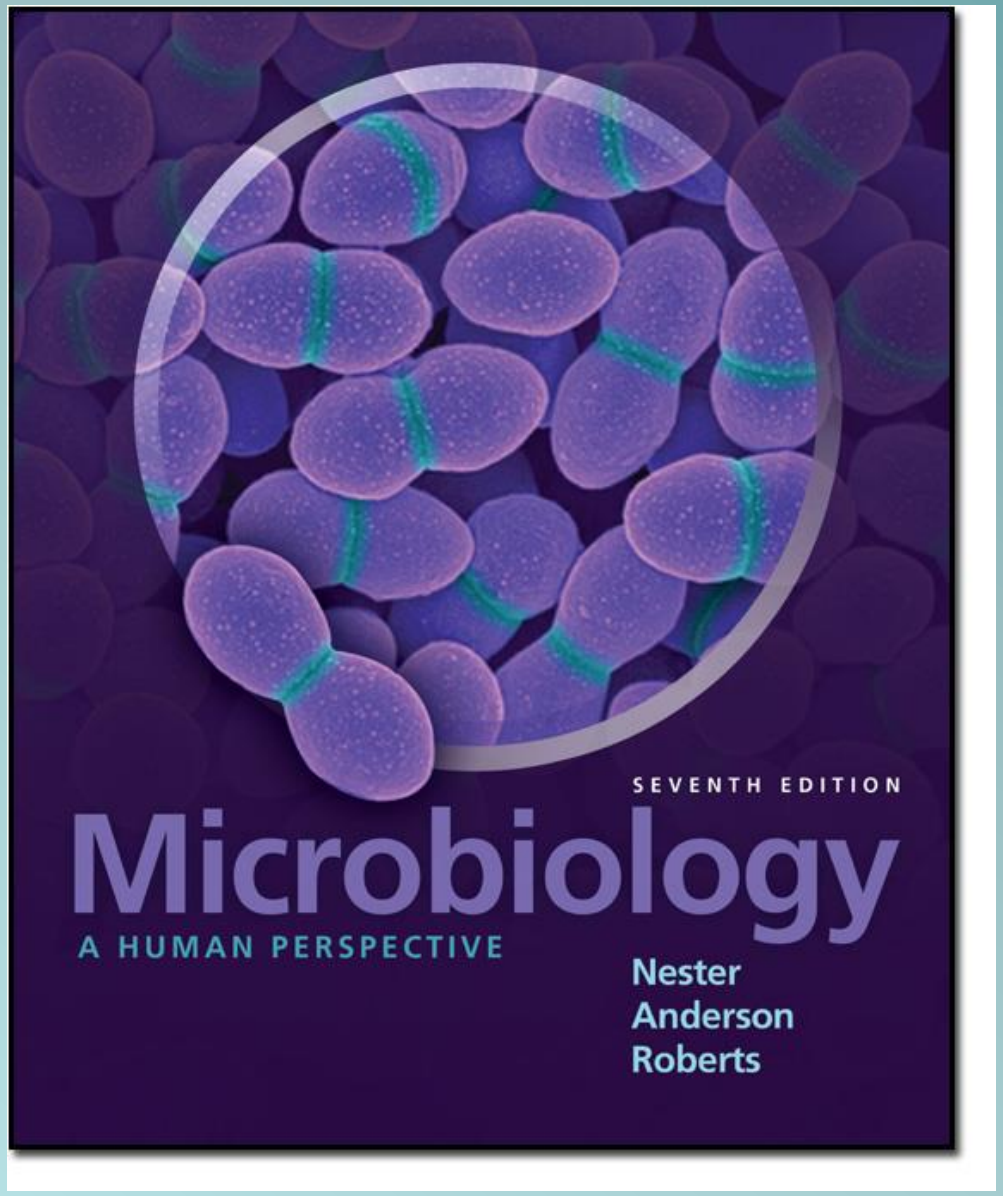


Chapter 16

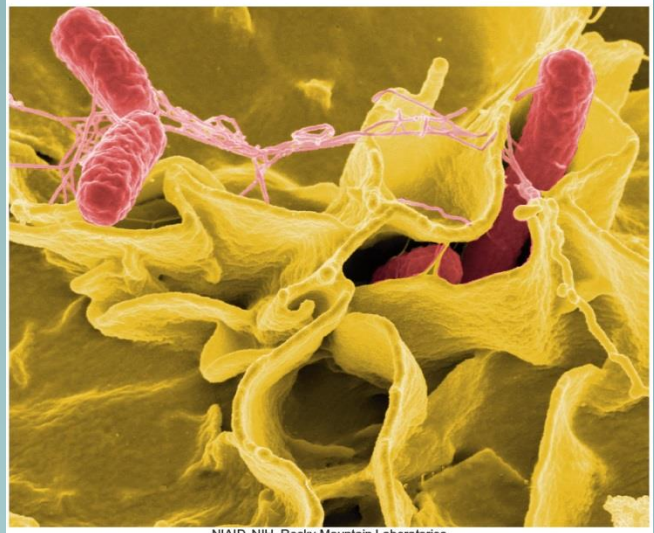
Host-Microbe Interactions

A Glimpse of History

- Ancients thought diseases were divine punishment
  - By the time of Moses, Egyptians and Hebrews believed leprosy could be transmitted by contact
  - Thucydides (430 B.C.) concluded some plagues contagious; many accepted by Middle Ages
  - Fracastorius (1546) proposed that communicable diseases caused by living agents passed from one person or animal to another, but no way to test
  - Leeuwenhoek's discovery of microorganisms in 17th century led people to suspect they might cause disease
  - Robert Koch (1876) offered proof of what is now considered germ theory of disease; showed *Bacillus anthracis* causes anthrax
    - Formalized criteria for establishing cause of disease, now known as Koch's postulates

Bacteria Are Ubiquitous

- We contact numerous microorganisms daily
  - Breathe in, ingest with food and drink, pick up on skin
  - Vast majority generate no ill effects
  - Some may colonize body surfaces; others slough off with dead epithelial cells
  - Most that are swallowed die in stomach or are eliminated in feces
  - Relatively few are pathogens that cause damage
    - Distinct characteristics allow avoidance of some body defenses



