Cestode Infections (Caused By the Larval Stages) 736**
*Taenia solium*—Cysticercosis/Neurocysticercosis **736**
*Echinococcus granulosus* (Hydatid Cyst) **736**
Review Questions **737**

SECTION VII
**DIAGNOSTIC MEDICAL MICROBIOLOGY AND CLINICAL CORRELATION 741**

*Karen C. Carroll, MD and Steve Miller, MD, PhD*

47. **Principles of Diagnostic Medical Microbiology 741**
Communication Between Physician and Laboratory **741**
Diagnosis of Bacterial and Fungal Infections **742**
The Importance of Normal Bacteria l and Fungal Microbiota 753
Laboratory Aids in the Selection of Antimicrobial Therapy **754**
Diagnosis of Infection By Anatomic Site **755**
Anaerobic Infections **761**
Diagnosis of Chlamydial Infections **761**
Diagnosis of Viral Infections **762**
Review Questions **769**

48. **Cases and Clinical Correlations 773**
**Central Nervous System 773**
**Respiratory 777**
**Heart 782**
**Abdomen 783**
**Urinary Tract 785**
**Bone and Soft Tissue 790**
**Sexually Transmitted Diseases 792**
***Mycobacterium tuberculosis* Infections 795**
***Myocobacterium avium* Complex 798**
**Infections in Transplant Patients 799**
Emerging Infections **805**

Index **809**

# Understand the clinically relevant aspects of microbiology with *Jawetz, Melnick, & Adelberg's Medical Microbiology, Twenty-Seventh Edition*

- Delivers a concise, up-to-date overview of the roles microorganisms play in human health and illness
- Links fundamental principles with the diagnosis and treatment of microbial infections
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- Includes brief descriptions of each organism, along with vital perspectives on pathogenesis, diagnostic laboratory tests, clinical findings, treatment, and epidemiology
- Features an entire chapter of case studies that focuses on differential diagnosis and management of microbial infections
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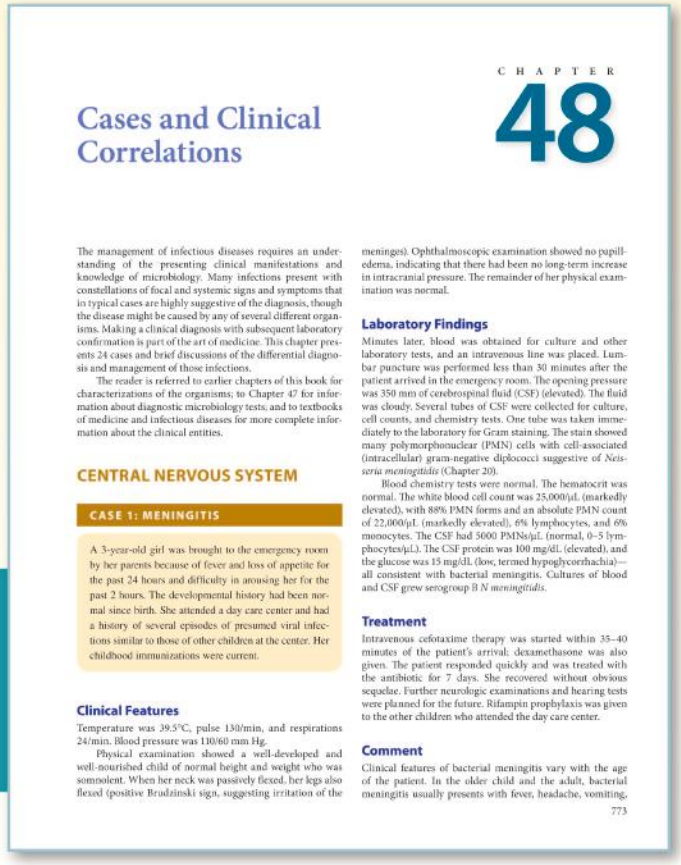

CHAPTER 48

## Cases and Clinical Correlations

The management of infectious diseases requires an understanding of the presenting clinical manifestations and knowledge of microbiology. Many infections present with constellations of focal and systemic signs and symptoms that in typical cases are highly suggestive of the diagnosis, though the disease might be caused by any of several different organisms. Making a clinical diagnosis with subsequent laboratory confirmation is part of the art of medicine. This chapter presents 24 cases and brief discussions of the differential diagnosis and management of those infections.

The reader is referred to earlier chapters of this book for characterizations of the organisms; to Chapter 47 for information about diagnostic microbiology tests; and to textbooks of medicine and infectious diseases for more complete information about the clinical entities.

### CENTRAL NERVOUS SYSTEM

#### CASE 1: MENINGITIS

A 3-year-old girl was brought to the emergency room by her parents because of fever and loss of appetite for the past 24 hours and difficulty in arousing her for the past 2 hours. The developmental history had been normal since birth. She attended a day care center and had a history of several episodes of presumed viral infections similar to those of other children at the center. Her childhood immunizations were current.

**Clinical Features**

Temperature was 39.5°C, pulse 130/min, and respirations 24/min. Blood pressure was 110/60 mm Hg.

Physical examination showed a well-developed and well-nourished child of normal height and weight who was somnolent. When her neck was passively flexed, her legs also flexed (positive Brudzinski sign, suggesting irritation of the meninges). Ophthalmoscopic examination showed no papilledema, indicating that there had been no long-term increase in intracranial pressure. The remainder of her physical examination was normal.

**Laboratory Findings**

Minutes later, blood was obtained for culture and other laboratory tests, and an intravenous line was placed. Lumbar puncture was performed less than 30 minutes after the patient arrived in the emergency room. The opening pressure was 350 mm of cerebrospinal fluid (CSF) (elevated). The fluid was cloudy. Several tubes of CSF were collected for culture, cell counts, and chemistry tests. One tube was taken immediately to the laboratory for Gram staining. The stain showed many polymorphonuclear (PMN) cells with cell-associated (intracellular) gram-negative diplococci suggestive of *Neisseria meningitidis* (Chapter 20).

Blood chemistry tests were normal. The hematocrit was normal. The white blood cell count was 25,000/μL (markedly elevated), with 88% PMN forms and an absolute PMN count of 22,000/μL (markedly elevated), 6% lymphocytes, and 6% monocytes. The CSF had 5000 PMNs/μL (normal, 0–5 lymphocytes/μL). The CSF protein was 100 mg/dL (elevated), and the glucose was 15 mg/dL (low, termed hypoglycorrhachia)—all consistent with bacterial meningitis. Cultures of blood and CSF grew serogroup B *N meningitidis*.

**Treatment**

Intravenous cefotaxime therapy was started within 35–40 minutes of the patient's arrival; dexamethasone was also given. The patient responded quickly and was treated with the antibiotic for 7 days. She recovered without obvious sequelae. Further neurologic examinations and hearing tests were planned for the future. Rifampin prophylaxis was given to the other children who attended the day care center.

