BRS
BOARD REVIEW SERIES

INCLUDES
Online Access to Full Text and Questions from the Book!

Microbiology & Immunology

FIFTH EDITION

Arthur G. Johnson
Richard J. Ziegler
Louise Hawley

- Outline format—highlights the most tested topics for Step 1
- More than 350 board-style questions to help test your memorization and mastery
- Online access—offers greater study flexibility

Wolters Kluwer Health | Lippincott Williams & Wilkins

thePoint

BRS BOARD REVIEW SERIES

Microbiology and Immunology

FIFTH EDITION

Arthur G. Johnson, Ph.D
Professor Emeritus
Department of Anatomy, Microbiology, and Pathology
University of Minnesota Medical School-Duluth
Duluth, Minnesota

Richard J. Ziegler, Ph.D.
Professor of Microbiology
Department of Anatomy, Microbiology, and Pathology
University of Minnesota Medical School-Duluth
Duluth, Minnesota

Louise Hawley, Ph.D.
Professor and Chair
Department of Microbiology and Immunology
Ross University School of Medicine
Dominica, West Indies

Wolters Kluwer Health | Lippincott Williams & Wilkins
Philadelphia • Baltimore • New York • London
Buenos Aires • Hong Kong • Sydney • Tokyo

Acquisitions Editor: Charles W. Mitchell
Product Manager: Stacey L. Sebring
Marketing Manager: Jennifer Kuklinski
Compositor: Cadmus Communications

351 West Camden Street
Baltimore, Maryland 21201-2436 USA

530 Walnut Street
Philadelphia, PA 19106

Printed in the United States of America

Library of Congress Cataloging-in-Publication Data

Johnson, Arthur G.
Microbiology and immunology / Arthur G. Johnson, Richard J. Ziegler, Louise Hawley. — 5th ed.
p. ; cm. — (Board review series)
Rev. ed. of: Microbiology and immunology / Arthur G. Johnson … [et al.]. 4th ed. c2002.
Includes index.
ISBN 978-0-7817-8912-7
1. Medical microbiology—Outlines, syllabi, etc. 2. Medical microbiology—Examinations, questions, etc. 3. Immunology—Outlines, syllabi, etc. 4. Immunology—Examinations, questions, etc. I. Johnson, Arthur G. II. Ziegler, Richard J. III. Hawley, Louise. IV. Microbiology and immunology. V. Title. VI. Series: Board review series.
[DNLM: 1. Microbiological Phenomena—Examination Questions. 2. Immune System Phenomena—Examination Questions. QW 18.2 J66m 2010]
QR46.M5387 2010
616.9′041076—dc22 2009020327

The publishers have made every effort to trace the copyright holders for borrowed material. If they have inadvertently overlooked any, they will be pleased to make the necessary arrangements at the first opportunity.

We'd like to hear from you! If you have comments or suggestions regarding this Lippincott Williams & Wilkins title, please contact us at the appropriate customer service number listed below, or send correspondence to **book_comments@lww.com.** If possible, please remember to include your mailing address, phone number, and a reference to the book title and author in your message. To purchase additional copies of this book call our customer service department at **(800) 638-3030** or fax orders to **(301) 824-7390.** International customers should call **(301) 714-2324.**

Dedication

The authors dedicate this book to their many students who have been a source of stimulation over the years, and to their many colleagues whose research and insight has resulted in the knowledge described herein. We also note the seminal contributions to previous editions of this review of two colleagues, the late Omelan Lukasewycz, Ph.D. and Thomas Fitzgerald, Ph.D.

Acknowledgments

The authors are grateful for the excellent organizational and secretarial skills of Wendy Schwartz who aided in the preparation of this edition.

Preface

This concise review of microbiology and immunology is designed specifically for medical and graduate students for successful preparation for the United States Medical Licensing Examination (USMLE) as well as other examinations. This newest edition remains a succinct description of the most important microbiological and immunological concepts and critical details needed to understand important human infections and the immune system function and malfunction.

ORGANIZATION

The book is divided into 12 chapters starting with basic information and bringing the student quickly to the level of detail and comprehension needed for Step 1. There is both a ''bug'' approach followed by an organ-systems approach. They include critical signs/symptoms, epidemiology, etiology, pathogenesis of infections and immune diseases along with the mechanisms of preventing infection and means of identifying and diagnosing the causative agent.

The outline format facilitates rapid review of important information. Numerous tables with clinical correlations have been added along with updated images. Each chapter is followed by review questions and answers and explanations that reflect the style and content of the USMLE. We have added four 50 question comprehensive examinations at the end of the book. Each has the same subject distribution generally found on Step 1 and so may be used as a practice exam and self-assessment tool to help students diagnose their weaknesses prior to, during, and after reviewing microbiology and immunology.

KEY FEATURES

- Both ''bug'' and organ-systems approaches in one small book
- 4-color tables and figures summarize essential information for quick recall
- End-of-chapter review tests feature updated USMLE-style questions
- Four USMLE comprehensive exams (in 50 question blocks like Step 1) with explanations are included
- Updated and current information in all chapters

Arthur G. Johnson, Ph.D.
Richard J. Ziegler, Ph.D.
Louise Hawley, Ph.D.

Contents

Dedication iii
Acknowledgments iii
Preface iv

1. GENERAL PROPERTIES OF MICROORGANISMS 1

I. The Microbial World 1
II. Host–Parasite Relationship 3
III. Sterilization and Disinfection 4

Review Test 5

2. BACTERIA 7

I. Bacterial Structure 7
II. Bacterial Growth and Replication 12
III. Bacterial Viruses 16
IV. Genetics 21
V. Bacterial Pathogenesis 28
VI. Host Defenses to Bacteria 29
VII. Antimicrobial Chemotherapy 29

Review Test 34

3. BACTERIAL TAXONOMY 38

I. Diagnostic Bacteriology 38
II. Introduction to Major Bacterial Genera 46
III. Gram-Positive Bacteria 46
IV. Gram-Negative Bacteria 49
V. Poorly Gram-Staining Bacteria 53

Review Test 57

4. BACTERIAL DISEASES 62

I. Major Recurring Species 62
II. Eye Infections 65
III. Dental Disease 67

IV. Ear and Sinus Infections 67
V. Bacterial Pharyngitis 68
VI. Infections of the Respiratory System 69
VII. Pneumonia/Pneumonitis 70
VIII. Nervous System Infections: Meningitis 76
IX. Nervous System Infections: Nonmeningitis Conditions 79
X. Cardiovascular Infections: Vasculitis 79
XI. Cardiovascular Infections: Endocarditis 79
XII. Cardiovascular: Myocarditis 81
XIII. Gastrointestinal Infections 81
XIV. Urinary Tract Infections 87
XV. Skin, Mucosal, Soft Tissue, and Bone Infections 88
XVI. Sexually Transmitted Infections 90
XVII. Pregnancy, Congenital, and Perinatal Infections 93
XVIII. Arthropod-Borne and Zoonotic Diseases 94
XIX. Bacterial Vaccines 98

Review Test 103

5. VIRUSES 107

I. Nature of Human Viruses 107
II. Viral Classification 108
III. Viral Replication and Genetics 108
IV. Viral Pathogenesis 110
V. Host Defenses to Viruses 114
VI. Immunotherapy, Antivirals, and Interferon 115
VII. Diagnostic Virology 119
VIII. DNA Viruses 121
VIX. RNA Viruses 124
X. Slow Viruses and Prions 132
XI. Oncogenic Viruses 133

Review Test 136

6. SYSTEMS-BASED AND SITUATIONAL VIRAL INFECTIONS 140

I. Eye Infections 140
II. Ear Infections 140
III. Upper Respiratory Tract (Mouth and Throat) Infections 141
IV. Lower Respiratory Tract Infections 142
V. Gastrointestinal Infections 143
VI. Liver Infection 144
VII. Urinary Tract Infections 145
VIII. Cardiovascular Infections 145
IX. Nervous System Infections 146
X. Skin, Mucosal, and Soft Tissue Infections 148
XI. Childhood Infections 149
XII. Congenital and Neonatal Infections 150
XIII. Sexually Transmitted Diseases 151

XIV. Postinfectious Disease 151
XV. Organ Transplant-Associated Diseases 152
XVI. Arboviral and Zoonotic Diseases 152
Review Test 153

7. MYCOLOGY 156

I. Overview of Fungi 156
II. Fungal Groups 160
III. Overview of Fungal Diseases 160
IV. Diagnosis of Fungal Infections 160
V. Antifungal Drugs 161
Review Test 164

8. FUNGAL DISEASES 165

I. Superficial Skin Infections 165
II. Cutaneous Mycoses 166
III. Mucocutaneous Candidiasis/*C. albicans* 167
IV. Subcutaneous Mycoses 168
V. Pneumonias/Systemic Mycoses 168
VI. Opportunistic Mycoses 172
VII. Tables for Self-Testing 175
Review Test 176

9. PARASITOLOGY 181

I. Characteristics of Parasites and Their Hosts 181
II. Protozoan Parasites 181
III. Worms 182
Review Test 184

10. PARASITIC DISEASES 185

Review Test 196

11. CLUES FOR DISTINGUISHING CAUSATIVE INFECTIOUS AGENTS 200

I. Conjunctivitis 200
II. Pneumonias 200
III. Diarrheas and Dysentery 205
IV. Acute Meningitis 206

V. Bacterial and Viral Skin Infection and Rashes 206
VI. Genitourinary Tract Infections 208

Review Test 219

12. IMMUNOLOGY 222

I. Overview 222
II. Innate (native) immunity 222
III. Adaptive (Acquired) Immunity 226
IV. Antigens 229
V. Antibodies 230
VI. Properties of Antibodies 231
VII. Immunogenetics 235
VIII. Immunologic Assays 241
IX. The Response to Antigen 245
X. Clinical Immunological Disorders 249

Review Test 261

Comprehensive Examination: Block 1 265
Comprehensive Examination: Block 2 275
Comprehensive Examination: Block 3 285
Comprehensive Examination: Block 4 295

Index 305

chapter 1

General Properties of Microorganisms

I. THE MICROBIAL WORLD

A. Microorganisms

1. Belong to the Protista biologic kingdom.
2. Include some eukaryotes and prokaryotes, viruses, viroids, and prions.
3. Are classified according to their structure, chemical composition, and biosynthetic and genetic organization.