NIAID, NIH, Rocky Mountain Laboratories

Microbes, Health, and Disease

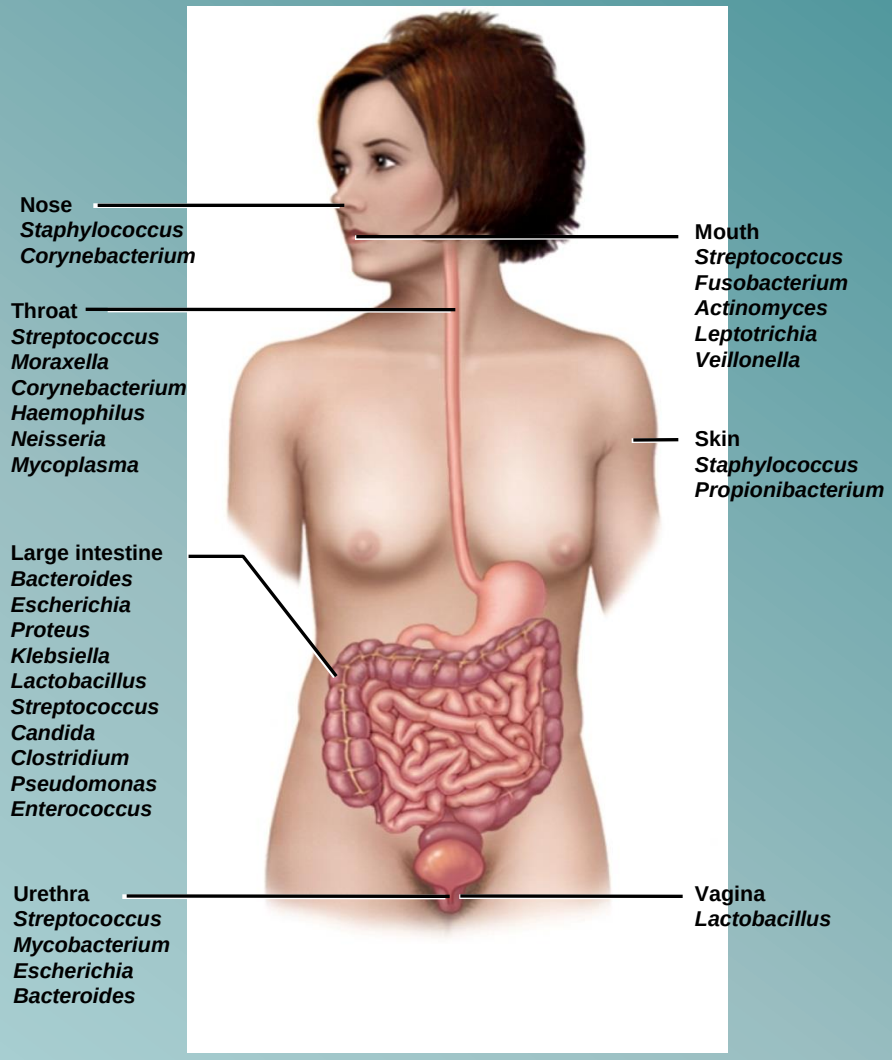
- Most microbes are harmless
  - Many are beneficial
  - Normal microbiota (normal flora) are organisms that routinely reside on body's surfaces
    - Relationship is delicate balance; some can cause disease should opportunity arise
    - Weaknesses or defects in innate or adaptive defenses can leave individuals vulnerable to invasion
      - Individuals said to be immunocompromised
      - Factors include malnutrition, cancer, AIDS or other disease, surgery, wounds, genetic defects, alcohol or drug abuse, and immunosuppressive therapy following procedures such as organ transplants

16.1. The Anatomical Barriers as Ecosystems

- Skin, mucous membranes are barriers
  - Also host complex ecosystem of microorganisms
    - Example of symbiosis, or “living together”
    - Mutualism: both partners benefit
      - E.g., in large intestine, some bacteria synthesize vitamin K and B vitamins, which host can absorb; bacteria are supplied with warmth, energy sources
    - Commensalism: one partner benefits, other is unharmed
      - Many microbes living on skin neither harmful nor helpful, but obtain food and necessities from host
    - Parasitism: one organism benefits at expense of other
      - All pathogens are parasites, but medical microbiologists often reserve for eukaryotic pathogens (e.g., protozoa, helminths)

16.2. The Normal Microbiota

- Normal microbiota
  - Resident microbiota inhabit sites for extended periods
  - Transient microbiota inhabit temporarily
  - Important to human health
  - Relatively little is known
  - Human Microbiome Project aimed at studying



16.2. The Normal Microbiota

- The Protective Role of the Normal Microbiota
  - Significant contribution is protection against pathogens
    - Covering of binding sites prevents attachment
    - Consumption of available nutrients
    - Production of compounds toxic to other bacteria
  - When killed or suppressed (e.g., during antibiotic treatment), pathogens may colonize, cause disease
    - Some antibiotics inhibit *Lactobacillus* (predominate vagina of mature females, suppress growth of *Candida albicans*); results in vulvovaginal candidiasis
    - Oral antibiotics can inhibit intestinal microbiota, allow overgrowth of toxin-producing *Clostridium difficile*

16.2. The Normal Microbiota

- The Protective Role of the Normal Microbiota (continued…)
  - Stimulation of adaptive immune system
    - Mice reared in microbe-free environment have greatly underdeveloped mucosal-associated lymphoid tissue (MALT); antibodies against normal microbiota bind to pathogens as well
  - Important in development of oral tolerance
    - Immune system learns to lessen response to many microbes that routinely inhabit gut as well as food
      - Basis of hygiene hypothesis, which proposes insufficient exposure to microbes can lead to allergies

16.2. The Normal Microbiota

- The Dynamic Nature of the Normal Microbiota
  - Healthy human fetus sterile until just before birth
    - Exposed to microbes during passage through birth canal
    - These take up residence; others from food, humans, environment soon also become established on newborn
  - Composition of normal microbiota is dynamic
    - Changes occur in response to physiological variations within host (e.g., hormonal changes) and as result of activities of host (e.g., consuming food)
      - Intestinal microbiota of obese and lean people differs
      - Obese have more members of phylum *Firmicutes*; thin have more members of phylum *Bacteroidetes*
      - Microbiota changed following weight loss in study to resemble that of typically lean people

16.3. Principles of Infectious Disease

- Colonization refers to microbe establishing itself on body surface
  - Term infection can be used to refer to pathogen
    - Can be subclinical: no or mild symptoms
    - Infectious disease yields noticeable impairment
      - Symptoms are subjective effects experienced by patient (e.g., pain and nausea)
      - Signs are objective evidence (e.g., rash, pus formation, swelling)
    - Initial infection is primary infection
      - Damage can predispose individual to developing a secondary infection (e.g., respiratory illness impairing mucociliary escalator)

16.3. Principles of Infectious Disease

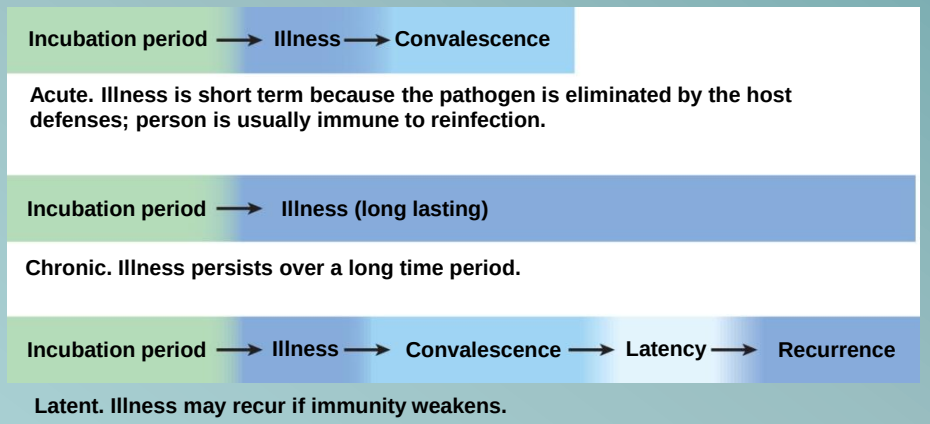
- Pathogenicity
  - Primary pathogen is microbe or virus that causes disease in otherwise healthy individual
    - Diseases such as plague, malaria, measles, influenza, diphtheria, tetanus, tuberculosis, etc.
  - Opportunistic pathogen (opportunist) causes disease only when body's innate or adaptive defenses are compromised or when introduced into unusual location
    - Can be members of normal microbiota or common in environment (e.g., *Pseudomonas*)
  - Virulence refers to degree of pathogenicity
  - Virulence factors are traits that allow microorganism to cause disease