**Comment**

Clinical features of bacterial meningitis vary with the age of the patient. In the older child and the adult, bacterial meningitis usually presents with fever, headache, vomiting,

773

*Cases and Clinical Correlations* show readers how to apply the material to real-world situations

## Here's why *Jawetz, Melnick, & Adelberg's Medical Microbiology* is essential for USMLE review:

- 650+ USMLE-style review questions
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- An easy-to-access list of medically important microorganisms
- Coverage that reflects the latest techniques in laboratory and diagnostic technologies
- Full-color images and micrographs
- Chapter-ending summaries
- Chapter concept checks

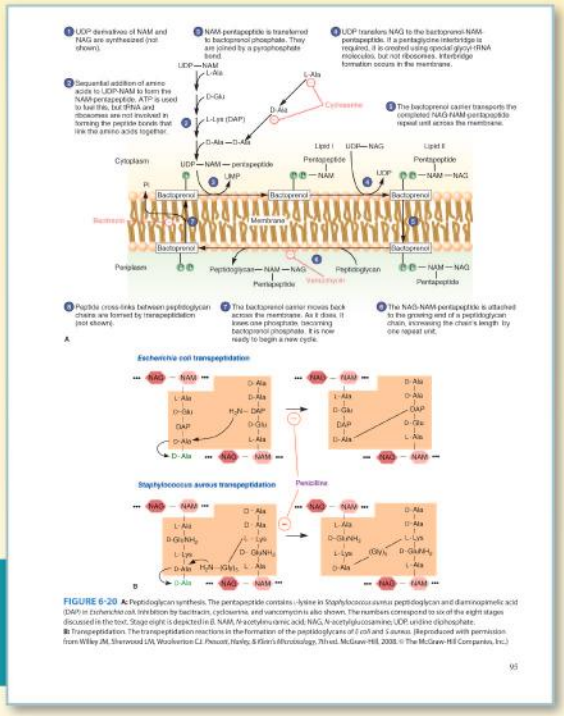

FIGURE 6-20 **A:** Peptidoglycan synthesis. The pentapeptide contains L-lysine in *Staphylococcus aureus* peptidoglycan and diaminopimelic acid (DAP) in *Escherichia coli*. Inhibition by bacitracin, cycloserine, and vancomycin is also shown. The numbers correspond to six of the eight stages discussed in the text. Stage eight is depicted in B. NAM, *N*-acetylmuramic acid; NAG, *N*-acetylglucosamine; UDP, uridine diphosphate. **B:** Transpeptidation. The transpeptidation reactions in the formation of the peptidoglycans of *E coli* and *S aureus*. (Reproduced with permission from Wilkey JM, Sherwood LM, Woolverton CJ. *Prescott, Harley, & Klein's Microbiology*, 7th ed. McGraw-Hill, 2008. © The McGraw-Hill Companies, Inc.)

Diagrams that crystallize what is stated in the text

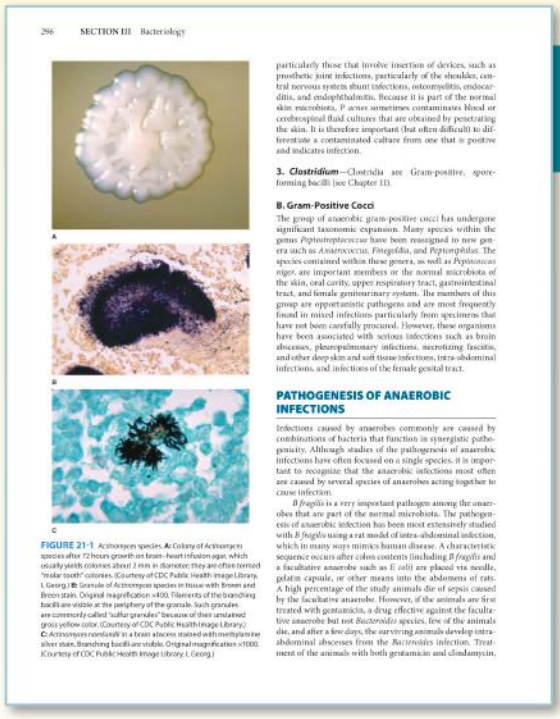

FIGURE 21-1 *Actinomyces* species. **A:** Colony of *Actinomyces* species after 72 hours growth on brain–heart infusion agar, which usually yields colonies about 2 mm in diameter; they are often termed "molar tooth" colonies. (Courtesy of CDC Public Health Image Library, L Georg.) **B:** Granule of *Actinomyces* species in tissue with Brown and Brenn stain. Original magnification ×400. Filaments of the branching bacilli are visible at the periphery of the granule. Such granules are commonly called "sulfur granules" because of their unstained gross yellow color. (Courtesy of CDC Public Health Image Library.) **C:** *Actinomyces naeslundii* in a brain abscess stained with methylamine silver stain. Branching bacilli are visible. Original magnification ×1000. (Courtesy of CDC Public Health Image Library, L Georg.)

Full-color images bring the subject matter to life

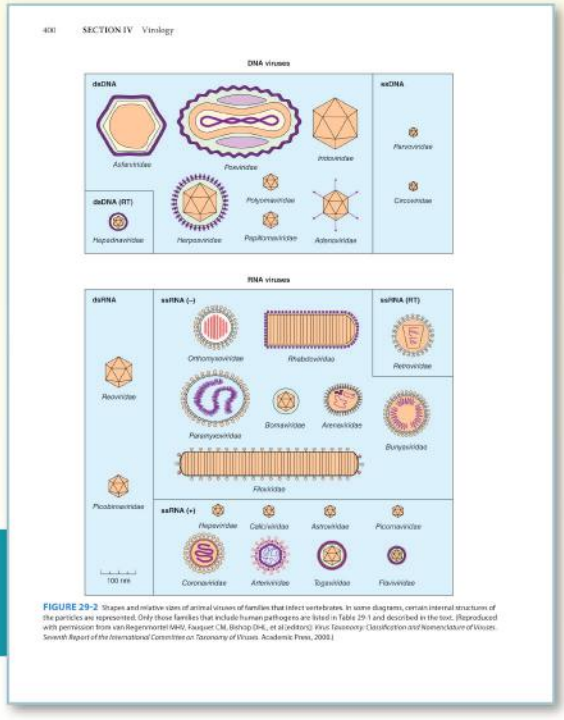

FIGURE 29-2 Shapes and relative sizes of animal viruses of families that infect vertebrates. In some diagrams, certain internal structures of the particles are represented. Only those families that include human pathogens are listed in Table 29-1 and described in the text. (Reproduced with permission from van Regenmortel MHV, Fauquet CM, Bishop DHL, et al (editors): *Virus Taxonomy: Classification and Nomenclature of Viruses. Seventh Report of the International Committee on Taxonomy of Viruses*. Academic Press, 2000.)

Complete coverage of essentials such as *Virology*

# Preface

The twenty-seventh edition of *Jawetz, Melnick, & Adelberg's Medical Microbiology* remains true to the goals of the first edition published in 1954 "to provide a brief, accurate and up-to-date presentation of those aspects of medical microbiology that are of particular significance to the fields of clinical infections and chemotherapy."