B. Eukaryotic cells (Table 1.1)

1. Contain organelles and a nucleus bounded by a nuclear membrane.
2. Contain complex phospholipids, sphingolipids, histones, and sterols.
3. Lack a cell wall. (Plant cells and fungi have a cell wall.)
4. Have multiple diploid chromosomes and nucleosomes.
5. Have relatively long-lived mRNA formed from the processing of precursor mRNA, which contains exons and introns.
6. Have 80s ribosomes and uncoupled transcription and translation.
7. Include **protozoa** and **fungi**.
   - **a.** Organisms in **kingdom Protozoa** are classified into seven phyla; three of these phyla (Sarcomastigophora, Apicomplexa, Ciliophora) contain medically important species that are human parasites.
   - **b.** Organisms in **kingdom Fungi**:
     - **(1)** Are **eukaryotic** cells with a complex carbohydrate cell wall.
     - **(2)** Have ergosterol as the dominant membrane sterol.
     - **(3)** May be **monomorphic,** existing as single-celled **yeast** or multicellular, filamentous **molds**.
     - **(4)** May be **dimorphic,** existing as **yeasts or molds depending on temperature and nutrition**.
     - **(5)** May have both asexual and sexual reproduction capabilities. Deuteromycetes, or Fungi Imperfecti, have no known sexual stages.

C. Prokaryotic cells (see Table 1.1)

1. Have no organelles, no membrane-enclosed nucleus, and no histones; in rare cases, they contain complex phospholipids, sphingolipids, and sterols.
2. Have 70S ribosomes composed of 30S and 50S subunits.
3. Have a cell wall composed of peptidoglycan-containing muramic acid.
4. Are haploid with a single chromosome.
5. Have short-lived, unprocessed mRNA.
6. Have coupled transcription and translation.
7. Include **typical bacteria, mycoplasmas,** and **obligate intracellular bacteria**.
   - **a. Typical bacteria:**
     - **(1)** Have a **cell wall**.
     - **(2)** May be normal flora or may be pathogenic in humans.
     - **(3)** Do not have a sexual growth cycle; however, some can produce asexual spores.

table 1.1 Components of Microbial Cells

Structure	Composition	Fungi	Gram-Positive Bacteria	Gram-Negative Bacteria	Mycoplasmas	Chlamydia*	Rickettsia*
		Cell Type					
Envelope capsule	Polysaccharide or polypeptide	–	+ or –	+ or –	–	–	–
Wall							
Chitin	Poly-*N*-acetylglucosamine	+	–	–	–	–	–
Peptidoglycan	Poly-*N*-acetyl/glucosamine-*N* acetylmuramic acid tetrapeptide	–	+	+	–	–	+
Periplasm	Proteins and oligosaccharides	–	–	+	–	+	+
Lipoprotein	Lipoprotein	–	–	+	–	+	+
Outer membrane	Proteins, phospholipids, and lipopolysaccharide	–	–	+	–	+	+
Appendages							
Pili	Protein	–	+ or –	+ or –	–	–	–
Flagella	Protein	–	+ or –	+ or –	–	–	–
Cell membrane	Proteins and phospholipids	+ (plus ergosterol)	+	+	+	+	+
Cytosol							
Organelles	Protein, phospholipids, and nucleic acids	+	–	–	–	–	–
80S Ribosomes	Protein and RNA	+	–	–	–	–	–
70S Ribosomes	Protein and RNA	–	+	+	+	+	+
Genetic Material							
Nucleus	Protein, phospholipids, and Nucleic acids	+	–	–	–	–	–
Nucleoid	Protein and nucleic acids	–	+	+	+	+	+
Plasmids	DNA	+ or –	+ or –	+ or –	+ or –	+ or –	+ or –
Transposons	DNA	+	+	+	+	+	+
Spores							
Reproductive Spores	All cellular components	+	–	–	–	–	–
Endospores	All cellular components plus dipicolinic acid	–	+ or –	–	–	–	–

*Obligate intracellular pathogens

b. **Mycoplasmas:**
   (1) Are the smallest and simplest of the bacteria that are self-replicating.
   (2) Lack a cell wall.
   (3) Are the only prokaryotes that contain **sterols**.

c. **Obligate intracellular bacteria** include **Rickettsia** and **Chlamydia**.
   (1) **Rickettsia** are incapable of self-replication and depend on the host cell for adenosine triphosphate (ATP) production.
   (2) **Chlamydia** are bacteria-like pathogens with a complex growth cycle involving intracellular and extracellular forms. They depend on the host cell for ATP production.

D. Viruses

1. Are not cells and are not visible with the light microscope.
2. Are **obligate intracellular parasites**.
3. Contain no organelles or biosynthetic machinery, except for a few enzymes.
4. Contain either RNA or DNA as genetic material.
5. Are called **bacteriophages** (or **phages**) if they have a bacterial host.

E. Viroids

1. Are not cells and are not visible with the light microscope.
2. Are **obligate intracellular parasites**.
3. Are single-stranded, covalently closed, circular RNA molecules that exist as base-paired, rod-like structures.
4. Cause plant diseases but have not been proven to cause human disease, although the RNA of the hepatitis D virus (HDV) is viroid-like.

F. Prions

1. Are infectious particles associated with subacute progressive, degenerative diseases of the central nervous system (e.g., Creutzfeldt-Jakob disease).
2. Copurify with a specific glycoprotein (PrP) that has a molecular weight of 27 to 30 kDa. They are resistant to nucleases but are inactivated with proteases and other agents that inactivate proteins.
3. Are altered conformations of a normal cellular protein that can autocatalytically form more copies of itself.

II. HOST–PARASITE RELATIONSHIP

A. Normal flora consist mainly of bacteria, but fungi and protozoa may be present in some individuals. They can provide useful nutrients (e.g., vitamin K) and release compounds (e.g., colicins) with antibacterial activity against pathogenic bacteria.

1. They reside in the skin, mouth, nose, oropharynx, large intestine, urethra, and vagina.
2. Normal flora may produce disease if they invade normally sterile areas of the body or are not properly controlled by the immune system.

B. Microbial pathogenicity *refers to a microbe's ability to cause disease, which depends on genetically determined virulence factors.* A microbe's pathogenicity is related to its:

1. Entry
2. Colonization
3. Escape from host defense mechanisms
4. Multiplication
5. Damage to host tissues

C. Virulence factors are *chromosomal and extrachromosomal (plasmid) gene products that affect aspects related to an organism's*:

1. Invasion *properties*
2. Adherence and colonization

3. Tissue damage induced by toxins, immune system reactions, and intracellular growth
4. Eluding host defense mechanisms
5. Antibiotic resistance

III. STERILIZATION AND DISINFECTION

A. Terminology

1. **Sterility**—total absence of viable microorganisms as assessed by no growth on any medium
2. **Bactericidal**—kills bacteria
3. **Bacteriostatic**—inhibits growth of bacteria
4. **Sterilization**—removal or killing of all microorganisms
5. **Disinfection**—removal or killing of disease-causing microorganisms
6. **Sepsis**—infection
7. **Aseptic**—without infection
8. **Antisepsis**—any procedure that inhibits the growth and multiplication of microorganisms

B. Kinetics of killing

1. Killing is affected by the medium, the concentration of organisms and antimicrobial agents, temperature, pH, and the presence of endospores.
2. It can be exponential (logarithmic); can result in a killing curve that becomes asymptotic, requiring extra considerations in killing final numbers, especially if the population is heterogeneous relative to sensitivity.