16.3. Principles of Infectious Disease

- Characteristics of Infectious Disease
  - Communicable or contagious diseases easily spread
  - Infectious dose is number of microbes necessary to establish infection
    - ID_{50} is number of cells that infects 50% of population
    - Shigellosis results from ~10–100 ingested *Shigella*
    - Salmonellosis results from as many as 10^6 ingested *Salmonella enterica* serotype Enteritidis
      - Difference partially reflects ability to survive stomach acid

16.3. Principles of Infectious Disease

- Course of Infectious Disease
  - Incubation period: time between infection and onset
    - Varies considerably: few days for common cold to even years for Hansen's disease (leprosy)
    - Depends on growth rate, host's condition, infectious dose
  - Illness: signs and symptoms of disease
    - May be preceded by prodromal phase (vague symptoms)
  - Convalescence: recuperation, recovery from disease
  - Carriers may harbor and spread infectious agent for long periods of time in absence of signs or symptoms



16.3. Principles of Infectious Disease

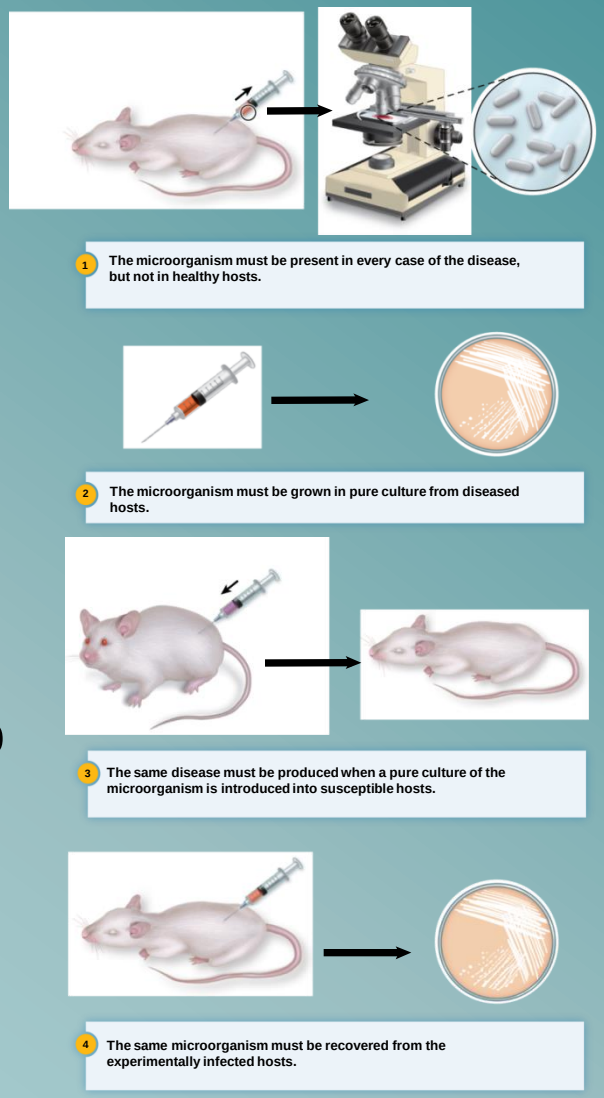
- Duration of Symptoms
  - Acute infections: symptoms develop quickly, last a short time (e.g., strep throat)
  - Chronic infections: develop slowly, last for months or years (e.g., tuberculosis)
  - Latent infections: never completely eliminated; microbe exists in host tissues without causing symptoms
    - Decrease in immunity may allow reactivation
    - Chicken pox (acute illness) results from varicella-zoster virus; immune response stops, but virus takes refuge in sensory nerves, can later produce viral particles resulting in shingles
    - Tuberculosis, cold sores, genital herpes also examples

16.3. Principles of Infectious Disease

- Distribution of Pathogen
  - Localized infection: microbe limited to small area (e.g., boil caused by *Staphylococcus aureus*)
  - Systemic infection: agent disseminated throughout body (e.g., measles)
  - Suffix *-emia* means “in the blood”
    - Bacteremia: bacteria circulating in blood
      - Not necessarily a disease state (e.g., can occur transiently following vigorous tooth brushing
    - Toxemia: toxins circulating in bloodstream
    - Viremia: viruses circulating in bloodstream
    - Septicemia or sepsis: acute, life-threatening illness caused by infectious agents or products in bloodstream

16.4. Establishing the Cause of Infectious Disease

- Koch's Postulates
  - Criteria Robert Koch used to establish that *Bacillus anthracis* causes anthrax
    - Microorganism must be present in every case of disease
    - Organism must be grown in pure culture from diseased host
    - Same disease must be produced when pure culture is introduced into susceptible hosts
    - Organisms must be recovered from experimentally infected hosts



16.4. Establishing the Cause of Infectious Disease

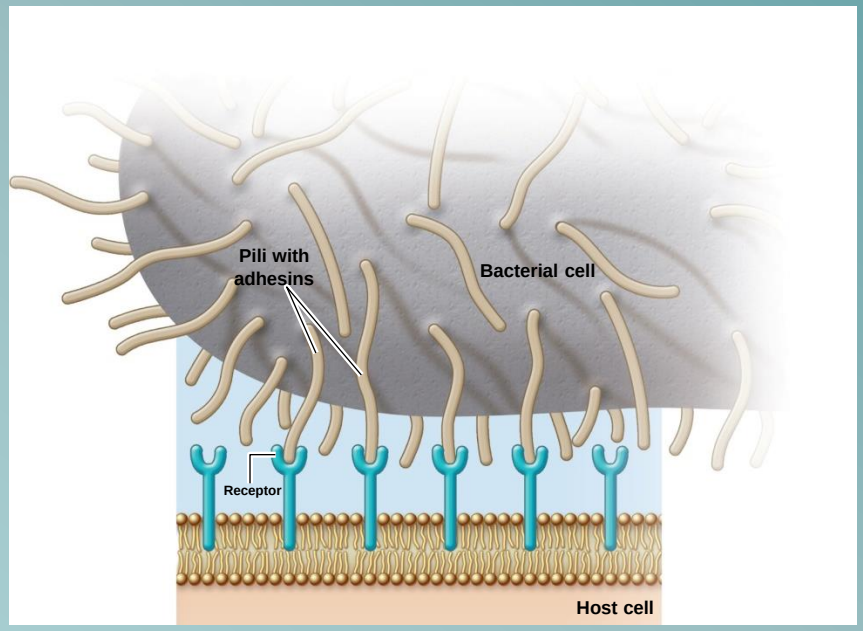
- Koch's Postulates (continued…)
  - Some limitations
    - Some organisms cannot be grown in laboratory medium (e.g., causative agent of syphilis)
    - Infected individuals do not always have symptoms (e.g., cholera, polio)
    - Some diseases are polymicrobial (e.g., periodontal)
    - Suitable animal hosts not always available for testing
- Molecular Koch's Postulates
    - Virulence factor gene or product found in pathogenic strains of organism
    - Mutating gene to disrupt function should reduce virulence
    - Reversion or replacement of gene should restore