All chapters have been revised extensively, consistent with the tremendous expansion of medical knowledge afforded by molecular mechanisms, advances in our understanding of microbial pathogenesis, and the discovery of novel pathogens. Chapter 47, "Principles of Diagnostic Medical Microbiology," and Chapter 48, "Cases and Clinical Correlations," have been updated to reflect the current explosion in novel diagnostics over the last several years as well as new therapies in the treatment of infectious diseases.

New to this edition are Steve Miller, MD, PhD, and Jeffery Hobden, PhD. Dr. Miller is the Medical Director of the University of California, San Francisco Clinical Microbiology Laboratory and Health Science Associate Professor of Clinical Laboratory Medicine, UCSF, and he brings extensive expertise in virology. Dr. Hobden is an Associate Professor in the Department of Microbiology, Immunology, & Parasitology, Louisiana State University Health Sciences Center, New Orleans, Louisiana, and his interest is in bacterial pathogens, especially *Pseudomonas aeruginosa*. We welcome their participation.

The authors hope that the changes to this edition will be helpful to the student of microbiology.

SECTION I FUNDAMENTALS OF MICROBIOLOGY

CHAPTER 1

# The Science of Microbiology

## INTRODUCTION

Microbiology is the study of microorganisms, a large and diverse group of microscopic organisms that exist as single cells or cell clusters; it also includes viruses, which are microscopic but not cellular. Microorganisms have a tremendous impact on all life and the physical and chemical makeup of our planet. They are responsible for cycling the chemical elements essential for life, including carbon, nitrogen, sulfur, hydrogen, and oxygen; more photosynthesis is carried out by microorganisms than by green plants. Furthermore, there are 100 million times as many bacteria in the oceans ($13 \times 10^{28}$) as there are stars in the known universe. The rate of viral infections in the oceans is about $1 \times 10^{23}$ infections per second, and these infections remove 20–40% of all bacterial cells each day. It has been estimated that $5 \times 10^{30}$ microbial cells exist on earth; excluding cellulose, these cells constitute about 90% of the biomass of the entire biosphere. Humans also have an intimate relationship with microorganisms; more than 90% of the cells in our bodies are microbes. The bacteria present in the average human gut weigh about 1 kg, and a human adult will excrete his or her own weight in fecal bacteria each year. The number of genes contained within this gut flora outnumber that contained within our genome 150-fold, and even in our own genome, 8% of the DNA is derived from remnants of viral genomes.

## BIOLOGIC PRINCIPLES ILLUSTRATED BY MICROBIOLOGY

Nowhere is **biologic diversity** demonstrated more dramatically than by microorganisms, creatures that are not directly visible to the unaided eye. In form and function, be it biochemical property or genetic mechanism, analysis of microorganisms takes us to the limits of biologic understanding. Thus, the need for **originality**—one test of the merit of a scientific **hypothesis**—can be fully met in microbiology. A useful hypothesis should provide a basis for **generalization**, and microbial diversity provides an arena in which this challenge is ever present.

**Prediction**, the practical outgrowth of science, is a product created by a blend of technique and theory. **Biochemistry**, **molecular biology**, and **genetics** provide the tools required for analysis of microorganisms. **Microbiology**, in turn, extends the horizons of these scientific disciplines. A biologist might describe such an exchange as **mutualism**, that is, one that benefits all of the contributing parties. Lichens are an example of microbial mutualism. Lichens consist of a fungus and phototropic partner, either an alga (a eukaryote) or a cyanobacterium (a prokaryote) (Figure 1-1). The phototropic component is the primary producer, and the fungus provides the phototroph with an anchor and protection from the elements. In biology, mutualism is called **symbiosis**, a continuing association of different organisms. If the exchange operates primarily to the benefit of one party, the association is described as **parasitism**, a relationship in which a **host** provides the primary benefit to the parasite. Isolation and characterization of a parasite—such as a pathogenic bacterium or virus—often require effective mimicry in the laboratory of the growth environment provided by host cells. This demand sometimes represents a major challenge to investigators.

The terms *mutualism*, *symbiosis*, and *parasitism* relate to the science of **ecology**, and the principles of environmental biology are implicit in microbiology. Microorganisms are

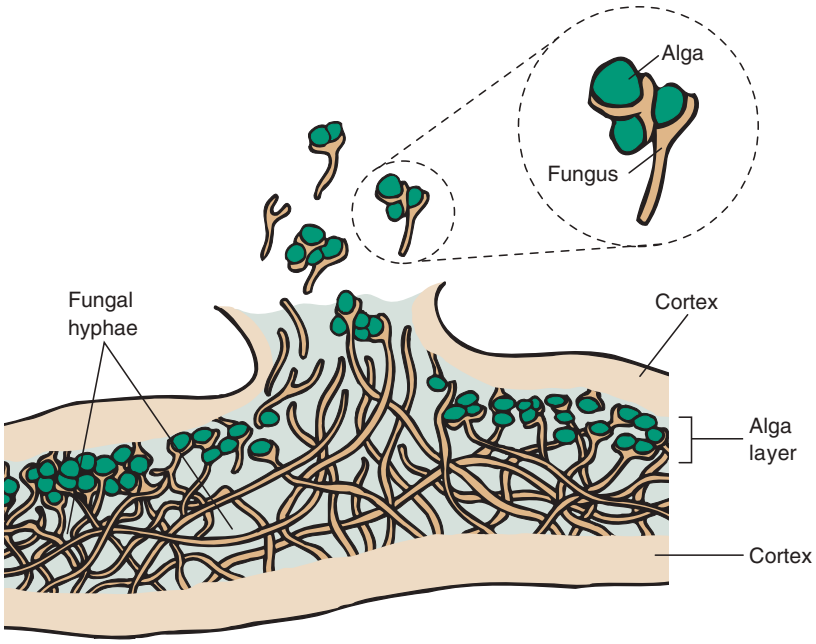


**FIGURE 1-1** Diagram of a lichen, consisting of cells of a phototroph, either an alga or a cyanobacterium, entwined within the hyphae of the fungal partner. (Reproduced with permission from Nester EW, Anderson DG, Roberts CE, Nester MT (editors): *Microbiology: A Human Perspective*, 6th ed. McGraw-Hill, 2009, p. 293.)

the products of **evolution**, the biologic consequence of **natural selection** operating on a vast array of genetically diverse organisms. It is useful to keep the complexity of natural history in mind before generalizing about microorganisms, the most heterogeneous subset of all living creatures.

A major biologic division separates the eukaryotes, organisms containing a membrane-bound nucleus, from prokaryotes, organisms in which DNA is not physically separated from the cytoplasm. As described in this chapter and in Chapter 2, further major distinctions can be made between eukaryotes and prokaryotes. Eukaryotes, for example, are distinguished by their relatively large size and by the presence of specialized membrane-bound organelles such as mitochondria.

As described more fully later in this chapter, eukaryotic microorganisms—or, phylogenetically speaking, the Eukarya—are unified by their distinct cell structure and phylogenetic history. Among the groups of eukaryotic microorganisms are the **algae**, the **protozoa**, the **fungi**, and the **slime molds**.

