Chapter 27

Bacterial Infections

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KEY TERMS AND DEFINITIONS

Antibiotic—a substance that kills or inhibits the growth of bacteria.

Bacteria—unicellular (single-celled) microorganisms. The singular of this term is bacterium.

Bactericidal—able to kill bacteria.

Bacteriostatic—suppressing the growth of bacteria.

Broad-spectrum—a term describing an agent that has activity against a wide variety of microorganisms.

Infection—invasion by pathogenic microorganisms, which multiply in a host.

Microorganism—a life form of microscopic size (not visible to the unaided eye).

Normal flora—microorganisms inhabiting the human body that under normal circumstances do not cause illness or disease.

Nosocomial—acquired in or associated with a healthcare facility.

Pathogen—organism that causes illness or disease.

Prophylaxis—prevention of illness or disease. (adjective = Prophylactic).

Resistance—the ability of microorganisms to withstand the effects of antibiotics.

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LEARNING OBJECTIVES

After completing this chapter, you should be able to

1. Define:
   - Infection
   - Bacteria
   - Normal flora
   - Pathogen
   - Resistance
2. Outline the concept of normal flora bacteria and the mechanism behind the development of pathogenicity.
3. Describe host defense mechanisms.
4. Recognize the types of bacteria and bacterial infections.
5. Explain the therapeutic effects of antibiotics and the most common indications for each class.
6. Identify factors relevant to antibiotic selection.
7. Outline the management of patients with bacterial infections, including monitoring for efficacy and safety.

CASE STUDY

G. F. is a 16-year-old male who presents to the emergency room (ER) with shortness of breath and increased sputum production. G. F. states he has not felt well for the past couple of days but today has trouble breathing. Upon examination in the ER, breath sounds are positive for wheezing with crackles, temperature 102.1°F, oxygen saturation 89%, and white blood cell (WBC) count = 15.7 (normal WBC count = 4–10). Blood and sputum cultures are obtained and sent to the laboratory for analysis.

Bacteria are single-celled microscopic organisms that live in soil, water, and humans. Bacteria are found everywhere on earth and in all types of environments. There are approximately five nonillion (5×10^{30}) bacteria on earth.[1]

In humans, bacteria reside on the skin and in the digestive tract, genitourinary tract, airways, and mouth. When these bacteria stay in a particular part of the body and do not cause harm or **infection**, they are referred to as **normal flora** or colonizing bacteria. Normal flora protects the body against disease-causing organisms. Normal flora also performs tasks that are useful to the human host. Skin flora prevents pathogenic organisms from colonizing the surface of the skin by utilizing nutrients for themselves and/or being hostile to pathogenic organisms. The flora that resides in the gastrointestinal (GI) tract are often referred to as *gut flora*. These organisms are responsible for many functions, such as preventing the overgrowth of pathogenic organisms, carbohydrate metabolism, production of certain vitamins (biotin, vitamin K), and various other functions. It is important to understand that not all bacteria are infectious when they reside in their normal environment and that they perform many important functions.

Bacteria that cause illness or disease are known as **pathogens**; they are referred to as pathogenic. Bacteria become pathogenic when they produce toxins and/or gain access to a body location where they are not tolerated as *normal flora*. Toxin production or invasion by pathogenic organisms are considered infection. Many host factors may influence the likelihood of infection. Host defense mechanisms can be classified as natural barriers, nonspecific immune responses, and specific immune responses.

Natural barriers to infection include the skin, mucous membranes, respiratory tract, and GI tract. The skin usually provides protection unless its barrier is physically disrupted (eg, injury, abrasion, incision, burns, or intravenous catheter). Mucous membrane barriers include secretions that are produced by the body (eg, cervical mucus, tears, or saliva). Many of these secretions contain immunoglobulins, which are proteins that are used by the immune system to identify and neutralize foreign substances, such as IgA and IgG that prevent organisms from attaching to host cells. The respiratory tract barrier consists of cilia (short hair-like structures that extend from a cell and move in locomotion). The lining of the respiratory tract serves as a filter mechanism as it transports invading organisms away from the lung. In addition, coughing serves as a barrier to remove these organisms. GI barriers include the acidic content of the GI tract and antibacterial activity of pancreatic enzymes, bile, and secretions released by the intestine. As mentioned earlier, the normal flora of the GI tract can serve as a barrier because they inhibit pathogenic organisms by competing for environmental resources.

Once a pathogenic organism is recognized, the body's natural defenses are initiated. Nonspecific immune responses

are usually produced first. This response involves fever and the increased production of neutrophils, WBCs capable of ingesting **microorganisms** or particles (discussed in Chapter 25). The inflammation that occurs during an infection directs the immune system response to the site of injury or infection by increasing blood flow to that site and increasing vascular permeability. This allows the WBCs to penetrate tissues and access the site to begin inhibiting the spread of the infectious organism.