Mechanisms of Pathogenesis

- Several general patterns
  - Produce toxins that are ingested
    - E.g., *Clostridium botulinum*, *Staphylococcus aureus*
  - Colonize mucous membranes, produce toxins
    - E.g., *Vibrio cholerae*, *E. coli* O157:H7, *Corynebacterium diphtheriae*
  - Invade host tissues, avoid defenses
    - E.g., *Mycobacterium tuberculosis*, *Yersinia pestis*, *Salmonella enterica*
  - Invade host tissues, produce toxins
    - E.g., *Shigella dysenteriae*, *Clostridium tetani*
  - Pathogens and hosts generally evolve toward balanced pathogenicity (e.g., myxoma virus and rabbits)

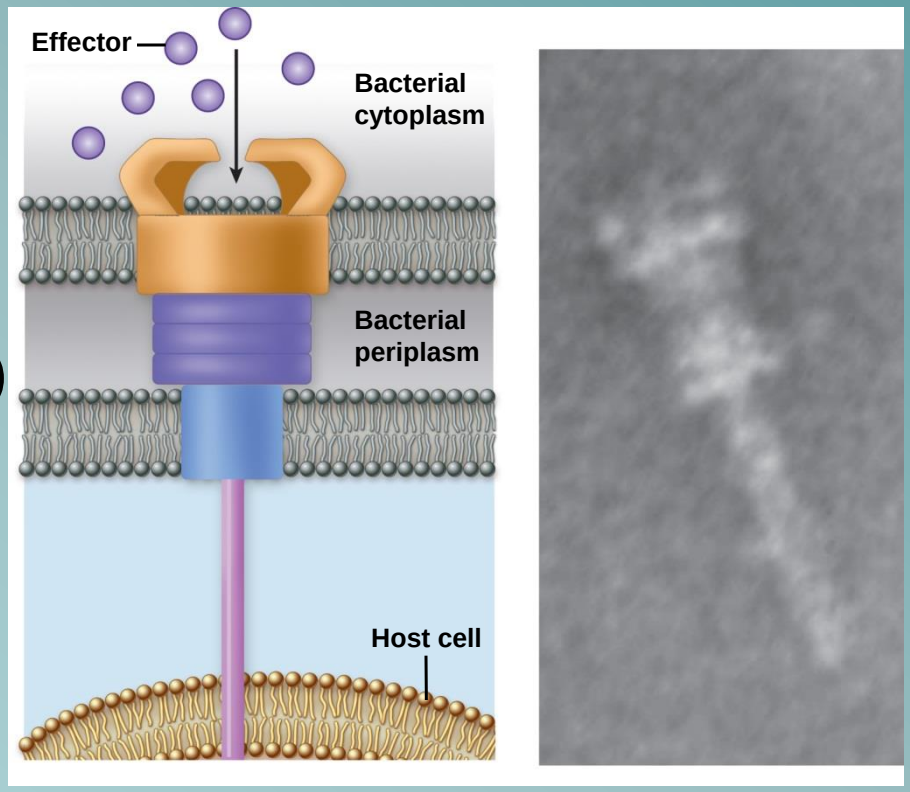
16.5. Establishing Infection

- Adherence
  - Adhesins attach to host cell receptor
    - Often located at tips of pili (called fimbriae)
    - Can be component of capsules or various cell wall proteins
    - Binding highly specific; exploits host cell receptor
- Colonization
  - Growth in biofilms
  - Siderophores
  - Avoidance of secretory IgA
    - Rapid pili turnover, antigenic variations, IgA proteases
  - Compete with normal microbiota, tolerate toxins



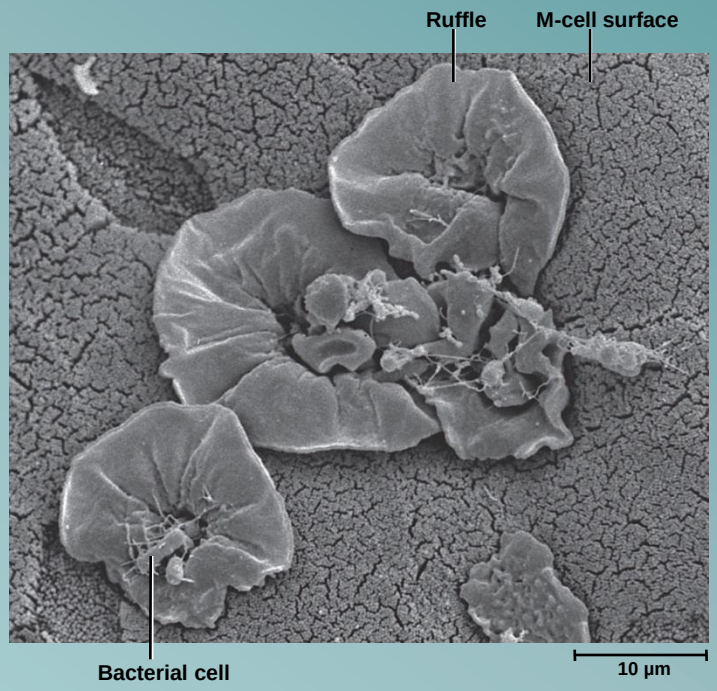
16.5. Establishing Infection

- Delivering Effector Proteins to Host Cells
  - Secretion systems in Gram-negatives
    - Several types discovered; some can inject molecules other than proteins
    - Type III secretion system (injectisome)
      - Effector proteins induce changes (e.g., altering of cell's cytoskeleton structure)
      - Can induce uptake of bacterial cells



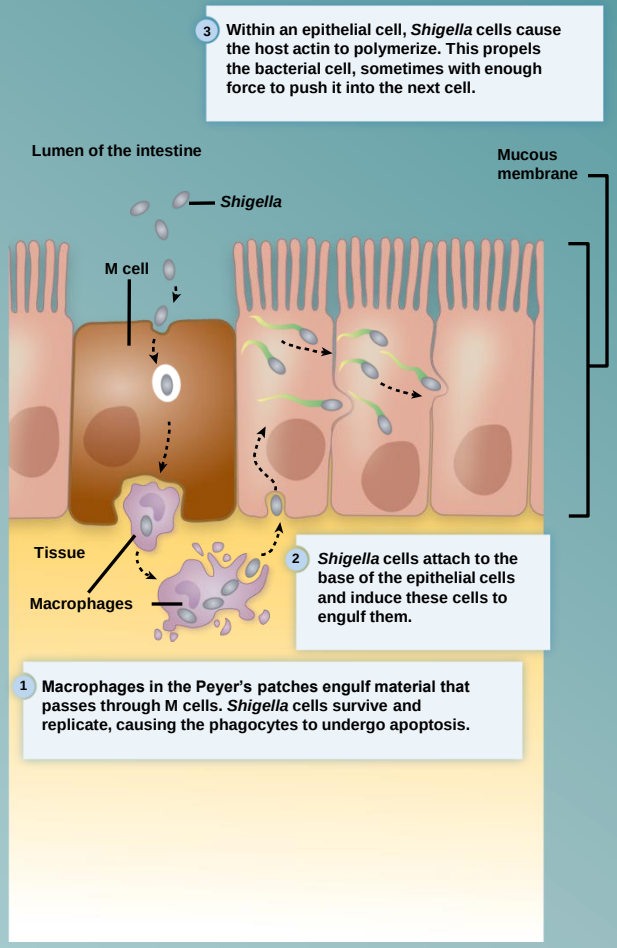
16.6. Invasion—Breaching the Anatomical Barriers