## VIRUSES

The unique properties of viruses set them apart from living creatures. Viruses lack many of the attributes of cells, including the ability to replicate. Only when it infects a cell does a virus acquire the key attribute of a living system—reproduction. Viruses are known to infect all cells, including microbial cells. Recently, viruses called **virophages** have been discovered that infect other viruses. Host–virus interactions tend to be highly specific, and the biologic range of viruses mirrors the diversity of potential host cells. Further diversity of viruses is exhibited by their broad array of strategies for replication and survival.

Viral particles are generally small (eg, adenovirus is 90 nm) and consist of a nucleic acid molecule, either DNA or RNA, enclosed in a protein coat, or capsid (sometimes itself enclosed by an envelope of lipids, proteins, and carbohydrates). Proteins—frequently glycoproteins—in the capsid determine the specificity of interaction of a virus with its host cell. The capsid protects the nucleic acid and facilitates attachment and penetration of the host cell by the virus. Inside the cell, viral nucleic acid redirects the host's enzymatic machinery to functions associated with replication of the virus. In some cases, genetic information from the virus can be incorporated as DNA into a host chromosome. In other instances, the viral genetic information can serve as a basis for cellular manufacture and release of copies of the virus. This process calls for replication of the viral nucleic acid and production of specific viral proteins. **Maturation** consists of assembling newly synthesized nucleic acid and protein subunits into mature viral particles, which are then liberated into the extracellular environment. Some very small viruses require the assistance of another virus in the host cell for their duplication. The delta agent, also known as hepatitis D virus, is too small to code for even a single capsid protein and needs help from hepatitis B virus for transmission. Viruses are known to infect a wide variety of plant and animal hosts as well as protists, fungi, and bacteria. However,

most viruses are able to infect specific types of cells of only one host species.

Some viruses are large and complex. For example, Mimivirus, a DNA virus infecting *Acanthamoeba*, a free-living soil ameba, has a diameter of 400–500 nm and a genome that encodes 979 proteins, including the first four aminoacyl tRNA synthetases ever found outside of cellular organisms and enzymes for polysaccharide biosynthesis. An even larger marine virus has recently been discovered (Megavirus); its genome (1,259,197-bp) encodes 1120 putative proteins and is larger than that of some bacteria (see Table 7-1). Because of their large size, these viruses resemble bacteria when observed in stained preparations by light microscopy; however, they do not undergo cell division or contain ribosomes.

A number of transmissible plant diseases are caused by **viroids**—small, single-stranded, covalently closed circular RNA molecules existing as highly base-paired rodlike structures. They range in size from 246 to 375 nucleotides in length. The extracellular form of the viroid is naked RNA—there is no capsid of any kind. The RNA molecule contains no protein-encoding genes, and the viroid is therefore totally dependent on host functions for its replication. Viroid RNA is replicated by the DNA-dependent RNA polymerase of the plant host; preemption of this enzyme may contribute to viroid pathogenicity.

The RNAs of viroids have been shown to contain inverted repeated base sequences at their 3′ and 5′ ends, a characteristic of transposable elements (see Chapter 7) and retroviruses. Thus, it is likely that they have evolved from transposable elements or retroviruses by the deletion of internal sequences.

The general properties of animal viruses pathogenic for humans are described in Chapter 29. Bacterial viruses are described in Chapter 7.

## PRIONS

A number of remarkable discoveries in the past three decades have led to the molecular and genetic characterization of the transmissible agent causing **scrapie**, a degenerative central nervous system disease of sheep. Studies have identified a scrapie-specific protein in preparations from scrapie-infected brains of sheep that is capable of reproducing the symptoms of scrapie in previously uninfected sheep (Figure 1-2). Attempts to identify additional components, such as nucleic acid, have been unsuccessful. To distinguish this agent from viruses and viroids, the term **prion** was introduced to emphasize its proteinaceous and infectious nature. The cellular form of the prion protein ($PrP^c$) is encoded by the host's chromosomal DNA. $PrP^c$ is a sialoglycoprotein with a molecular mass of 33,000–35,000 Da and a high content of α-helical secondary structure that is sensitive to proteases and soluble in detergent. $PrP^c$ is expressed on the surface of neurons via a glycosylphosphatidyl inositol anchor in both infected and uninfected brains. A conformational change occurs in the prion protein, changing it from its normal or cellular form $PrP^c$ to the disease-causing conformation, $PrP^{Sc}$ (Figure 1-3). When $PrP^{Sc}$ is present in an individual (owing to spontaneous conformational conversion or to infection), it is capable of recruiting $PrP^c$ and converting it to the disease form. Thus, prions replicate using the $PrP^c$ substrate that is present in the host.

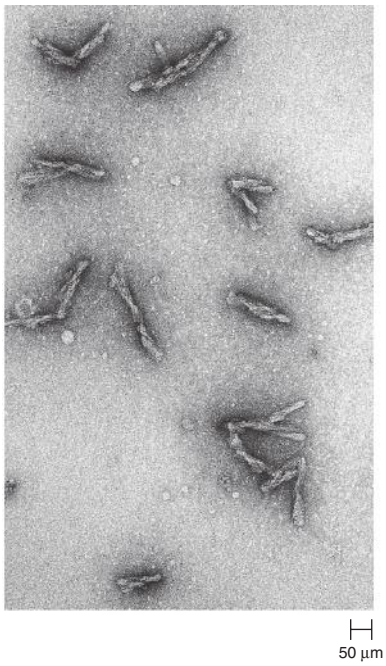


**FIGURE 1-2** Prion. Prions isolated from the brain of a scrapie-infected hamster. This neurodegenerative disease is caused by a prion. (Reproduced with permission from Stanley B. Prusiner.)

There are additional prion diseases of importance (Table 1-1 and see Chapter 42). Kuru, Creutzfeldt-Jakob disease (CJD), Gerstmann-Sträussler-Scheinker disease, and fatal familial insomnia affect humans. Bovine spongiform encephalopathy, which is thought to result from the ingestion of feeds and bone meal prepared from rendered sheep offal, has been responsible for the deaths of more than 184,000 cattle in Great Britain since its discovery in 1985. A new variant of CJD (vCJD) has been associated with human ingestion of prion-infected beef in the United Kingdom and France. A common feature of all of these diseases is the conversion of a host-encoded sialoglycoprotein to a protease-resistant form as a consequence of infection.

Human prion diseases are unique in that they manifest as sporadic, genetic, and infectious diseases. The study of prion biology is an important emerging area of biomedical investigation, and much remains to be learned.

The distinguishing features of the nonliving members of the microbial world are given in Table 1-2.