C. Methods of control

1. **Moist heat** (autoclaving at 121°C/250°F for 15 minutes at a steam pressure of 15 pounds per square inch) kills microorganisms, including endospores.
2. **Dry heat** and i**ncineration** are both methods that oxidize proteins, killing bacteria.
3. **Ultraviolet radiation** blocks DNA replication.
4. **Chemicals**
   a. **Phenol** is used as a disinfectant standard that is expressed as a phenol coefficient, which compares the rate of the minimal sterilizing concentration of phenol to that of the test compound for a particular organism.
   b. **Chlorhexidine** is a diphenyl cationic analog that is a useful topical disinfectant.
   c. **Iodine** is bactericidal in a 2% solution of aqueous alcohol containing potassium iodide. It acts as an oxidizing agent and combines irreversibly with proteins. It can cause hypersensitivity reactions.
   d. **Chlorine** inactivates bacteria and most viruses by oxidizing free sulfhydryl groups.
   e. **Quaternary ammonium compounds** (e.g., **benzalkonium chloride**) inactivate bacteria by their hydrophobic and lipophilic groups, interacting with the cell membrane to alter metabolic properties and permeability.
   f. **Ethylene oxide** is an alkylating agent that is especially useful for sterilizing heat-sensitive hospital instruments. It requires exposure times of 4 to 6 hours, followed by aeration to remove absorbed gas.
   g. **Alcohol** requires concentrations of 70% to 95% to kill bacteria given sufficient time. Isopropyl alcohol (90% to 95%) is the major form in use in hospitals.

Review Test

Directions: *Each of the numbered items or incomplete statements in this section is followed by answers or completions of the statement. Select the ONE lettered answer that is BEST in each case.*

1. A pharmaceutical company has developed a new compound that is well tolerated by the body and inhibits the sterol ergosterol synthesis. Screening of anti-infectious agent activity should be directed toward

(A) Bacteria
(B) Chlamydia species
(C) Fungi
(D) Rickettsia species
(E) Viruses

2. 50S ribosomal subunits are found in

(A) Bacteria
(B) Fungi
(C) Prions
(D) Protozoa
(E) Viruses

3. The normal flora of the large intestine consists mainly of

(A) Bacteria
(B) Fungi
(C) Protozoa
(D) Viruses
(E) No microbial agents

4. The minimal concentration of alcohol necessary to kill bacteria and enveloped viruses is

(A) 30%
(B) 40%
(C) 50%
(D) 60%
(E) 70%

5. Human obligate intracellular pathogens that depend on the host cell for ATP production are

(A) Bacteriophages
(B) Mycoplasma species
(C) Prions
(D) Rickettsia species
(E) Viroids

6. Dimorphism is a characteristic of

(A) Bacteria
(B) Fungi
(C) Prions
(D) Rickettsia species
(E) Viruses

7. A new infectious agent has been isolated from deer ticks. It lacks a cell wall but has 70S ribosomes. This agent is most likely a

(A) Bacterium
(B) Chlamydia species
(C) Mycoplasma species
(D) Rickettsia species
(E) Virus

Answers and Explanations

1. **The answer is C.** Fungi have ergosterol as their dominant membrane sterol. Mycoplasmas are the only prokaryotes with sterols in their cytoplasmic membrane, but they do not synthesize their own sterols.
2. **The answer is A.** Bacteria have 70S ribosomes composed of 30S and 50S subunits. Fungi and protozoa have 80S ribosomes, and prions and viruses do not have ribosomes.
3. **The answer is A.** Bacteria form the majority of the normal flora of the large intestine. Other types of human infectious agents are not usually present except in time of disease.
4. **The answer is E.** An alcohol concentration of 70% to 95% is necessary to kill bacteria.
5. **The answer is D.** Chlamydia and rickettsia are obligate intracellular pathogens because they depend on the host cell to provide them with ATP.
6. **The answer is B.** Certain species of pathogenic fungi are dimorphic (i.e., existing as yeast or mold forms depending on their environment).
7. **The answer is C.** Mycoplasmas are the only microbes that lack a cell wall, but they do have 70S ribosomes.

chapter 2

Bacteria

I. BACTERIAL STRUCTURE

A. Shape. Along with other properties, shape is used to identify bacteria. It is determined by the mechanism of cell wall assembly.

1. Bacterial shape usually can be determined with appropriate staining and a light microscope.
2. **Types**
   a. **Round** (coccus)
   b. **Rod-like** (bacillus)
   c. **Spiral**
3. Cocci and bacilli often grow in doublets (diplococci) or chains (streptococci). Cocci that grow in clusters are called staphylococci.
4. Some bacterial species are **pleomorphic**, such as *Bacteroides*.
5. Antibiotics that affect cell wall biosynthesis (e.g., penicillin) may alter a bacteria's shape.

B. Nucleus. In bacteria, the nucleus generally is called a **nucleoid** or **nuclear body.**

1. The bacterial nucleus is not surrounded by a nuclear membrane, nor does it contain a mitotic apparatus.
2. **Composition.** The nucleus consists of polyamine and magnesium ions bound to negatively charged, circular, supercoiled, double-stranded DNA; small amounts of RNA; RNA polymerase; and other proteins.

C. Cytoplasm

1. Bacterial cytoplasm contains ribosomes and various types of nutritional storage granules.
2. It contains **no organelles**.

D. Ribosomes. Bacterial ribosomes contain proteins and RNAs that differ from those of their eukaryotic counterparts.

1. **Types.** Bacterial ribosomes have a sedimentation coefficient of 70S and are composed of 30S and 50S subunits containing 16S, and 23S and 5S RNA, respectively.
2. Ribosomes engaged in protein biosynthesis are membrane bound.
3. Many antibiotics target ribosomes, inhibiting protein biosynthesis. Some antibiotics selectively target the 70s ribosomes (e.g., erythromycin), but not 80s ribosomes.

E. Cell (cytoplasmic) membrane

1. **Structure.** The cell membrane is a typical phospholipid bilayer that contains the following constituents:
   a. Cytochromes and enzymes involved in electron transport and oxidative phosphorylation.
   b. Carrier lipids, enzymes, and **penicillin-binding proteins (PCP)** involved in cell wall biosynthesis.
   c. Enzymes involved in phospholipid synthesis and DNA replication.
   d. Chemoreceptors.

2. Functions

a. Selective permeability and active transport facilitated by membrane-bound permeases, binding proteins, and various transport systems.

b. Site of action of certain antibiotics such as polymyxin.

F. Mesosomes are controversial structures that are **convoluted invaginations** of the plasma membrane.

1. Septal mesosomes occur at the septum (cross-wall); **lateral mesosomes** are nonseptal.

2. Functions: participate in DNA replication, cell division, and secretion.

G. Plasmids

1. Plasmids are small, circular, nonchromosomal, double-stranded DNA molecules that are:

a. Capable of self-replication.

b. Most frequently extrachromosomal but may become integrated into bacterial DNA.

2. Function: contain genes that confer protective properties such as antibiotic resistance or virulence factors or their own transmissibility to other bacteria.

H. Transposons

1. Transposons are small pieces of DNA that move between the DNA of bacteria and plasmids; they do not self-replicate.

2. Functions

a. Code for antibiotic resistance enzymes, metabolic enzymes, or toxins.

b. May alter expression of neighboring genes or cause mutations to genes into which they are inserted.

I. Cell envelope (Figs. 2.1 and 2.2)

1. General structure. The cell envelope is composed of the macromolecular layers that surround the bacterium. It includes:

a. A cell membrane and a peptidoglycan layer except for mycoplasma.

b. An outer membrane layer in Gram-negative bacteria.

c. A capsule, a glycocalyx layer, or both (sometimes).

d. Antigens that frequently induce a specific antibody response.

2. Cell wall

a. The cell wall refers to that portion of the cell envelope that is **external to the cytoplasmic membrane** and **internal to the capsule or glycocalyx.**

b. It confers osmotic protection and Gram-staining characteristics.

c. In **Gram-positive bacteria** it is composed of:

(1) Peptidoglycan

(2) Teichoic and teichuronic acids

(3) Polysaccharides

d. In **Gram-negative bacteria,** it is composed of:

(1) Peptidoglycan

(2) Lipoprotein

(3) An outer phospholipid membrane that contains lipopolysaccharide

3. Peptidoglycan (also called **mucopeptide** or **murein**) is unique to prokaryotes. It is found in all bacterial cell walls except *Mycoplasma.*

a. Structure

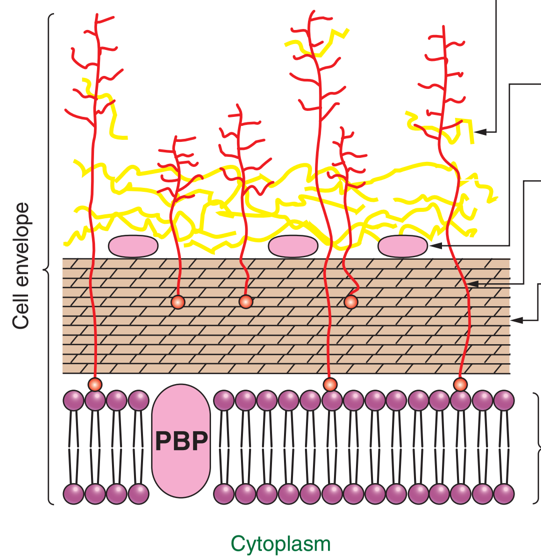
(1) This **complex polymer** consists of a **backbone** composed of alternating *N*-acetylglucosamine and *N*-acetylmuramic acid and a set of identical tetrapeptide **side chains**.