- Penetrating the Skin
  - Difficult barrier to penetrate; bacteria rely on injuries
    - *Staphylococcus aureus* enters via cut or wound; *Yersinia pestis* is injected by fleas
- Penetrating Mucous Membranes
  - Entry point for most pathogens
  - <u>Directed Uptake by Cells</u>
    - Pathogen induces cells to engulf via endocytosis
      - *Salmonella* uses type III secretion system to inject effector proteins; actin molecules rearrange, yield membrane ruffling



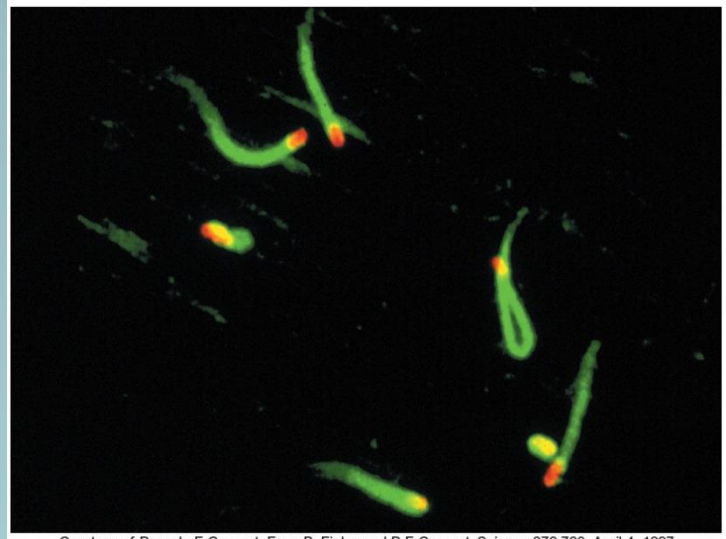
16.6. Invasion—Breaching the Anatomical Barriers

- Penetrating Mucous Membranes (continued…)
  - Exploiting Antigen-Sampling Processes
    - Mucosal-associated lymphoid tissue (MALT) samples
    - Some pathogens use M cells to cross intestinal barrier
    - *Shigella* survives phagocytosis by macrophages; induces apoptosis; binds to base of mucosal epithelial cells and induces uptake
    - Some invade by alveolar macrophages (e.g., *Mycobacterium tuberculosis* produces surface proteins, directs uptake, avoids macrophage activation)



16.7. Avoiding the Host Defenses

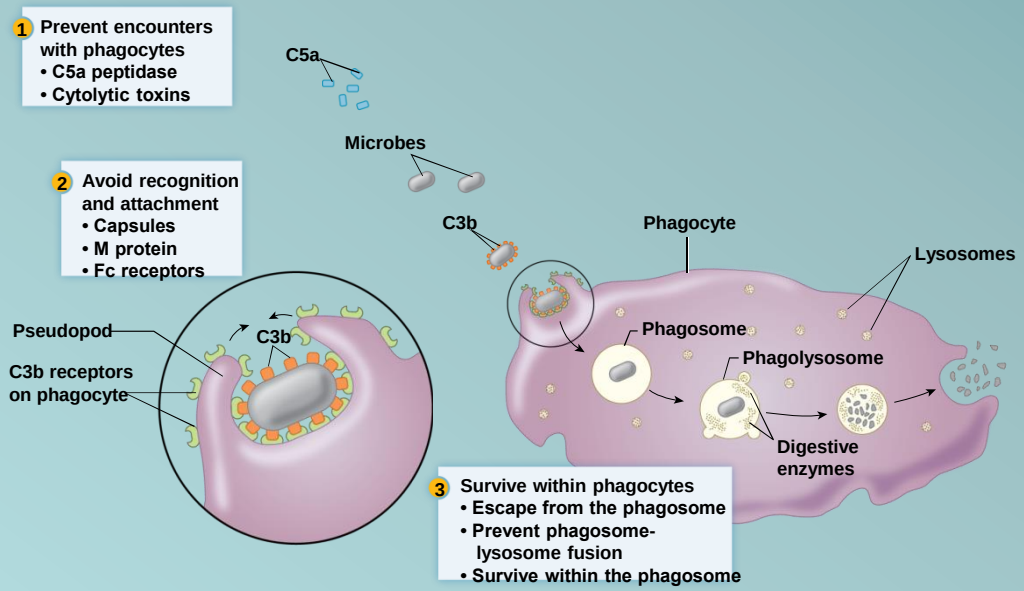
- Hiding Within a Host Cell
  - Allows avoidance of complement proteins, phagocytes, and antibodies
    - *Shigella* directs transfer from intestinal epithelial cell to adjacent cells by causing host cell actin polymerization
    - *Listeria monocytogenes* (meningitis) does the same
- Avoiding Killing by Complement System Proteins
  - Serum resistant bacteria resist
  - *Neisseria gonorrhoeae* hijacks host system, binds complement regulatory proteins to avoid activation of membrane attack complex



Courtesy of Pascale F. Cossart, From B. Finlay and P. F. Cossart, Science 276:720, April 4, 1997

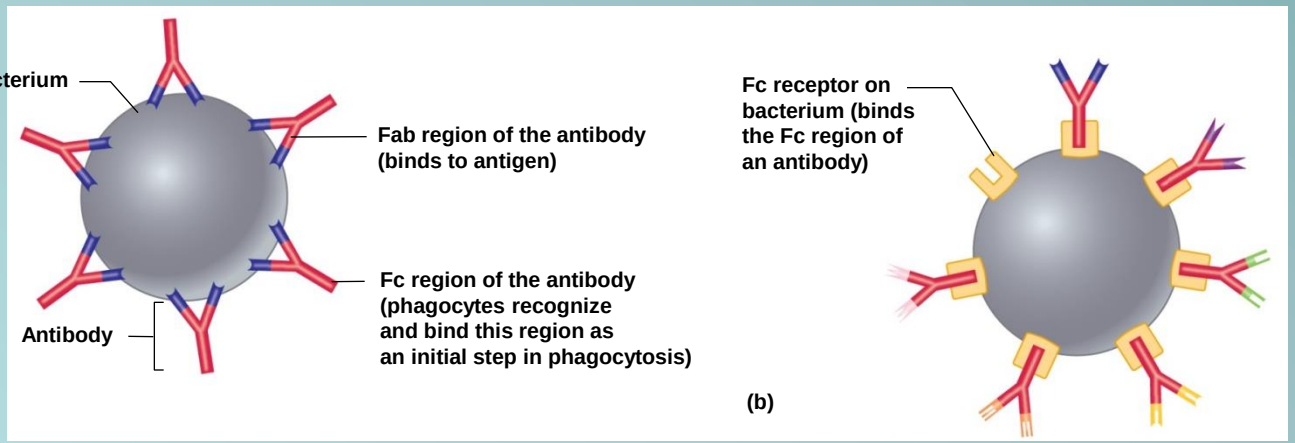
16.7. Avoiding the Host Defenses

- Avoiding Destruction by Phagocytes
  - Preventing Encounters with Phagocytes
    - C5a peptidase: degrades chemoattractant C5a
      - E.g., *Streptococcus pyogenes*
    - Membrane-damaging toxins: kill phagocytes, other cells
      - E.g., *S. pyogenes* makes streptolysin O