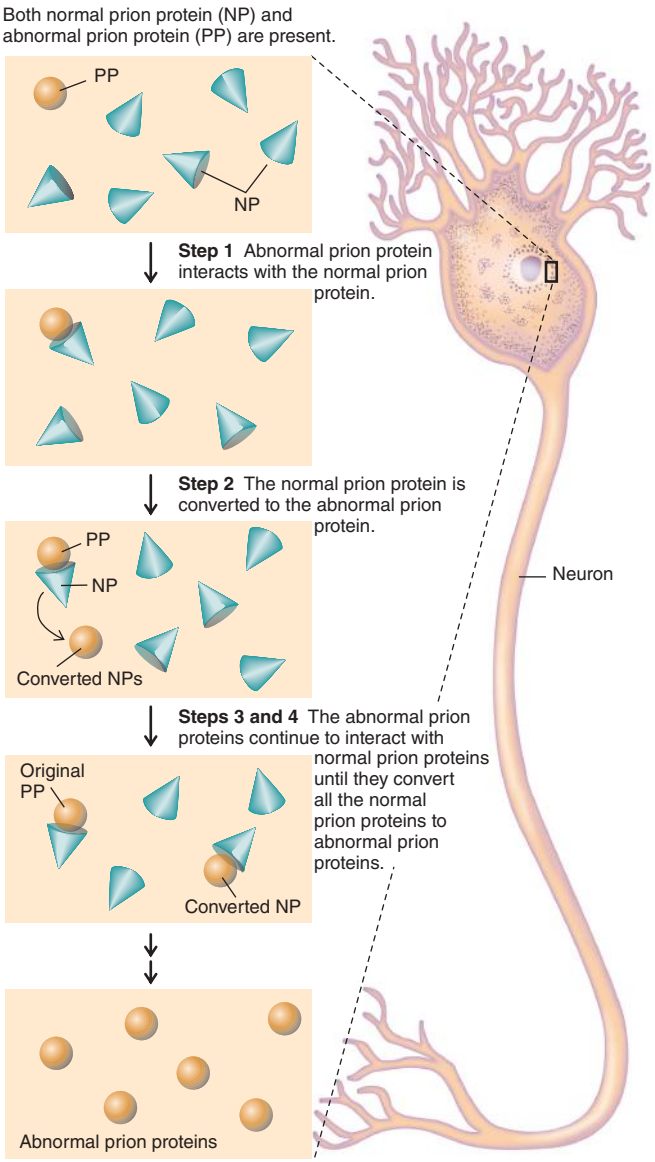


**FIGURE 1-3** Proposed mechanism by which prions replicate. The normal and abnormal prion proteins differ in their tertiary structure. (Reproduced with permission from Nester EW, Anderson DG, Roberts CE, Nester MT (editors): *Microbiology: A Human Perspective*, 6th ed. McGraw-Hill, 2009, p. 342.)

# PROKARYOTES

The primary distinguishing characteristics of the prokaryotes are their relatively small size, usually on the order of 1 μm in diameter, and the absence of a nuclear membrane. The DNA of almost all bacteria is a circle with a length of about 1 mm; this is the prokaryotic chromosome. Most prokaryotes have only a single chromosome. The chromosomal DNA must be folded more than 1000-fold just to fit within the prokaryotic cell membrane. Substantial evidence suggests that the folding may be orderly and may bring specified regions of the DNA into proximity. The specialized region of the cell containing DNA is termed the **nucleoid** and can be visualized by electron microscopy as well as by light microscopy after treatment of the cell to make the nucleoid visible. Thus, it would be a mistake to conclude that subcellular differentiation, clearly demarcated by membranes in eukaryotes, is lacking in prokaryotes. Indeed, some prokaryotes form membrane-bound subcellular structures with specialized function such as the chromatophores of photosynthetic bacteria (see Chapter 2).

## Prokaryotic Diversity

The small size of the prokaryotic chromosome limits the amount of genetic information it can contain. Recent data based on genome sequencing indicate that the number of genes within a prokaryote may vary from 468 in *Mycoplasma genitalium* to 7825 in *Streptomyces coelicolor*, and many of these genes must be dedicated to essential functions such as energy generation, macromolecular synthesis, and cellular replication. Any one prokaryote carries relatively few genes that allow physiologic accommodation of the organism to its environment. The range of potential prokaryotic environments is unimaginably broad, and it follows that the prokaryotic group encompasses a heterogeneous range of specialists, each adapted to a rather narrowly circumscribed niche.

The range of prokaryotic niches is illustrated by consideration of strategies used for generation of metabolic energy. Light from the sun is the chief source of energy for life. Some prokaryotes such as the purple bacteria convert light energy to metabolic energy in the absence of oxygen production. Other prokaryotes, exemplified by the blue-green bacteria (**Cyanobacteria**), produce oxygen that can provide energy through respiration in the absence of light. **Aerobic organisms** depend on respiration with oxygen for their energy. Some **anaerobic organisms** can use electron acceptors other than oxygen in respiration. Many anaerobes carry out **fermentations** in which energy is derived by metabolic rearrangement of chemical growth substrates. The tremendous chemical range of potential growth substrates for aerobic or anaerobic growth is mirrored in the diversity of prokaryotes that have adapted to their utilization.

## Prokaryotic Communities

A useful survival strategy for specialists is to enter into **consortia**, arrangements in which the physiologic characteristics of different organisms contribute to survival of the group as a whole. If the organisms within a physically interconnected community are directly derived from a single cell, the community is a **clone** that may contain up to $10^8$ cells. The biology of such a community differs substantially from that of a single cell. For example, the high cell number virtually ensures the presence within the clone of at least one cell carrying a variant of any gene on the chromosome. Thus, genetic variability—the wellspring of the evolutionary process called natural selection—is ensured within a clone.

**TABLE 1-1 Common Human and Animal Prion Diseases**

| Type | Name | Etiology |
|---|---|---|
| **Human prion diseases** | | |
| Acquired | Variant Creutzfeldt-Jakob disease[a] | Associated with ingestion or inoculation of prion-infected material |
| | Kuru | |
| | Iatrogenic Creutzfeldt-Jakob disease[b] | |
| Sporadic | Creutzfeldt-Jakob disease | Source of infection unknown |
| Familial | Gerstmann-Sträussler-Scheinker | Associated with specific mutations within the gene encoding PrP |
| | Fatal familial insomnia | |
| | Creutzfeldt-Jakob disease | |
| **Animal prion diseases** | | |
| Cattle | Bovine spongiform encephalopathy | Exposure to prion-contaminated meat and bone meal |
| Sheep | Scrapie | Ingestion of scrapie-contaminated material |
| Deer, elk | Chronic wasting disease | Ingestion of prion-contaminated material |
| Mink | Transmissible mink encephalopathy | Source of infection unknown |
| Cats | Feline spongiform encephalopathy[a] | Exposure to prion-contaminated meat and bone meal |

PrP, prion protein.

[a]Associated with exposure to bovine spongiform encephalopathy–contaminated materials.

[b]Associated with prion-contaminated biologic materials, such as dura mater grafts, corneal transplants, and cadaver-derived human growth hormone, or prion-contaminated surgical instruments.

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The high number of cells within clones also is likely to provide physiologic protection to at least some members of the group. Extracellular polysaccharides, for example, may afford protection against potentially lethal agents such as antibiotics or heavy metal ions. Large amounts of polysaccharides produced by the high number of cells within a clone may allow cells within the interior to survive exposure to a lethal agent at a concentration that might kill single cells.