Specific immune responses occur after infection. The body produces antibodies and immunoglobulins that adhere to specific targets on the infecting organisms. The antibodies help cells ingest antigens, inactivate toxic substances that are produced by bacteria, and attack bacteria directly. In addition, the specific immune response activates systems responsible for clearing pathogens from a host.

When there are breakdowns or deficiencies in the body's defense system, the host is vulnerable to many types of infections. Defects in natural barriers include impaired cough, loss of gastric acidity, loss of cutaneous (skin tissue) integrity, and loss of normal flora. Defects in immune barriers, which include disease states that limit or inhibit the production or replication of the body's immune cells, are referred to as immunosuppression or immunodeficiency. Diseases, such as HIV infection, lupus, leukemia, and megaloblastic anemia, and decreases in numbers of WBCs lead to immunosuppression. Additionally, certain medications can contribute to deficiencies in the host's immune response. These medication classes include some cancer chemotherapies, some biologics, and corticosteroids.

SIGNS AND SYMPTOMS OF BACTERIAL INFECTIONS

Signs and symptoms in the infected host are based on the location and the type of infection. Infection can be confirmed by fever, other signs and symptoms, and predisposing factors. Fever is defined as a controlled elevation of body temperature above the normal range of 36°C to 37.8°C (98.2°F to 99.5°F). The increase in body temperature is a defense mechanism. Some organisms are susceptible to moderate temperature elevations and, in addition, the elevation of temperature activates many of the body's other defense mechanisms. Recall from Chapter 25 that certain WBCs are responsible for providing defense against invading pathogens. Most infections cause an elevation of the body's WBC count, known as leukocytosis.

PRACTICE POINT

Not all infections result in an increase in WBC count.

Identification of the pathogen assists with confirming the presence of infection. Infected body materials are often sampled for this purpose. Such sampling is known as culturing. It is most effective if cultures are obtained prior to **antibiotic** therapy.

CASE?

What signs and symptoms of infection does G. F. have?

PRACTICE POINT

If cultures are obtained after antibiotics are started, the sample may reveal a false-negative culture or altered cellular and chemical composition of the infected sample, as a result of the antibiotic's action.

Several types of cultures can be obtained from the infected host. These include blood, sputum, tissue, wound, urine, stool, cerebral spinal fluid, and samples from other body fluids. The interpretation of the culture is important in determining whether the organisms identified (if any) are pathogenic, contaminant, or normal flora from the site of collection. Another test used to assist in obtaining useful information regarding the type of organism present is known as a Gram stain. Gram staining rapidly classifies bacteria into broad groups based on their shape and color and may provide useful information to assist in the initial selection of antibiotic therapy before culture results are completed.

For certain types of infections, such as pneumonia, other methods can be used to diagnose or confirm the presence of infection. This includes chest x-rays to review the patient's lungs for images that may reveal infiltration in the lobes of the lung. Computed tomography (CT) scans along with magnetic resonance imaging (MRI) can allow the clinician a better view of infectious processes in many parts of the body.

TABLE 27-1. Signs and Symptoms of Bacterial Infections

Type of Infection	Location	Signs and Symptoms
Meningitis	Central nervous system	Fever, stiffness of neck and back, altered mental status, headache
Brain and meningeal abscess	Central nervous system	Fever, altered mental status
Encephalitis	Central nervous system	Fever, altered mental status
Sinusitis (sinus infection)	Respiratory (upper)	Fever, nasal discharge, facial pain
Otitis media (ear infection)	Respiratory (upper)	Fever, irritability, discharge
Pneumonia	Respiratory (lower)	Fever, chills, shortness of breath, productive cough
Bronchitis	Respiratory (lower)	Persistent cough, malaise
Enteritis	Gastrointestinal tract	Fever, diarrhea, dehydration
Peritonitis	Intra-abdominal	Fever, nausea, vomiting, abdominal guarding
Bacteremia	Blood	Fever, chills, malaise
Cellulitis	Skin/soft tissue	Edema, erythema, fever
Gonorrhea	GU tract	Dysuria, urethritis, discharge
Urinary tract infection (UTI)	GU tract	Dysuria, urgency, frequency

There are many different types of infections that occur in humans. Bacterial infections can form in every system of the human body. Table 27-1 classifies various types of infections, location, and some of the most common signs and symptoms.

CASE?

What organisms are the most likely cause of G. F.'s infection?