16.7. Avoiding the Host Defenses

- Avoiding Destruction by Phagocytes (continued…)
  - Avoiding Recognition and Attachment
    - Capsules: interfere with opsonization; some bind host's regulatory proteins that inactivate C3b
      - E.g., *Streptococcus pneumoniae*
    - M protein: cell wall of *Streptococcus pyogenes* binds regulatory protein that inactivates C3b
    - Fc receptors: bind Fc region of antibodies
      - E.g., *Staphylococcus aureus*, *Streptococcus pyogenes*



16.7. Avoiding the Host Defenses

- Avoiding Destruction by Phagocytes (continued…)
  - Surviving Within Phagocytes
    - Escape from phagosome: prior to lysis with lysosomes
      - *Listeria monocytogenes* produces molecule that forms pores in membrane; *Shigella* species lyse phagosome
    - Prevent phagosome-lysosome fusion: avoid destruction
      - *Salmonella* sense ingestion by macrophage, produce protein that blocks fusion process
    - Survive within phagolysosome: few can survive destructive environment
      - *Coxiella burnetii* (Q fever) can withstand; delays fusion, allows time to equip itself to survive

16.7. Avoiding the Host Defenses

- Avoiding Destruction by Phagocytes (continued…)
  - Avoiding Antibodies
    - IgA protease: cleaves IgA, found in mucus, secretions
      - *Neisseria gonorrhoeae* and others produce
    - Antigenic variation: alter structure of surface antigens, stay ahead of antibody production
      - *Neisseria gonorrhoeae* varies antigenic structure of pili
    - Mimicking host molecules: cover surface with molecules similar to those found in host cell, appear to be “self”
      - *Streptococcus pyogenes* form capsule from hyaluronic acid, a polysaccharide found in tissues

16.8. Damage to the Host

- Direct or indirect effects
  - Direct (e.g., toxins produced)
  - Indirect (e.g., immune response)
  - Damage may help pathogen to exit and spread
    - *Vibrio cholerae* induces watery diarrhea, up to 20 liters/day, which can contaminate water supplies
    - *Bordetella pertussis* triggers severe coughing, pathogens released into air

16.8. Damage to the Host

- Exotoxins: proteins with damaging effects
  - Secreted or leak into tissue following bacterial lysis
    - Foodborne intoxication results from consumption
    - Destroyed by heating; most exotoxins heat-sensitive
  - Can act locally or systemically
  - Proteins, so immune system can generate antibodies
    - Many fatal before immune response mounted
    - Vaccines therefore critical: toxoids are inactivated toxin
    - Antitoxin is suspension of neutralizing antibodies to treat
  - Neurotoxins damage nervous system
  - Enterotoxins cause intestinal disturbance
  - Cytotoxins damage variety of cell types

16.8. Damage to the Host

TABLE 16.1 Exotoxins Produced by Various Primary Pathogens

Example	Name of Disease; Name of Toxin	Characteristics of the Disease	Mechanism	Page Reference
A-B TOXINS—Composed of two subunits, A and B. The A subunit is the toxic, or active, part; the B subunit binds to the target cell.				
Neurotoxins				
Clostridium botulinum	Botulism; botulinum toxin	Flaccid paralysis	Blocks transmission of nerve signals to the muscles by preventing the release of acetylcholine.	p. 652
Clostridium tetani	Tetanus; tetanospasmin	Spastic paralysis	Blocks the action of inhibitory neurons by preventing the release of neurotransmitters.	p. 555
Enterotoxins				
Enterotoxigenic *E. coli*	Traveler's diarrhea; heat-labile enterotoxin (cholera-like toxin)	Severe watery diarrhea	Modifies a regulatory protein in intestinal cells, causing those cells to continuously secrete electrolytes and water.	p. 590
Vibrio cholerae	Cholera; cholera toxin	Severe watery diarrhea	Modifies a regulatory protein in intestinal cells, causing those cells to continuously secrete electrolytes and water.	p. 586
Cytotoxins				
Bacillus anthracis	Anthrax; edema factor, lethal factor	Inhaled form—septic shock; cutaneous form—skin lesions	Edema factor modifies a regulatory protein in cells, causing accumulation of fluids. Lethal factor inactivates proteins involved in cell signaling functions.	p. 497
Bordetella pertussis	Pertussis (whooping cough); pertussis toxin	Sudden bouts of violent coughing	Modifies a regulatory protein in respiratory cells, causing accumulation of respiratory secretions and mucus. Other factors also contribute to the symptoms.	p. 501
Corynebacterium diphtheriae	Diphtheria; diphtheria toxin	Pseudomembrane in the throat; heart, nervous system, kidney damage	Inhibits protein synthesis by inactivating an elongation factor of eukaryotic cells. Kills local cells (in the throat) and is carried in the bloodstream to various organs.	p. 490
E. coli O157:H7	Bloody diarrhea, hemolytic uremic syndrome; shiga toxin	Diarrhea that may be bloody; kidney damage	Inactivates the 60S subunit of eukaryotic ribosomes, halting protein synthesis.	p. 590
Shigella dysenteriae	Dysentery, hemolytic uremic syndrome; shiga toxin	Diarrhea that contains blood, pus, and mucus; kidney damage	Inactivates the 60S subunit of eukaryotic ribosomes, halting protein synthesis.	p. 588

(continued)

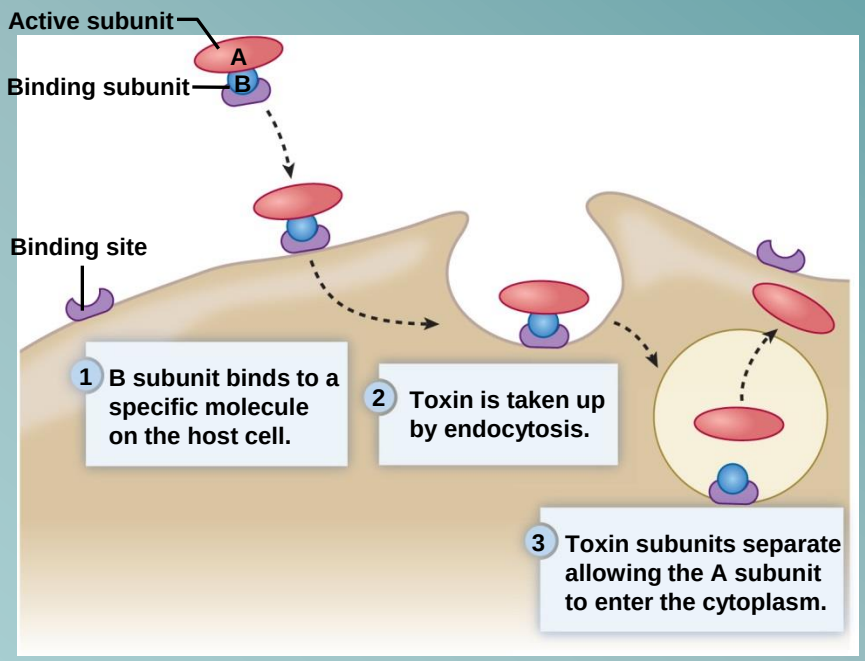
16.8. Damage to the Host

TABLE 16.1 Exotoxins Produced by Various Primary Pathogens (*Continued*)