Many bacteria exploit a cell–cell communication mechanism called **quorum sensing** to regulate the transcription of genes involved in diverse physiologic processes, including bioluminescence, plasmid conjugal transfer, and the production of virulence determinants. Quorum sensing depends on the production of one or more diffusible signal molecules (eg, acetylated homoserine lactone [AHL]) termed **autoinducers** or **pheromones** that enable a bacterium to monitor its own cell population density (Figure 1-4). The cooperative activities leading to **biofilm** formation are controlled by quorum sensing. It is an example of multicellular behavior in prokaryotes.

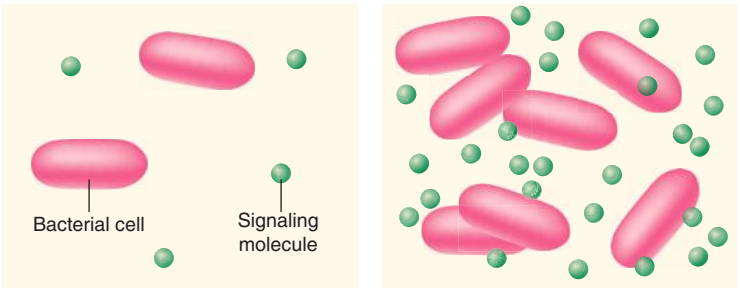
**TABLE 1-2 Distinguishing Characteristics of Viruses, Viroids, and Prions**

| Viruses | Viroids | Prions |
|---|---|---|
| Obligate intracellular agents | Obligate intracellular agents | Abnormal form of a cellular protein |
| Consist of either DNA or RNA surrounded by a protein coat | Consist only of RNA; no protein coat | Consist only of protein; no DNA or RNA |

Reproduced with permission from Nester EW, Anderson DG, Roberts CE, Nester MT (editors): *Microbiology: A Human Perspective*, 6th ed. McGraw-Hill; 2009:13.

A distinguishing characteristic of prokaryotes is their capacity to exchange small packets of genetic information. This information may be carried on **plasmids**, small and specialized genetic elements that are capable of replication within at least one prokaryotic cell line. In some cases, plasmids may be transferred from one cell to another and thus may carry sets of specialized genetic information through a population. Some plasmids exhibit a **broad host range** that allows them to convey sets of genes to diverse organisms. Of particular concern are **drug resistance plasmids** that may render diverse bacteria resistant to antibiotic treatment.

The survival strategy of a single prokaryotic cell line may lead to a range of interactions with other organisms. These may include symbiotic relationships illustrated by complex nutritional exchanges among organisms within the human gut. These exchanges benefit both the microorganisms and their human host. Parasitic interactions can be quite deleterious to the host. Advanced symbiosis or parasitism can lead to loss of functions that may not allow growth of the symbiont or parasite independent of its host.




When few cells are present, the concentration of the signaling molecule acylated homoserine lactone (AHL) is low.

When many cells are present, the concentration of the AHL is high. High concentrations of AHL induce expression of specific genes.

**FIGURE 1-4** Quorum sensing. (Reproduced with permission from Nester EW, Anderson DG, Roberts CE, Nester MT (editors): *Microbiology: A Human Perspective*, 6th ed. McGraw-Hill, 2009, p. 181.)

The **mycoplasmas**, for example, are parasitic prokaryotes that have lost the ability to form a cell wall. Adaptation of these organisms to their parasitic environment has resulted in incorporation of a substantial quantity of cholesterol into their cell membranes. Cholesterol, not found in other prokaryotes, is assimilated from the metabolic environment provided by the host. Loss of function is exemplified also by obligate intracellular parasites, the **chlamydiae** and **rickettsiae**. These bacteria are extremely small (0.2–0.5 μm in diameter) and depend on the host cell for many essential metabolites and coenzymes. This loss of function is reflected by the presence of a smaller genome with fewer genes (see Table 7-1).

The most widely distributed examples of bacterial symbionts appear to be chloroplasts and mitochondria, the energy-yielding organelles of eukaryotes. A substantial body of evidence points to the conclusion that ancestors of these organelles were **endosymbionts**, prokaryotes that established symbiosis within the cell membrane of the ancestral eukaryotic host. The presence of multiple copies of the organelles may have contributed to the relatively large size of eukaryotic cells and to their capacity for specialization, a trait ultimately reflected in the evolution of differentiated multicellular organisms.

## Classification of the Prokaryotes

An understanding of any group of organisms requires their **classification**. An appropriate classification system allows a scientist to choose characteristics that allow swift and accurate categorization of a newly encountered organism. The categorization allows prediction of many additional traits shared by other members of the category. In a hospital setting, successful classification of a pathogenic organism may provide the most direct route to its elimination. Classification may also provide a broad understanding of relationships among different organisms, and such information may have great practical value. For example, elimination of a pathogenic organism will be relatively long-lasting if its habitat is occupied by a nonpathogenic variant.

The principles of prokaryotic classification are discussed in Chapter 3. At the outset, it should be recognized that any prokaryotic characteristic might serve as a potential criterion for classification. However, not all criteria are equally effective in grouping organisms. Possession of DNA, for example, is a useless criterion for distinguishing organisms because all cells contain DNA. The presence of a broad host range plasmid is not a useful criterion because such plasmids may be found in diverse hosts and need not be present all of the time. Useful criteria may be structural, physiologic, biochemical, or genetic. **Spores**—specialized cell structures that may allow survival in extreme environments—are useful structural criteria for classification because well-characterized subsets of bacteria form spores. Some bacterial groups can be effectively subdivided on the basis of their ability to ferment specified carbohydrates. Such criteria may be ineffective when applied to other bacterial groups that may lack any fermentative capability. A biochemical test, the **Gram stain**, is an effective criterion for classification because response to the stain reflects fundamental and complex differences in the bacterial cell surface that divide most bacteria into two major groups.

Genetic criteria are increasingly used in bacterial classification, and many of these advances are made possible by the development of DNA-based technologies. It is now possible to design DNA probe or DNA amplification assays (eg, polymerase chain reaction [PCR] assays) that swiftly identify organisms carrying specified genetic regions with common ancestry. Comparison of DNA sequences for some genes led to the elucidation of **phylogenetic relationships** among prokaryotes. Ancestral cell lines can be traced, and organisms can be grouped on the basis of their evolutionary affinities. These investigations have led to some striking conclusions. For example, comparison of cytochrome c sequences suggests that all eukaryotes, including humans, arose from one of three different groups of purple photosynthetic bacteria. This conclusion in part explains the evolutionary origin of eukaryotes, but it does not fully take into account the generally accepted view that the eukaryotic

cell was derived from the evolutionary merger of different prokaryotic cell lines.