(2) The tetrapeptide side chains are attached to the *N*-acetylmuramic acid and are frequently linked to adjacent tetrapeptides by identical peptide **cross-bridges** or by direct peptide **bonds**.

(3) The β-1, 4 glycosidic bond between *N*-acetylmuramic acid and *N*-acetylglucosamine is cleaved by the bacteriolytic enzyme **lysozyme** (found in mucus, saliva, and tears).

(4) It may contain **diaminopimelic acid**, an amino acid unique to prokaryotic cell walls.

Gram-Positive Cell Envelope



Structure/Chemistry	Function
Capsule* Polysaccharides, except for polypeptide capsule of *Bacillus anthracis*	**Antiphagocytic** and **immunogenic** (except for hyaluronic acid capsule of *Strep. pyogenes*)
Surface proteins (e.g., *Staph. aureus* A protein or *Strep. pyogenes* M protein)	Many are **antiphagocytic** and **immunogenic**.
Teichoic acids (TA) **Lipoteichoic acids (LTA)** LTAs are attached to the membrane.	**Attachment** to epithelial surfaces; "chunks" from lysis **trigger complement** (alt C') and cytokines.
Cell wall/Peptidoglycan (PG) Thick layer, highly cross-linked, pentaglycine bridges; small and moderate-sized molecules diffuse across cell wall	**Rigid support** of cell; osmotic protection; lysis "chunks" of PG and TA **trigger alt C'** and cytokines → shock and, if in CNS, high PMN response
Cytoplasmic membrane Hydrophobic phospholipid bilayer	Membranous **matrix for enzymes** of many pathways, such as **respiration** and final stages of **cell wall synthesis** (Penicillin Binding Proteins [PBPs] = transpeptidases and carboxypeptidases)

* Not all Gram-positive cells have capsules or surface proteins.

FIGURE 2.1. Gram-positive cell envelope showing structures and describing their chemistry and function. (Modified from Hawley LB. *High-yield microbiology and infectious diseases*. 2nd ed. Baltimore: Lippincott Williams & Wilkins, 2006:2-1.)

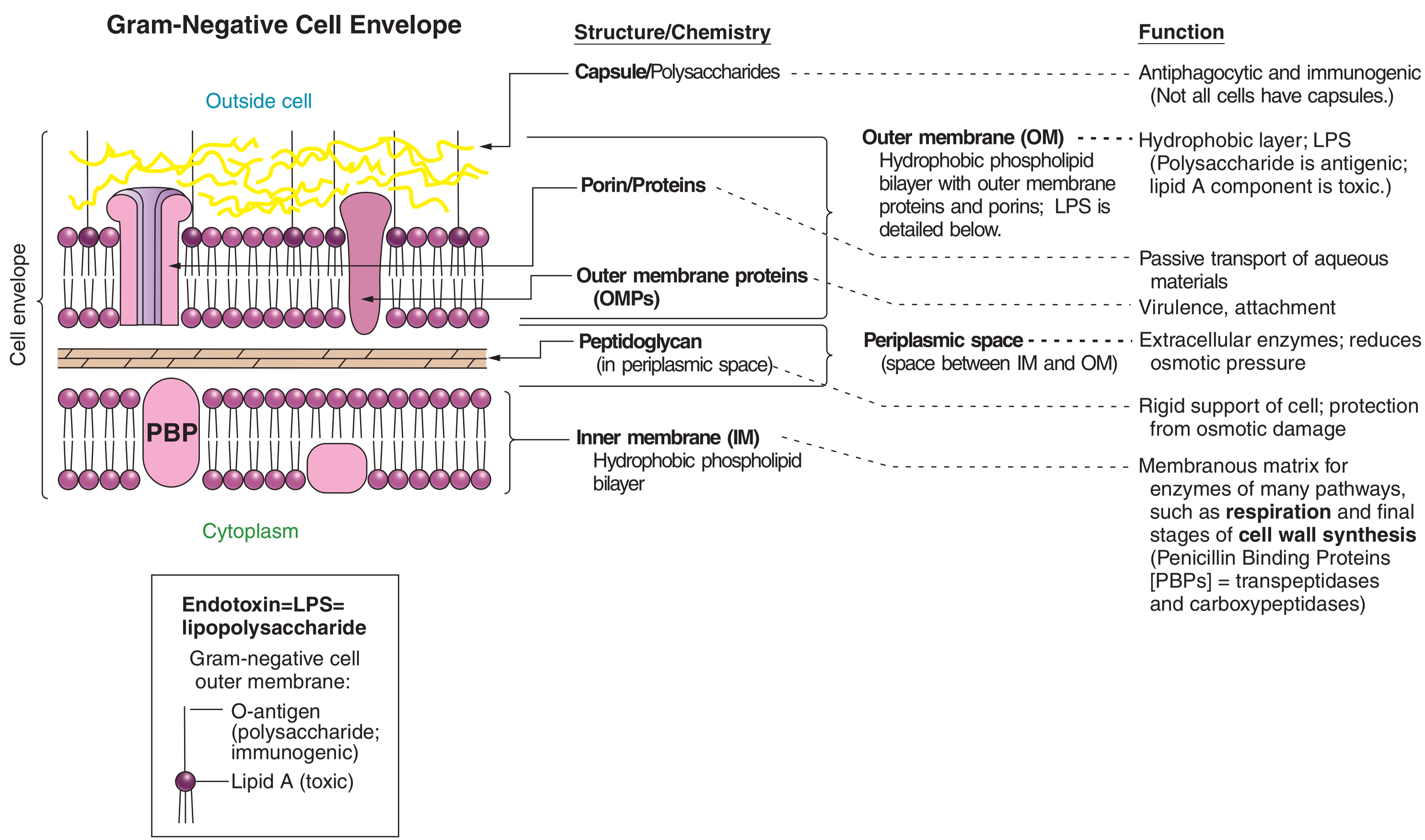


FIGURE 2.2. Gram-negative cell envelope showing structures and describing their chemistry and function. (Modified from Hawley LB. *High-yield microbiology and infectious diseases*. 2nd ed. Baltimore: Lippincott Williams & Wilkins, 2006:2-2.)

b. Peptidoglycan is the site of action of certain antibiotics such as **penicillin** and the **cephalosporins**.

c. In Gram-positive bacteria, it comprises up to 50% of the cell wall. In Gram-negative bacteria, it comprises only 2% to 10% of the cell wall.

4. Teichoic and **teichuronic acids** are **water-soluble polymers**, containing a ribitol or glycerol residue linked by phosphodiester bonds.

a. They are found in **Gram-positive** cell walls or membranes.

(1) Teichoic acid is found in cell walls and is chemically bonded to peptidoglycan.

(2) Lipoteichoic acid is found in cell membranes and is chemically bonded to membrane glycolipid, particularly in mesosomes.

b. Functions

(1) Contain important bacterial surface antigenic determinants, and lipoteichoic acid helps anchor the wall to the membrane.

(2) May account for 50% of the dry weight of a Gram-positive cell wall.

5. Lipoprotein is found in **Gram-negative** bacteria.

a. Lipoprotein cross-links the peptidoglycan and outer membrane.

b. A peptide bond links the lipoprotein to diaminopimelic acid residues of peptidoglycan tetrapeptide side chains; the lipid portion is noncovalently inserted into the outer membrane.

6. The **periplasmic space** is found in **Gram-negative** cells.

a. It refers to the area between the cell membrane and the outer membrane.

b. Hydrated peptidoglycan, hydrolytic **enzymes including β-lactamases, specific carrier molecules**, and oligosaccharides are found in the periplasmic space.

7. An **outer membrane** is found in **Gram-negative** cells.

a. Structure. The outer membrane is a phospholipid bilayer in which the phospholipids of the outer portion are replaced by lipopolysaccharides. It contains:

(1) Embedded proteins, including matrix **porins** (nonspecific pores)

(2) Some nonpore proteins (phospholipases and proteases)

(3) Transport proteins for small molecules

b. Functions

(1) Protects cells from harmful enzymes and some antibiotics

(2) Prevents leakage of periplasmic proteins.

8. Lipopolysaccharide is found in the outer leaflet of the outer membrane of **Gram-negative** cells.

a. Structure

(1) Lipopolysaccharide consists of **lipid A**, several long-chain fatty acids attached to phosphorylated glucosamine disaccharide units, and a polysaccharide composed of a core and terminal repeating units.

(2) It is negatively charged and noncovalently cross-bridged by divalent cations.

b. Functions

(1) Also called **endotoxin**; the toxicity is associated with the lipid A.

(2) Contains major surface antigenic determinants, including **O antigen** found in the polysaccharide component.