Toxins	Name of Disease; Name of Toxin	Characteristics of the Disease	Mechanism	Page Reference
MEMBRANE-DAMAGING TOXINS (cytotoxins)—Disrupt plasma membranes.				
Clostridium perfringens	Gas gangrene; α-toxin	Extensive tissue damage	Removes the polar head group on the phospholipids in the membrane, destroying membrane integrity.	p. 558
Staphylococcus aureus	Wound and other infections; leukocidin	Accumulation of pus	Inserts into membranes, forming pores that allow fluids to enter the cells.	p. 551
Streptococcus pyogenes	Pharyngitis and other infections; streptolysin O	Accumulation of pus	Inserts into membranes, forming pores that allow fluids to enter the cells.	p. 487
SUPERANTIGENS—Override the specificity of the T-cell response.				
Staphylococcus aureus (certain strains)	Foodborne intoxication; staphylococcal enterotoxins	Nausea and vomiting	Not well understood with respect to how the ingested toxins lead to the characteristic symptoms of foodborne intoxication.	p. 757
Staphylococcus aureus (certain strains)	Staphylococcal toxic shock; toxic shock syndrome toxin (TSST)	Fever, vomiting, diarrhea, muscle aches, rash, low blood pressure	Systemic toxic effects due to the resulting massive release of cytokines.	p. 619
Streptococcus pyogenes (certain strains)	Streptococcal toxic shock; streptococcal pyrogenic exotoxins (SPE)	Fever, vomiting, diarrhea, muscle aches, rash, low blood pressure	Systemic toxic effects due to the resulting massive release of cytokines.	p. 553
OTHER TOXIC PROTEINS				
Staphylococcus aureus	Scalded-skin syndrome; exfoliatin	Separation of the outer layer of skin	Thought to break ester bonds that hold the layers of skin together.	p. 527
Various organisms	Various diseases; proteases, lipases, and other hydrolases	Tissue damage	Degrades proteins, lipids, and other compounds that make up tissues.	

16.8. Damage to the Host

- Exotoxins (continued…)
  - A-B toxins have two parts
    - A subunit is toxic, usually an enzyme
    - B subunit binds to cell, dictates cell type to be infected
      - Structure allows novel approaches for vaccines and therapies; can use B subunit to deliver medically useful compounds to specific cell type

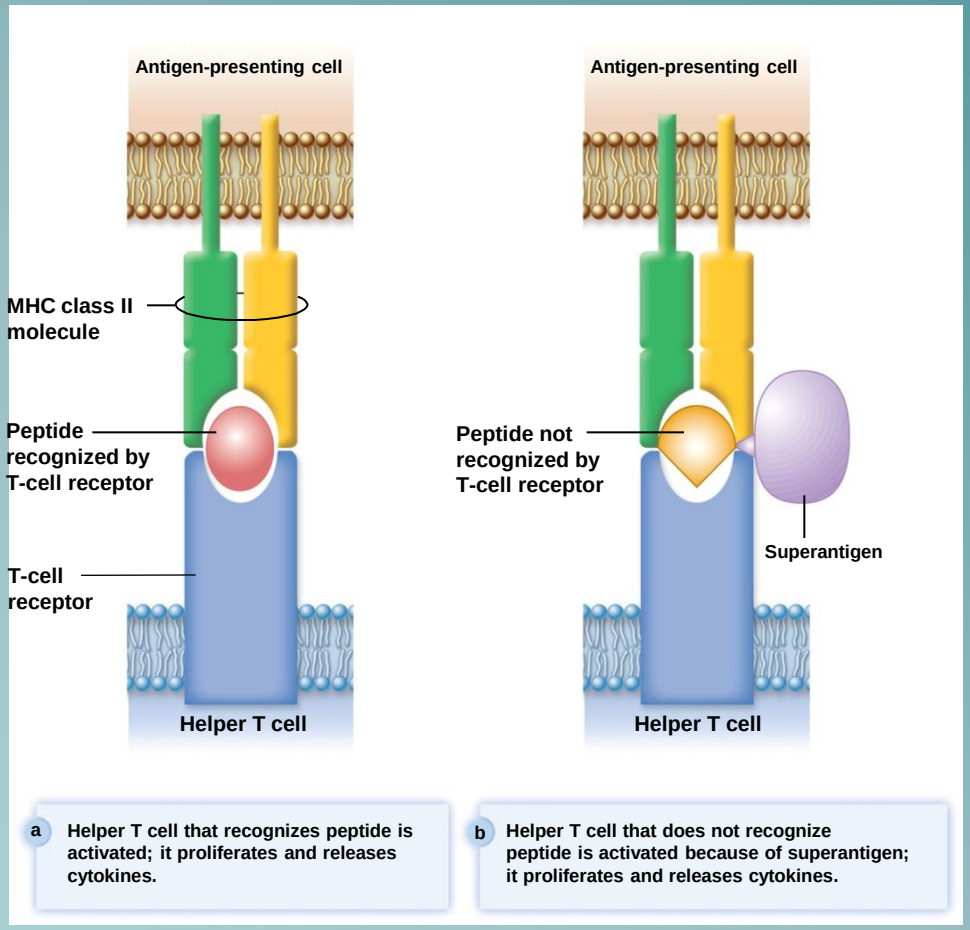


16.8. Damage to the Host

- Exotoxins (continued…)
  - Membrane-Damaging Toxins
    - Cytotoxins that disrupt plasma membranes, lyse cells
    - Hemolysins lyse red blood cells
    - Some insert into membranes, form pores
      - E.g., streptolysin O from *Streptococcus pyogenes*
    - Phospholipases hydrolyze phospholipids of membrane
      - E.g., α-toxin of *Clostridium perfringens* (gas gangrene)

16.8. Damage to the Host

- Exotoxins (continued…)
  - Superantigens: simultaneously bind MHC class II and T-cell receptor
    - T-cell interprets as antigen recognition
    - Toxic effect is from massive cytokine release from T_H
    - Include toxic shock syndrome toxin (TSST) and several by *Staphylococcus aureus*, *Streptococcus pyogenes*



16.8. Damage to the Host

- Exotoxins (continued…)
  - Other Toxic Proteins
    - Some damaging proteins are not A-B toxins, membrane-damaging toxins, or superantigens
    - E.g., exfoliatin from *Staphylococcus aureus* causes scalded skin syndrome
      - Destroys material that binds together skin layers
      - Bacteria may be growing in small lesion, but toxin spreads systemically
    - Various hydrolytic enzymes including proteases, lipases, and collagenases break down connective tissue
      - Destroy tissues, some help bacteria spread