### Bacteria and Archaebacteria: The Major Subdivisions Within the Prokaryotes

A major success in molecular phylogeny has been the demonstration that prokaryotes fall into two major groups. Most investigations have been directed to one group, the bacteria. The other group, the archaebacteria, has received relatively little attention until recently, partly because many of its representatives are difficult to study in the laboratory. Some archaebacteria, for example, are killed by contact with oxygen, and others grow at temperatures exceeding that of boiling water. Before molecular evidence became available, the major subgroupings of archaebacteria had seemed disparate. The methanogens carry out an anaerobic respiration that gives rise to methane, the halophiles demand extremely high salt concentrations for growth, and the thermoacidophiles require high temperature and acidity. It has now been established that these prokaryotes share biochemical traits such as cell wall or membrane components that set the group entirely apart from all other living organisms. An intriguing trait shared by archaebacteria and eukaryotes is the presence of **introns** within genes. The function of introns—segments of DNA that interrupts informational DNA within genes—is not established. What is known is that introns represent a fundamental characteristic shared by the DNA of archaebacteria and eukaryotes. This common trait has led to the suggestion that—just as mitochondria and chloroplasts appear to be evolutionary derivatives of the bacteria—the eukaryotic nucleus may have arisen from an archaebacterial ancestor.

## PROTISTS

The "true nucleus" of eukaryotes (from Gr *karyon*, "nucleus") is only one of their distinguishing features. The membrane-bound organelles, the microtubules, and the microfilaments of eukaryotes form a complex intracellular structure unlike that found in prokaryotes. The agents of motility for eukaryotic cells are flagella or cilia—complex multistranded structures that do not resemble the flagella of prokaryotes. Gene expression in eukaryotes takes place through a series of events achieving physiologic integration of the nucleus with the endoplasmic reticulum, a structure that has no counterpart in prokaryotes. Eukaryotes are set apart by the organization of their cellular DNA in chromosomes separated by a distinctive mitotic apparatus during cell division.

In general, genetic transfer among eukaryotes depends on fusion of **haploid gametes** to form a **diploid** cell containing a full set of genes derived from each gamete. The life cycle of many eukaryotes is almost entirely in the diploid state, a form not encountered in prokaryotes. Fusion of gametes to form reproductive progeny is a highly specific event and establishes the basis for eukaryotic **species**. This term can be applied only metaphorically to the prokaryotes, which exchange fragments of DNA through recombination. Taxonomic groupings of eukaryotes frequently are based on shared **morphologic properties**, and it is noteworthy that many taxonomically useful determinants are those associated with reproduction. Almost all successful eukaryotic species are those in which closely related cells, members of the same species, can recombine to form viable offspring. Structures that contribute directly or indirectly to the reproductive event tend to be highly developed and—with minor modifications among closely related species—extensively conserved.

Microbial eukaryotes—**protists**—are members of the four following major groups: algae, protozoa, fungi, and slime molds. It should be noted that these groupings are not necessarily phylogenetic: Closely related organisms may have been categorized separately because underlying biochemical and genetic similarities may not have been recognized.

### Algae

The term *algae* has long been used to denote all organisms that produce $O_2$ as a product of photosynthesis. One major subgroup of these organisms—the blue-green bacteria, or cyanobacteria—are prokaryotic and no longer are termed algae. This classification is reserved exclusively for photosynthetic eukaryotic organisms. All algae contain chlorophyll in the photosynthetic membrane of their subcellular chloroplast. Many algal species are unicellular microorganisms. Other algae may form extremely large multicellular structures. Kelps of brown algae sometimes are several hundred meters in length. A number of algae produce toxins that are poisonous to humans and other animals. Dinoflagellates, a unicellular alga, cause algal blooms, or red tides, in the ocean (Figure 1-5). Red tides caused by the dinoflagellate *Gonyaulax* species are serious because this organism produces neurotoxins such as **saxitoxin** and **gonyautoxins**, which accumulate in shellfish (eg, clams, mussels, scallops, oysters) that feed on this organism. Ingestion of these shellfish by humans results in symptoms of **paralytic shellfish poisoning** and can lead to death.

### Protozoa

Protozoa are unicellular nonphotosynthetic protists. The most primitive protozoa appear to be flagellated forms that in many respects resemble representatives of the algae. It seems likely that the ancestors of these protozoa were algae that became **heterotrophs**—the nutritional requirements of such organisms are met by organic compounds. Adaptation to a heterotrophic mode of life was sometimes accompanied by loss of chloroplasts, and algae thus gave rise to the closely related protozoa. Similar events have been observed in the laboratory to be the result of either mutation or physiologic adaptation.

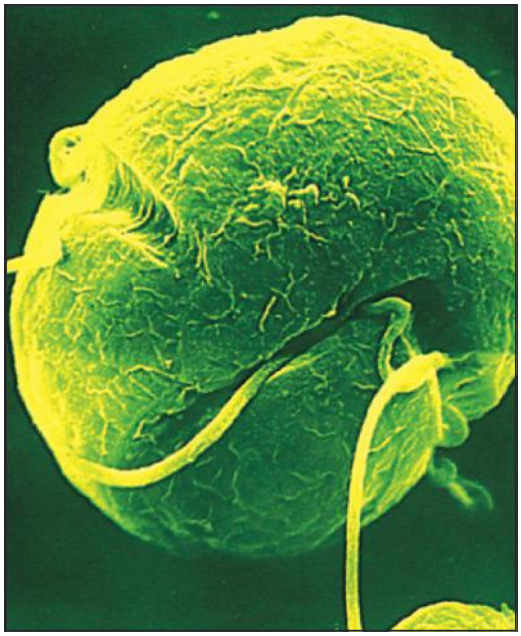


**FIGURE 1-5** The dinoflagellate *Gymnodinium* scanning electron micrograph (4000×). (Reproduced with permission from David M. Phillips/Visuals Unlimited.)

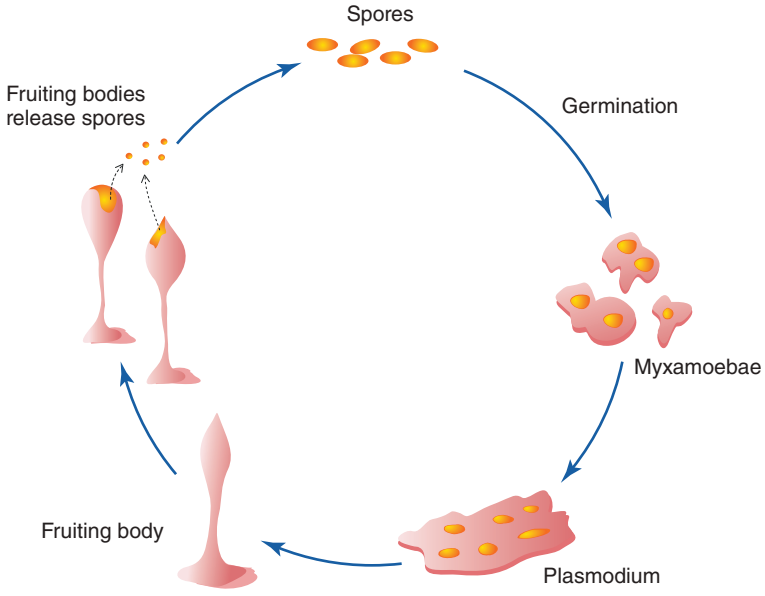
From flagellated protozoa appear to have evolved the ameboid and the ciliated types; intermediate forms are known that have flagella at one stage in the life cycle and pseudopodia (characteristic of the ameba) at another stage. A fourth major group of protozoa, the sporozoa, are strict parasites that are usually immobile; most of these reproduce sexually and asexually in alternate generations by means of spores. Protozoan parasites of humans are discussed in Chapter 46.