J. External layers

1. Surface proteins

a. These antiphagocytic proteins are external to the cell wall of some gram positive bacteria.

b. Functions: act as **adhesins** facilitating tissue colonization with several species (e.g., *Staphylococcus aureus* [fibronectin-binding proteins] and *Streptococcus pyogenes* [F proteins]).

2. Capsule

a. The capsule is a well-defined structure of polysaccharide surrounding a bacterial cell and is external to the cell wall. The one exception to the polysaccharide structure is the poly-D-glutamic acid capsule of *Bacillus anthracis.*

b. Functions: protects the bacteria from phagocytosis and plays a role in bacterial adherence.

3. Glycocalyx

a. The glycocalyx refers to a loose network of polysaccharide fibrils that surrounds some bacterial cell walls.

(1) It is sometimes called a **slime layer**.
(2) It is synthesized by surface enzymes.

b. **Functions**: associated with adhesive properties of the bacterial cell and contains prominent antigenic sites.

K. Appendages

1. **Flagella** are protein appendages for locomotion and contain prominent antigenic determinants.
   a. They consist of a basal body, hook, and a long filament composed of a polymerized protein called **flagellin**.
   b. Flagella may be located in only one area of a cell (**polar**) or over the entire bacterial cell surface (**peritrichous**).
2. **Pili (fimbriae)** are rigid surface appendages composed mainly of a protein called **pilin**.
   a. **Types**
      (1) **Ordinary pili (adhesins)** are involved in bacterial adherence and Gram-positive cell conjugation.
      (2) **Sex pili** are involved in attachment of donor and recipient bacteria in Gram-negative cell conjugation.
   b. **Functions**
      (1) Ordinary pili are the colonization antigens or **virulence factors** associated with some bacterial species such as *S. pyogenes* and *Neisseria gonorrhoeae*.
      (2) They also may confer antiphagocytic properties, such as the **M protein** of *S. pyogenes*.

L. Endospores

1. **General characteristics**. Endospores are formed as a survival response to certain adverse nutritional conditions, such as depletion of a certain resource. These metabolically **inactive bacterial cells** are highly resistant to desiccation, heat, and various chemicals. They are helpful in identifying some species of bacteria (e.g., *Bacillus* and *Clostridium*).
2. **Structure**
   a. Endospores possess a core that contains many cell components, a spore wall, a cortex, a coat, and an exosporium.
   b. The core contains **calcium dipicolinate**, which aids in heat resistance within the core.
3. **Function**: endospores germinate under favorable nutritional conditions after an activation process that involves damage to the spore coat. They are not reproductive structures.

M. Biofilms are aggregates of bacterial cells that form in soil and marine environments and the surface of **medical implants devices** (e.g., prostheses). They enhance nutrient uptake and often exclude antimicrobials.

II. BACTERIAL GROWTH AND REPLICATION

A. Growth

1. **General characteristics: bacterial growth**
   a. Bacterial growth refers to an increase in bacterial cell numbers (multiplication), which results from a programmed increase in the biomass of the bacteria.
   b. It results from bacterial reproduction due to binary fission, which may be characterized by a parameter called **generation time** (the average time required for cell numbers to double).
   c. It may be determined by measuring **cell concentration** (turbidity measurements or cell counting) or **biomass density** (dry weight or protein determinations).
   d. It usually occurs asynchronously (i.e., all cells do not divide at precisely the same moment).
2. **Cell concentration**
   a. Cell concentration may be measured by **viable cell counts** involving serial dilutions of sample followed by a determination of colony-forming units on an agar surface.
   b. It may be determined by **particle cell counting** or **turbidimetric density measurements** (includes both viable and nonviable cells).

3. Bacterial growth curve (Fig. 2.3)

a. The bacterial growth curve involves the inoculation of bacteria from a saturated culture into fresh liquid media. It is unique for a particular nutritional environment.

b. It is frequently illustrated in a plot of logarithmic number of the number of bacteria versus time; the **generation time** is determined by observing the time necessary for the cells to double in number during the log phase of growth.

c. The bacterial growth curve consists of **four phases**:

(1) Lag—metabolite-depleted cells adapt to new environment.

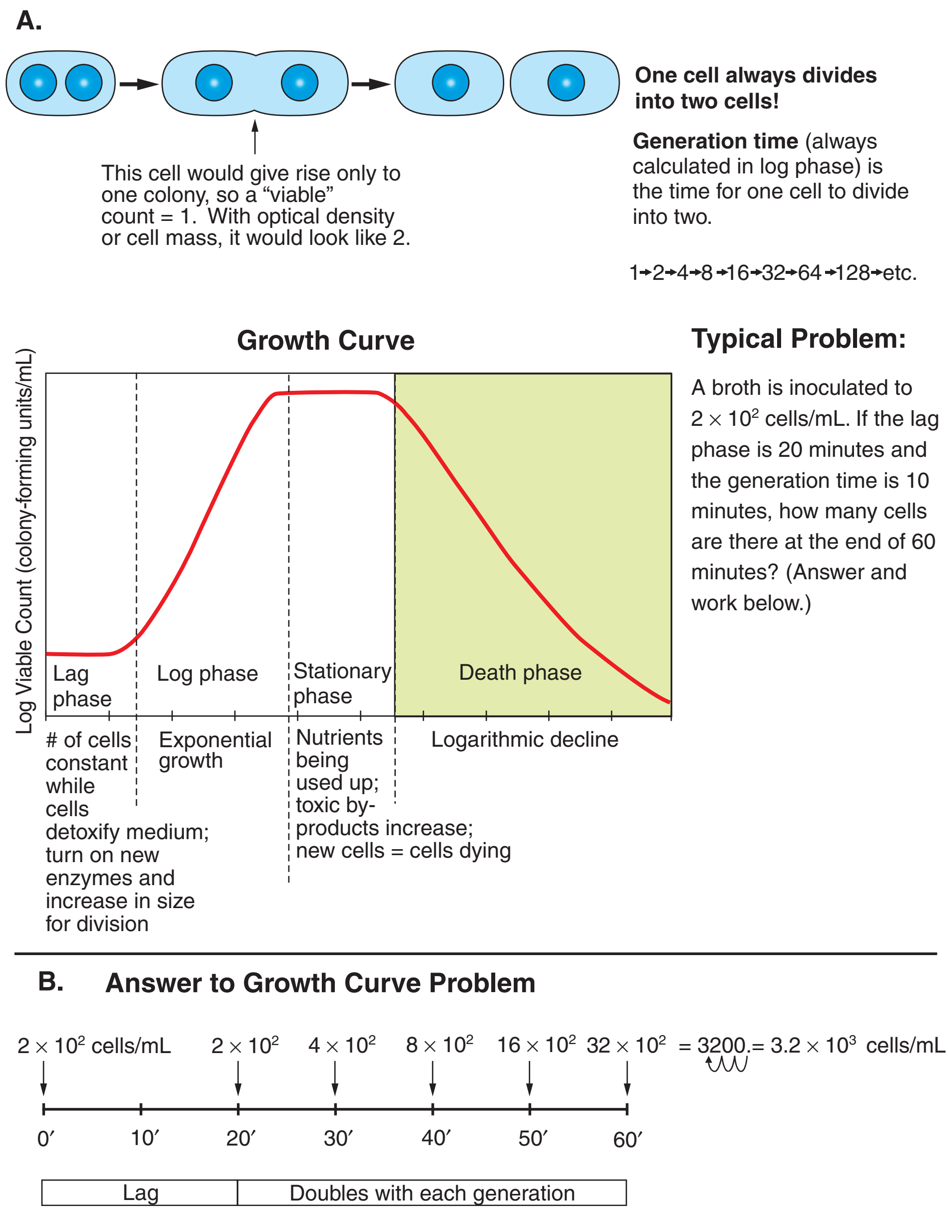


FIGURE 2.3. Bacterial growth and division. **(A)** Binary fission (which is asexual), growth curve, and typical problem. **(B)** Explanation of growth curve problem. (Modified from Hawley LB. *High-yield microbiology and infectious diseases*. 2nd ed. Baltimore: Lippincott Williams & Wilkins, 2006:3-1.)

(2) **Exponential or log**—cell biomass is synthesized at a constant rate, cells in this stage are generally more susceptible to antibiotics.
(3) **Stationary**—cells exhaust essential nutrients or accumulate toxic products.
(4) **Death or decline**—cells may die due to toxic products.

4. **Synchronous growth**
   a. This type of growth refers to a situation in which all the bacteria in a culture divide at the same moment.
   b. It may be achieved by several methods, including thymidine starvation (thymidine-requiring bacteria), alternate cycles of low and optimal incubation temperatures, spore germination, selective filtration of old (large) and young (small) cells, or ''trapped cell'' filtration.

