

# Contents

Preface **xii**

## SECTION I

### 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  $\beta$ -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 Carcinogenesis 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
- 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 V MYCOLOGY 657

Thomas G. Mitchell, PhD

- 45. Medical Mycology 657**  
 General Properties, Virulence, and Classification of Pathogenic Fungi 658

## 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  
Amoebae) 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) 734Larva 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 and  
Fungal Microbiota 753Laboratory 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*Mycobacterium avium* Complex 798**Infections in Transplant Patients 799****Emerging Infections 805**

Index 809