## Fungi

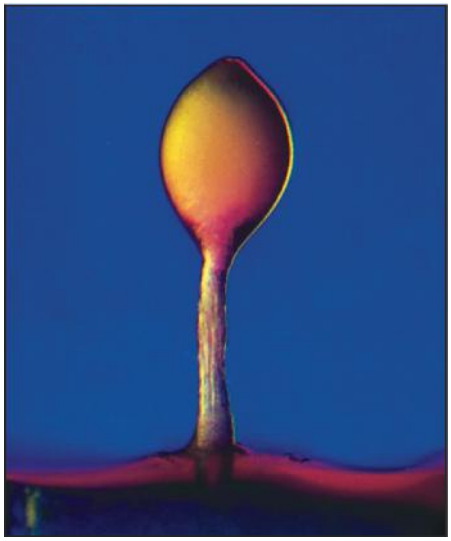
The fungi are nonphotosynthetic protists growing as a mass of branching, interlacing filaments ("hyphae") known as a **mycelium**. The largest known contiguous fungal mycelium covered an area of 2400 acres (9.7 $km^2$) at a site in eastern Oregon. Although the hyphae exhibit cross walls, the cross walls are perforated and allow free passage of nuclei and cytoplasm. The entire organism is thus a coenocyte (a multinucleated mass of continuous cytoplasm) confined within a series of branching tubes. These tubes, made of polysaccharides such as chitin, are homologous with cell walls. The mycelial forms are called **molds**; a few types, **yeasts**, do not form a mycelium but are easily recognized as fungi by the nature of their sexual reproductive processes and by the presence of transitional forms.

The fungi probably represent an evolutionary offshoot of the protozoa; they are unrelated to the actinomycetes, mycelial bacteria that they superficially resemble. The major subdivisions (phyla) of fungi are Chytridiomycota, Zygomycota (the zygomycetes), Ascomycota (the ascomycetes), Basidiomycota (the basidiomycetes), and the "deuteromycetes" (or imperfect fungi).

The evolution of the ascomycetes from the phycomycetes is seen in a transitional group, whose members form a zygote but then transform this directly into an ascus. The basidiomycetes are believed to have evolved in turn from the ascomycetes. The classification of fungi and their medical significance are discussed further in Chapter 45.




A



B

**FIGURE 1-6** Slime molds. **A:** Life cycle of an acellular slime mold. **B:** Fruiting body of a cellular slime mold. (Reproduced with permission from Carolina Biological Supply/Phototake, Inc.)

## Slime Molds

These organisms are characterized by the presence, as a stage in their life cycle, of an ameboid multinucleate mass of cytoplasm called a **plasmodium**. The plasmodium of a slime mold is analogous to the mycelium of a true fungus. Both are coenocytic. Whereas in the latter, cytoplasmic flow is confined to the branching network of chitinous tubes, in the former, the cytoplasm can flow in all directions. This flow causes the plasmodium to migrate in the direction of its food source, frequently bacteria. In response to a chemical signal, 3′, 5′-cyclic AMP (see Chapter 7), the plasmodium, which reaches macroscopic size, differentiates into a stalked body that can produce individual motile cells. These cells, flagellated or ameboid, initiate a new round in the life cycle of the slime mold (Figure 1-6). The cycle frequently is initiated by sexual fusion of single cells.

The life cycle of the slime molds illustrates a central theme of this chapter—the interdependency of living forms. The growth of slime molds depends on nutrients provided by bacterial or, in some cases, plant cells. Reproduction of the slime molds via plasmodia can depend on intercellular recognition and fusion of cells from the same species. Full understanding of a microorganism requires both knowledge of the other organisms with which it coevolved and an appreciation of the range of physiologic responses that may contribute to survival.

## CHAPTER SUMMARY

- Microorganisms are a large and diverse group of microorganisms existing as single cells or clusters; they also include viruses, which are microscopic but not cellular.
- A virus consists of a nucleic acid molecule, either DNA or RNA, enclosed in a protein coat, or capsid, sometimes enclosed by an envelope composed of lipids, proteins, and carbohydrates.
- A prion is an infectious protein, which is capable of causing chronic neurologic diseases.
- Prokaryotes consist of bacteria and archaebacteria.
- Prokaryotes are haploid.
- Microbial eukaryotes, or protists, are members of four major groups: algae, protozoa, fungi, and slime molds.
- Eukaryotes have a true nucleus and are diploid.

## REVIEW QUESTIONS

1. Which one of the following terms characterizes the interaction between herpes simplex virus and a human?
   (A) Parasitism
   (B) Symbiosis
   (C) Endosymbiosis
   (D) Endoparasitism
   (E) Consortia
2. Which one of the following agents lacks nucleic acid?
   (A) Bacteria
   (B) Viruses
   (C) Viroids
   (D) Prions
   (E) Protozoa
3. Which one of the following is a prokaryote?
   (A) Bacteria
   (B) Algae
   (C) Protozoa
   (D) Fungi
   (E) Slime molds
4. Which one of the following agents simultaneously contains both DNA and RNA?
   (A) Bacteria
   (B) Viruses
   (C) Viroids
   (D) Prions
   (E) Plasmids
5. Which of the following cannot be infected by viruses?
   (A) Bacteria
   (B) Protozoa
   (C) Human cells
   (D) Viruses
   (E) None of the above
6. Viruses, bacteria, and protists are uniquely characterized by their respective size. True or false?
   (A) True
   (B) False
7. Quorum sensing in prokaryotes involves
   (A) Cell–cell communication
   (B) Production of molecules such as acetylated homoserine lactone (AHL)
   (C) An example of multicellular behavior
   (D) Regulation of genes involved in diverse physiologic processes
   (E) All of the above
8. A 16-year-old female patient presented to her family physician with a complaint of an abnormal vaginal discharge and pruritus (itching). The patient denied having sexual activity and recently completed a course of doxycycline for the treatment of her acne. An examination of a Gram-stained vaginal smear revealed the presence of gram-positive oval cells about 4–8 μm in diameter. Her vaginitis is caused by which of the following agents?
   (A) Bacterium
   (B) Virus
   (C) Protozoa
   (D) Fungus
   (E) Prion
9. A 65-year-old man develops dementia, progressive over several months, along with ataxia and somnolence. An electroencephalographic pattern shows paroxysms with high voltages and slow waves, suggestive of Creutzfeldt-Jakob disease (CJD). By which of the following agents is this disease caused?
   (A) Bacterium
   (B) Virus
   (C) Viroid
   (D) Prion
   (E) Plasmid