B. Cultivation

1. **General characteristics: bacterial cultivation**
   a. Bacterial cultivation refers to the propagation of bacteria based on their specific pH, gaseous, and temperature preferences.
   b. It is performed in either liquid (broth) or solid (agar) growth medium and requires an environment that contains:
      (1) A carbon source
      (2) A nitrogen source
      (3) An energy source
      (4) Inorganic salts
      (5) Growth factors
      (6) Electron donors and acceptors
2. **Superoxide dismutase** is an enzyme in aerobes and facultative and aerotolerant anaerobes that allows them to grow in the presence of the superoxide free radical (O_2^-).
   a. This enzyme carries out the reaction $2O_2^- + 2H^+ \rightarrow H_2O_2 + O_2$.
   b. This reaction produces hydrogen peroxide (H_2O_2), which is toxic to cells but is destroyed by **catalase** or is oxidized by a peroxidase enzyme.

C. Oxygen requirements

1. **Obligate aerobes**: require oxygen for growth; contain superoxide dismutase, which protects them from the toxic O_2^-.
2. **Obligate anaerobes:** are killed by the O_2^-; grow maximally at a pO_2 concentration of less than 0.5% to 3%.
   a. They lack superoxide dismutase, catalase, and cytochrome-C oxidase (enzymes that destroy toxic products of oxygen metabolism).
   b. Instead of oxygen, they require another substance such as a hydrogen acceptor during the generation of metabolic energy and utilize **fermentation pathways** with distinctive metabolic products.
   c. **General characteristics**
      (1) Outnumber aerobes 1000:1 in the gut and 100:1 in the mouth
      (2) Comprise 99% of the total fecal flora (10^{11}/g of stool in the large bowel)
      (3) Usually cause polymicrobial infections, those involving more than one genus or species
      (4) Are foul smelling
   d. They generally are found proximal to mucosal surfaces, but can escape into tissues by:
      (1) Gastrointestinal obstruction or surgery
      (2) Diverticulitis
      (3) Bronchial obstruction
      (4) Tumor growth
      (5) Ulceration of the intestinal tract by chemotherapeutic agents
3. **Facultative anaerobes**: grow in the presence or absence of oxygen.
   a. They shift from a fermentative to a respiratory metabolism in the presence of air.
   b. Their energy needs are met by consuming less glucose under a respiratory metabolism than under a fermentative metabolism (**Pasteur effect**).
   c. Most **pathogenic bacteria** are facultative anaerobes.

4. **Aerotolerant anaerobes**: resemble facultative bacteria but have a fermentative metabolism both with and without an oxygen environment.

D. Nutritional requirements

1. **Heterotrophs** require preformed organic compounds (e.g., sugar, amino acids) for growth.
2. **Autotrophs** do not require preformed organic compounds for growth because they can synthesize them from inorganic compounds and carbon dioxide.

E. Growth media

1. **Minimal essential growth medium**
   a. This medium contains only the primary precursor compounds essential for growth.
   b. A bacterium grown in this medium must synthesize most of the organic compounds required for its growth.
   c. Generation time is relatively slow.
2. **Complex growth medium**
   a. This medium contains most of the organic compound building blocks (e.g., sugars, amino acids, nucleotides) necessary for growth.
   b. Generation time for a bacterium is faster relative to its generation time in minimal essential medium.
   c. Fastidious bacteria are grown in this medium.
3. **Differential growth medium** (Table 2.1)
   a. This medium contains a combination of nutrients and pH indicators to allow visual distinction of bacteria that grow on or in it.
   b. Colonies of particular bacterial species have a distinctive color.
4. **Selective growth medium** (see Table 2.1)
   a. This medium contains compounds that prevent the growth of some bacteria while allowing the growth of other bacteria.
   b. Dyes or sugars, high salt concentration, or pH are used to achieve selectivity.

F. Metabolism

1. **General characteristics**
   a. **Bacterial metabolism** is the sum of **anabolic processes** (synthesis of cellular constituents requiring energy) and **catabolic processes** (breakdown of cellular constituents with concomitant release of waste products and energy-rich compounds).
      (1) Pathogenic bacteria exhibit **heterotrophic** metabolism.
      (2) Metabolism can vary depending the nutritional environment.

table 2.1 Representative Differential and Selective Growth Medias

Media	Bacteria Identified	Identification Mechanism
Blood agar	Hemolytic Bacteria (Staphylococcal and Streptococcal species)	Defibrillated blood in nutrient agar base provides identification of α-hemolytic (green zone around colonies) and β-hemolytic (clear zone around colonies)
Hektoen-enteric agar	Enteric gram negative rods (E. coli, Klebsiella, **Salmonella**, and **Shigella**)	Contain bile salts, thiosulfate, ferric ammonium Citrate, and lactose and sucrose. Gram positives are inhibited and lactose/sucrose fermenters and H_2S producers are observed.
MacConkey agar	Enteric gram negative rods (E. coli, Klebsiella, Salmonella, Shigella and Proteins)	Contains bile salts, crystal violet, lactose, and neutral red pH indicator. Bile salts and crystal violet inhibit gram positives, only gram negatives that ferment lactose give the colonies a color that determines species.
Löwenstein-Jensen graft media	**Mycobacteria**	Is a glycerated egg-potato media (provides fatty acids and proteins) containing malachite green dye, penicillin and nalidixic acid to inhibit gram positive and some gram negative organisms.
Thayer-Martin and Martin-Lewis medium	**Neisseria species**	Variants of chocolate agar (blood agar containing gently heat-lysed RBCs to provide nutrients) and antibiotics to inhibit most normal respiratory and genital flora.

b. **Bacterial transport systems** involve membrane-associated binding or transport proteins for sugars and amino acids.
   (1) Energy is frequently required to concentrate substrates inside the cell.
   (2) Transport is usually inducible for nutrients that are catabolized; glucose, which is constitutive, is an exception.
   (3) Phosphotransferase systems are frequently used for sugar transport.

2. **Carbohydrate metabolism**
   a. **Fermentation** is a method of obtaining metabolic energy that is characterized by **substrate phosphorylation**.
      (1) **Adenosine triphosphate (ATP)** formation is not coupled to electron transfer.
      (2) An organic electron acceptor (e.g., pyruvate) is required.
      (3) Specific metabolic end products are synthesized, which may aid in the identification of bacterial species.
   b. **Respiration** refers to the method of obtaining metabolic energy that involves **oxidative phosphorylation**.
      (1) ATP is formed during electron transfer and the reduction of gaseous oxygen in aerobic respiration.
      (2) A cell membrane electron transport chain composed of cytochrome enzymes, lipid cofactors, and coupling factors is used during this process.

3. **Regulation**
   a. **Regulation of enzyme activity**
      (1) Enzymes are **allosteric proteins**, susceptible to binding of effector molecules that influence their activity.
      (2) **Feedback inhibition** involves the end product.
      (3) **Substrate-binding enhancement** regulates catalytic activity.
   b. **Regulation of enzyme synthesis** may involve the following mechanisms:
      (1) Allosteric regulatory proteins that activate (**activators**) or inhibit (**repressors**) gene transcription.
      (2) **End-product feedback repression** of biosynthetic pathway enzymes.
      (3) **Substrate induction** of catabolic enzymes.
      (4) **Attenuation control sequences** in enzyme mRNA.
      (5) **Catabolite repression**, which is under positive control of the **catabolite activator protein**.
   c. **Pasteur effect** is caused by oxygen blocking the fermentative capacity of **facultative bacteria**. The energy needs of the bacteria are met by using less glucose during aerobic growth.

G. Cell wall synthesis (Fig. 2.4)

1. Cell wall synthesis involves the cytoplasmic synthesis of peptidoglycan subunits, which are translocated by a membrane lipid carrier and cross-linked to existing cell wall by enzymes associated with the plasma membrane of Gram-positive bacteria or found in the periplasmic region of Gram-negative bacteria.
2. In Gram-positive cells, it involves the covalent linkage of teichoic acid to *N*-acetylmuramic acid residues.
3. In Gram-negative cells, three components (lipoprotein, outer membrane, lipopolysaccharide) are added, whose constituents or subunits are synthesized on or in the cytoplasmic membrane and assembled outside of the cell.