16.8. Damage to the Host

- Endotoxin, Other Bacterial Cell Wall Components
  - Endotoxin is lipopolysaccharide (LPS)
    - Lipid A triggers inflammatory response
      - When localized, response helps clear
      - When systemic, causes widespread response: septic shock or endotoxic shock
    - Lipid A typically released following cell lysis
      - Phagocytosis, MAC formation, certain antibiotics
    - Activates innate and adaptive defenses
      - Toll-like receptors (monocytes, macrophages, others) induce cytokine production; also T-independent antigen response of B-cells at high concentrations
    - Heat-stable; autoclaving does not destroy
  - Peptidoglycans, other components also trigger

16.8. Damage to the Host

- Comparison of Exotoxins and Endotoxin
  - Exotoxins from Gram-positives and Gram-negatives
    - Protein; potent; usually heat-inactivated
  - Endotoxins only from Gram-negatives
    - Lipid A component of LPS; small localized amounts yield appropriate response, but systemic distribution can be deadly; heat-stable

TABLE 16.2 Comparison of Exotoxins and Endotoxin

Property	Exotoxins	Endotoxin
Bacterial source	Gram-positive and Gram-negative species	Gram-negative species only
Location in the bacterium	Synthesized in the cytoplasm; may or may not be secreted	Component of the outer membrane of the Gram-negative cell wall
Chemical nature	Protein	Lipopolysaccharide (the lipid A component)
Ability to form a toxoid	Generally	No
Heat stability	Generally inactivated by heat	Heat-stable
Mechanism	A distinct toxic mechanism for each	Innate immune response; a systemic response leads to fever, a dramatic drop in blood pressure, and disseminated intravascular coagulation
Toxicity	Generally very potent; some are among the most potent toxins known.	Small amounts in a localized area lead to an appropriate immune response that helps clear an infection, but systemic distribution can be deadly

16.8. Damage to the Host

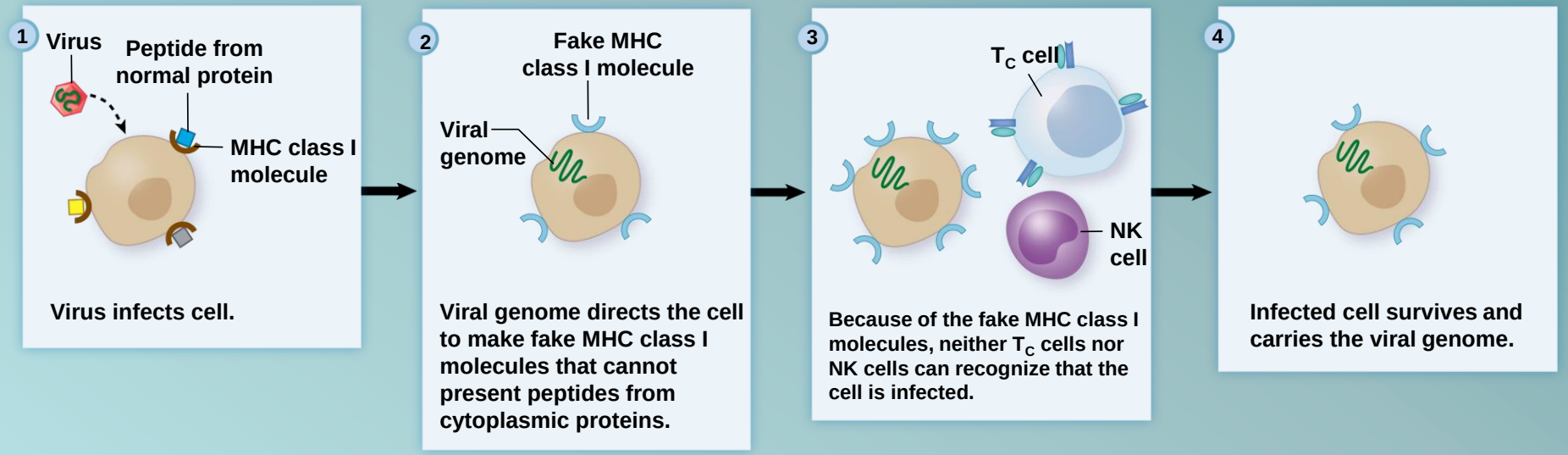
- Damaging Effects of the Immune Response
  - Damage Associated with Inflammation
    - Phagocytic cells can release enzymes and toxic products
  - Damage Associated with Adaptive Immunity
    - Immune complexes: antigen-antibody complexes can form, settle in kidneys and joints, and activate complement system leading to inflammation
      - E.g., acute glomerulonephritis following skin, throat infections of *S. pyogenes*
    - Cross-reactive antibodies: may bind to body's own tissues, promote autoimmune response
      - E.g., acute rheumatic fever following *S. pyogenes* infection

16.9. Mechanisms of Viral Pathogenesis

- Binding to Host Cells and Invasion
  - Viruses attach to target cells via specific receptors
- Avoiding Immune Responses
  - Avoiding the Antiviral Effects of Interferons
    - Viruses may block expression of host genes or block activation of enzymes
  - Antibodies and Viruses
    - Move cell to cell or cause cell fusion (syncytium) to avoid
    - Modify surface antigens, outpace body's capacity to produce effective antibodies
      - RNA virus replicases, HIV reverse transcriptase lack proofreading ability; mutations common
    - Use antibodies to facilitate macrophage uptake

16.9. Mechanisms of Viral Pathogenesis

- Avoiding Immune Responses (continued…)
  - Regulating Host Cell Death
    - Prevent or delay apoptosis, control regulatory protein p53
    - Block MHC class I presentation
    - Present “counterfeit” MHC class I molecules



16.10. Mechanisms of Eukaryotic Pathogenesis

- Colonization, evasion of defenses, damage to host
  - Fungi: most are saprophytes; those that cause disease are generally opportunists
    - Dermatophytes cause superficial infections of hair, skin, nails; have keratinase enzymes
    - Fungi of normal microbiota (e.g., *Candida albicans*) can cause disease in immunocompromised hosts
    - Most serious fungal infections caused by dimorphic fungi
      - Present as molds in environment, conidia inhaled deep into lungs, develop into other forms (e.g., yeasts)
      - Immune system usually controls unless compromised
    - Some fungi produce toxins: mycotoxins
      - E.g., *Aspergillus flavus* produces aflatoxin

16.10. Mechanisms of Eukaryotic Pathogenesis

- Colonization, evasion of defenses, damage to host
  - Protozoa and Helminths
    - Most live within intestinal tract or enter via arthropod bite
      - *Schistosoma* species can enter skin directly
    - Attach to host cells via specific receptors
    - Variety of mechanisms to avoid antibodies
      - Hide within cells (e.g., *Plasmodium* species produce enzyme to penetrate red blood cells; *Leishmania* species survive, multiply within macrophages)
      - Vary surface antigens (e.g., African trypanosomes)
      - Coat with host proteins (e.g., *Schistosoma* species)
    - Damage variable: can come from nutrient consumption in digestive tract; intestinal blockage; production of enzymes; immune response