III. BACTERIAL VIRUSES

A. General characteristics: bacteriophages are bacterial viruses that are frequently called **phages**.

1. These obligate intracellular parasites are host-specific infectious agents for bacteria.

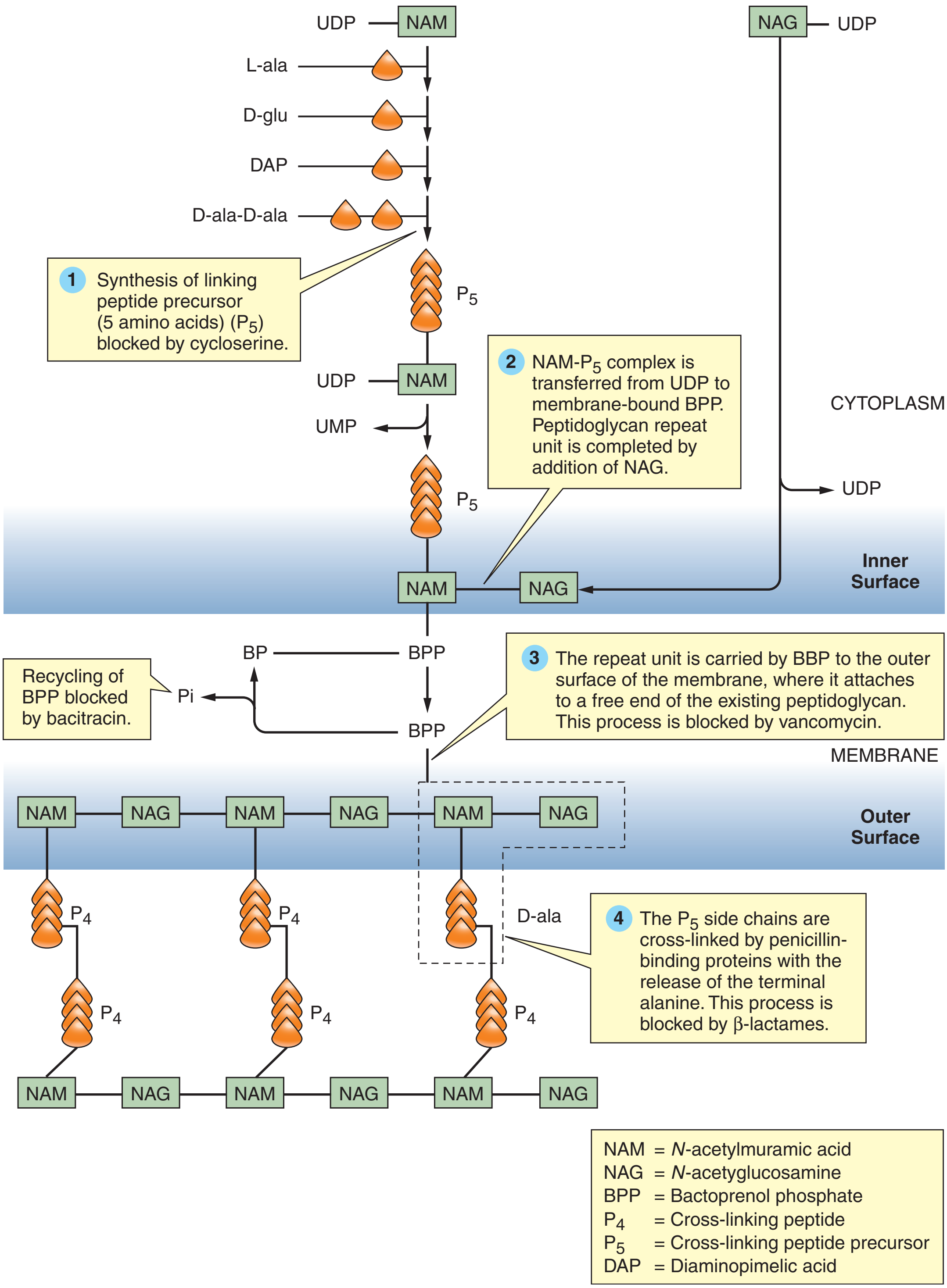


FIGURE 2.4. Synthesis of peptidoglycan.

2. **Bacteriophage virions** are complete (genetic material and capsid) infectious particles.
3. Major components are protein and RNA or DNA.

B. Morphologic classes of bacteriophages

1. **Polyhedral phages** are usually composed of an outer polyhedral-shaped protein coat (capsid), which surrounds the nucleic acid.
   a. They may contain a lipid bilayer between two protein capsid layers (PM-2 phage).
   b. Their **genetic material** consists of one of the following:
      (1) Circular double-stranded (PM-2) DNA
      (2) Single-stranded DNA (θX174 and M-12)
      (3) Linear single-stranded RNA (MS2 and Qβ)
      (4) One phage (θ6) that has three pieces of double-stranded RNA.
2. **Filamentous phages** have a filamentous protein capsid that surrounds a circular single-stranded DNA genome (f1 and M-13).
   a. They infect bacteria through the host's pili; thus, they are male-bacteria–specific. (Pili are only present on male bacteria.)
   b. They do not lyse their host cells during the replication process.
3. **Complex phages** have a protein polyhedral head containing linear double-stranded DNA and a protein tail and other appendages. They include the T and lambda phages of *Escherichia coli*.

C. Genetic classes of bacteriophages

1. **RNA phages** refer to all phages with RNA as their genetic material.
   a. These phages are specific for bacteria with male pili (male specific).
   b. The RNA is single-stranded (except for θ6, see X B-1). It can act as polycistronic mRNA.
2. **DNA phages** refer to all phages with DNA as their genetic material.
   a. They contain nucleic acid bases that are frequently glycosylated or methylated.
   b. Some of the nucleic acid bases are unusual, such as 5-hydroxymethyl cytosine or 5-hydroxymethyl uracil.
   c. Two classes are recognized: **virulent** or **temperate**, depending on whether their pattern of replication is strictly lytic (virulent) or alternates between lytic and lysogenic (temperate).

D. Bacteriophage replication

1. **General characteristics**: phages replicate by using the biosynthetic machinery of the host cell. During replication, the phage genome is injected into the host cell. (Filamentous phages are the exception.)
   a. The basic sequence of events includes adsorption; penetration; phage-specific transcription, translation, or both; assembly; and release.
   b. It is initiated by interaction of phage receptors and specific bacterial surface receptor sites.
   c. Two patterns are recognized for DNA phages: **lytic** or **lysogenic**.
   d. For virulent phages, replication is usually complete in 30 to 60 minutes
2. **Lytic replication** occurs in virulent phages (*E. coli* T phages) and results in **lysis of the host cell**.
   a. Strains of bacteria can be identified based on their lysis by a selected set of phages a process called **phage typing**.
   b. **One-step growth curve** is the result of an experimental situation in which one cycle of lytic phage replication is monitored.
      (1) It plots the amount of infectious virus produced versus time after infection using a **plaque assay**, an infectious-center assay in which counts are made of focal areas of phage-induced lysis on a lawn of bacteria.
      (2) **Data** obtained from the one-step growth curve includes:
         (a) **Replication time**: average time necessary for a phage to replicate within a specific host cell and be released from that cell.
         (b) **Burst size**: number of infectious phages produced from each infecting phage.
         (c) **Eclipse period**: time from infection to the synthesis of the first intracellular infectious virus.

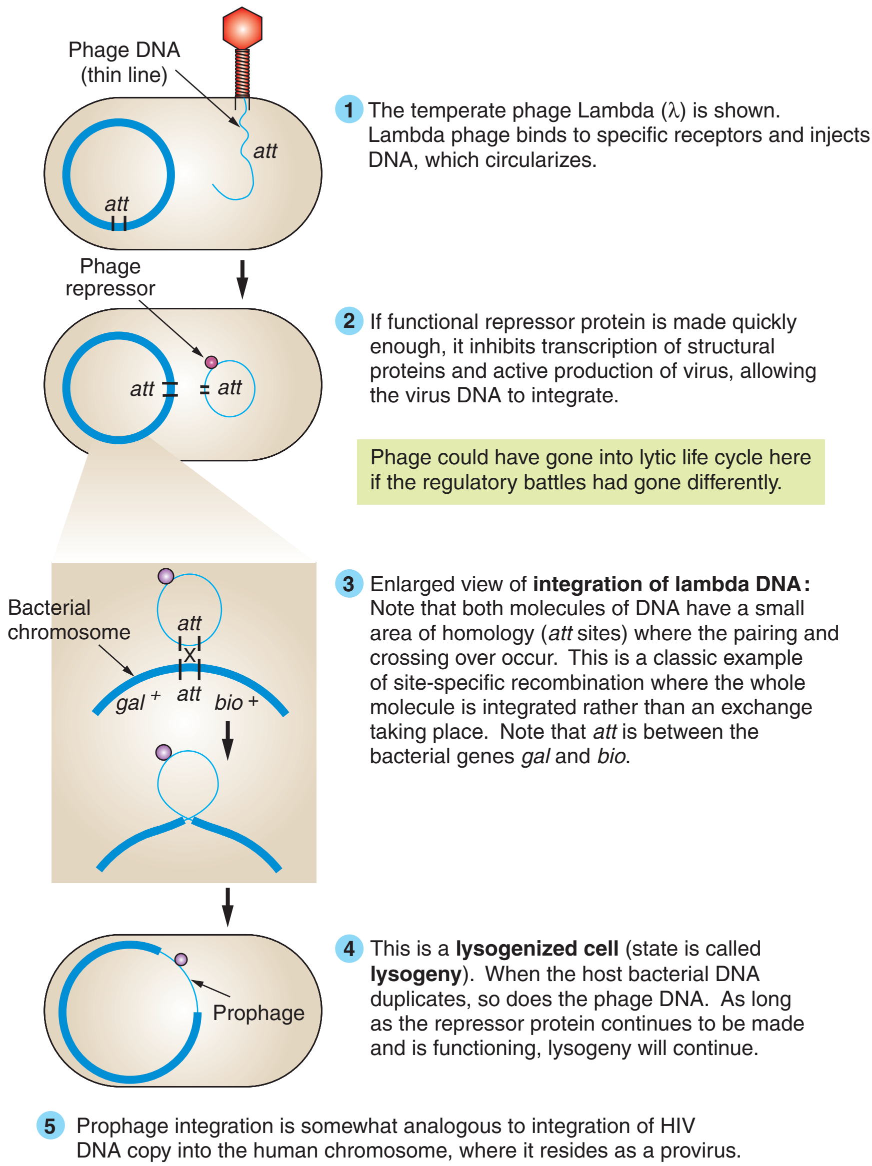


FIGURE 2.5. Transduction: temperate phage and lysogeny. (Modified from Hawley LB. *High-yield microbiology and infectious diseases*. 2nd ed. Baltimore: Lippincott Williams & Wilkins, 2006:5-9.)

3. Lysogenic replication occurs only in **temperate phages** (*E. coli* phage lambda) (Fig. 2.5).

- **a.** The synthesis of a phage-specific **repressor protein** inhibits phage-specific transcription, thus limiting phage-specific protein synthesis. If the phage repressor protein is destroyed, the phage can revert to lytic replication.
- **b. Prophage** (phage DNA) is incorporated into specific attachment sites in the host cell DNA.
  - **(1)** The incorporation of prophage confers immunity to infection by phages of a type similar to the infecting phage.
  - **(2)** The prophage is passed to succeeding generations of the bacteria.
- **c. Specialized or restricted transducing phages** may be generated (Fig. 2.6).
- **d.** Lysogenic replication may result in **lysogenic phage conversion**, a change in the phenotype of the bacteria as a result of limited expression of genes within a prophage. This mechanism occurs in the following situations:

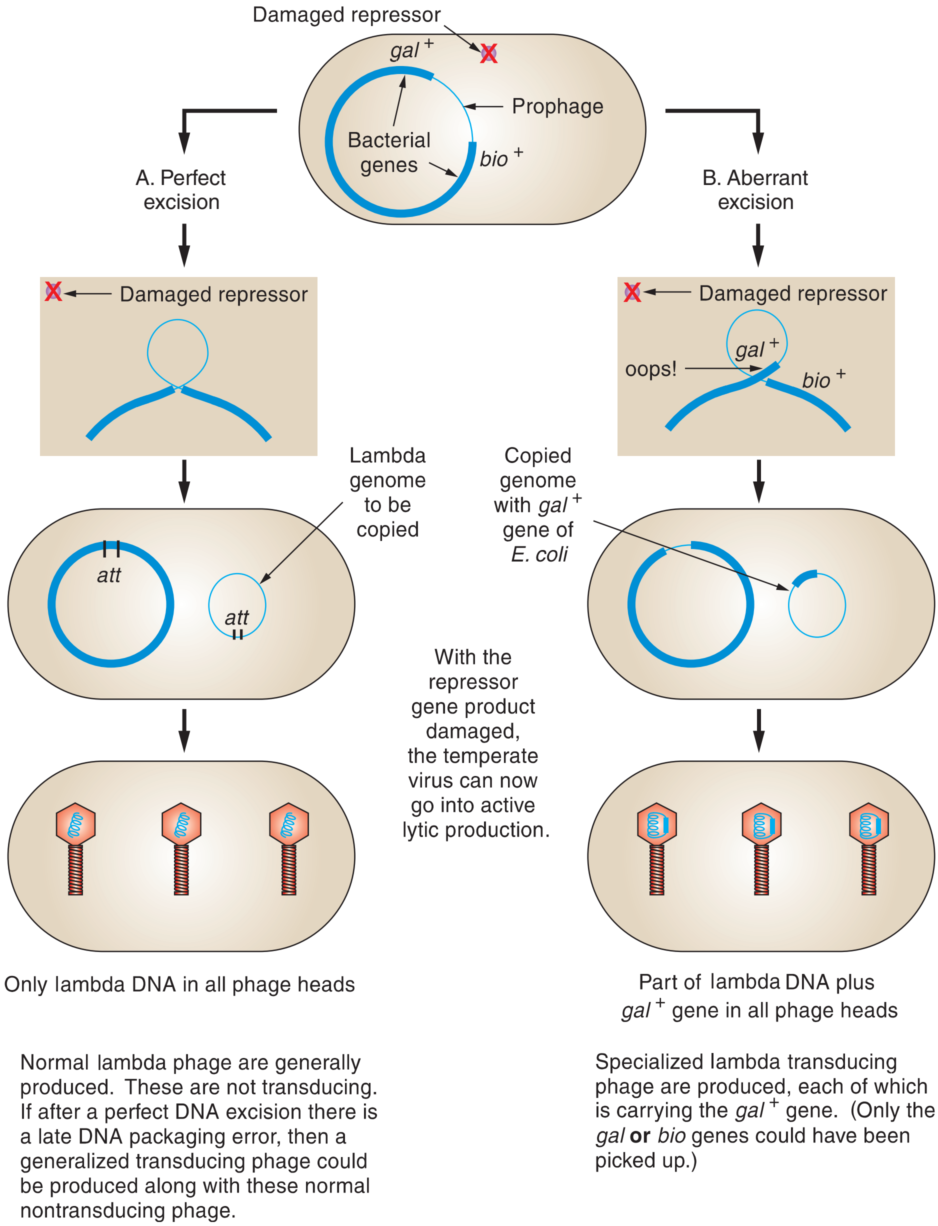


FIGURE 2.6. Transduction: induction/excision of prophage. If the repressor in a lysogenized cell is damaged by ultraviolet light, cold, or alkylating agents, the cell is "induced" into active virus production, which begins with the excision of the prophage DNA. Excision is the reverse of site-specific integration. The normal process of induction/excision of a prophage leading to active temperate phage replication is shown in **(A)**. Aberrant excision leading to production of a specialized transducing phage is shown in **(B)**. (Modified from Hawley LB. *High-yield microbiology and infectious diseases.* 2nd ed. Baltimore: Lippincott Williams & Wilkins, 2006:5-10.)

(1) In *Salmonella polysaccharides* as a result of infection with the epsilon prophage.
(2) Conversion of nontoxigenic strains of *Corynebacterium diphtheriae* to toxin-producing strains.
(3) Conversion of nontoxigenic *Clostridium botulinum* types C and D to toxin-producing strains.

IV. GENETICS

A. Comparison of bacterial and eukaryotic genomes

1. Eukaryotic genome

a. Structure: The eukaryotic genome:

(1) Is **diploid** with two homologous copies of each chromosome, except in some fungi.
(2) Is contained in two or more linear chromosomes located within a membrane-bound nucleus.
(3) Contains **introns** (DNA sequences not translated into gene products) and redundant genetic information.

b. Replication

(1) Begins at several points along the linear DNA molecule.
(2) Is regulated by specific gene inducer or repressor substances.
(3) Involves a specialized structure, the **spindle**, which pulls newly formed chromosomes into separate nuclei during mitosis.

2. Prokaryotic genome

a. Structure: The prokaryotic genome is **haploid** (single, circular chromosome encoding several thousand genes). It may contain extra chromosomal pieces of DNA called **plasmids** and moveable genetic elements called **transposons** and **integrons**.

(1) Plasmids

(a) These DNA pieces replicate independently of chromosomal replication.
(b) They may exist in an **episome** form that can integrate into the bacterial chromosome and replicate with it.
(c) Plasmids may carry **antibiotic resistance** genes (e.g., EM-1 β-lactamase gene of *E. coli*) **toxin genes**, (e.g., enterotoxins of *E. coli*), and transposons.

(2) Transposons

(a) These **moveable genetic elements** are incapable of independent replication.
(b) They contain insertion sequences and can transfer genetic information by insertion into bacterial chromosome or plasmids.
(c) They may contain antibiotic resistance genes like *Neisseria gonococcus*, β-lactamase, or virulence factors like the heat-stable enterotoxin of ***E. coli***.

(3) Integrons

(a) These **mobile genetic elements** consist of an integrase gene and a series (cassettes) of antibiotic resistance genes plus insertion sequences (attachment sites) and a promoter region controlling all resistance genes (observed in *Mycobacterium tuberculosis* resistance).
(b) They are not capable of independent replication.

(4) Pathogenicity islands

(a) These **groups of virulence-associated** genes code for unique secretion systems, toxins, adhesins, and regulatory proteins and contain integrase and transposase genes.
(b) They are associated with t-RNA genes on bacterial chromosomes or plasmids.

b. Replication

(1) **Replicon** is a general term for a double-stranded DNA circle (chromosomes, plasmids) capable of self replication.
(2) Replicons replicate bidirectionally (5′ PO_4 to 3′ OH) from a fixed origin.

B. Gene transfer between organisms

1. General characteristics

a. Genetic variability in microbes is maintained through the **exchange** and **recombination** of allelic forms of genes.
b. Exchange is most efficient between cells of the same species.
c. Gene exchange may also occur as the crossing over of homologous chromosomes or by nonhomologous means (e.g., movement of plasmids or transposons, insertion of viral genes).