CLASSIFICATION OF BACTERIA

There are several types of bacteria that are responsible for causing infections. The classification of bacteria includes the association of bacteria into an organized form of naming referred to as taxonomy. This includes the genus and species names of the bacteria. For example, with the bacterium known as *Staphylococcus aureus*, *Staphylococcus* is the genus or family name and *aureus* is the specific species. In addition, bacteria are classified by their shapes, known as morphology. There are three basic morphologies of bacteria: round (coccus), rod-shaped (bacillus), or spiral-shaped (spirillum). Bacteria are also classified by their color after a stain is applied. This staining process is referred to as a Gram stain. As mentioned previously, Gram staining is an empirical method of differentiating between the main groups of bacteria: Gram positive, Gram negative, and acid fast. Gram-positive bacteria have a thick cell wall that stains purple. Gram-negative bacteria have a thin cell wall that stains pink. Acid-fast bacteria resist Gram staining because the cell walls contain a high concentration of lipids. Finally, bacteria can be classified based on oxygen requirements. Those bacteria that require oxygen to live and grow are referred to as aerobic and those not needing oxygen are referred to as anaerobic.

The two most common groups of Gram-positive cocci (round) are staphylococci and streptococci. These are the genus names and there are several species within each group. When viewed microscopically, staphylococci appear in clumps (clusters) like a bunch of grapes and streptococci form chains. The most common pathogen in the *Staphylococcus* group is *Staphylococcus aureus*. Further tests can differentiate *Staphylococcus aureus* from other staphylococci. All species of staphylococci are normal flora and colonize on the skin and mucous membranes of humans.

Streptococci are classified according to their ability to break down blood in fresh blood agar plates. Some streptococci have no effect on blood and are termed *nonhemolytic* streptococci. The most important of the nonhemolytic streptococci are the enterococci, such as *Enterococcus faecalis*

and *Enterococcus faecium,* both of which are normal flora in the GI tract. Other streptococci cause partial breakdown of blood and are called alpha-hemolytic streptococci, which are often referred to as viridans (green) streptococci. The viridans streptococci are a large and heterogeneous group of bacteria and include organisms that play a role in tooth decay and those that can cause endocarditis (infection of the tissue surrounding the heart) and brain abscesses. The most common pathogen of the alpha-hemolytic streptococci family is *Streptococcus pneumoniae* (the cause of pneumococcal pneumonia and meningitis). The beta-hemolytic streptococci cause the complete breakdown of blood in fresh blood agar plates. Clinically, the most important of the beta-hemolytic streptococci is *Streptococcus pyogenes*, the infecting organism for strep throat.

The Gram-positive bacilli (rods) can be divided according to their ability to produce spores. Spores of Gram-positive rods are highly resistant structures that may add considerably to their pathogenic capacity. Gram-positive rods that are spore forming are grouped in the genus *Bacillus*. Important members of this genus include *Bacillus anthracis* (the cause of anthrax) and *Bacillus cereus* (a cause of food poisoning). Gram-positive rods that are anaerobic spore formers are grouped in the class clostridia. These include *Clostridium perfringens*, a principal cause of gangrene, *Clostridium tetani* (the cause of tetanus), *Clostridium botulinum* (the cause of the fatal food poisoning botulism), and *Clostridioides difficile* (*C. diff*), a growing cause of infectious diarrhea following antibiotic therapy.

The non-spore-forming Gram-positive rods include coryneform bacteria and lactobacilli. Some lactobacilli are important members of the normal vaginal flora of women of child-bearing age. A common pathogen of this group includes *Listeria monocytogenes*, which is one of the most virulent foodborne pathogens. Table 27-2 organizes the Gram-positive bacteria by shape, oxygen use (ie, aerobic or anaerobic), and enzyme-producing groups.

The Gram-negative bacteria have an outer thin cell wall and stain pink on a Gram stain. The Gram-negative cocci include the genera *Moraxella* and *Neisseria*.[2] The most pathogenic *Neisseria* organisms include *Neisseria meningitidis* (the cause of bacterial meningitis) and *Neisseria gonorrhoeae* (the cause of gonorrhea). These organisms are most often seen in pairs and are commonly referred to as diplococci.

Gram-negative bacilli include the order enterobacterales. This group is differentiated into types based on whether they can grow in the presence (aerobic) or absence (anaerobic) of oxygen and are frequently found in the GI tract of humans and animals. Some pathogens in this group include *Yersinia pestis* (the cause of plague), *Salmonella typhi* (the cause of typhoid), *Shigella dysenteriae* (the cause of bacillary dysentery), *Pseudomonas aeruginosa* (the cause of many types of infections associated with high mortality rates), and *Salmonella enteritidis* (the cause of food poisoning). Additional members of this class include *Escherichia coli* and members of the genus *Klebsiella*. The *Vibrio* and *Campylobacters* are Gram-negative rods that appear curved or spiral in shape. These bacteria are commonly found in natural waters, both

TABLE 27-2. Classification of Common Gram-Positive Microorganisms

Aerobic Gram Positive
Cocci Streptococci: *Streptococcus pneumoniae, Streptococcus viridans* Enterococci: *Enterococcus faecalis, Enterococcus faecium* Staphylococci: *Staphylococcus aureus, Staphylococcus epidermidis* Bacilli (rods) *Corynebacterium* *Listeria*
Anaerobic Gram Positive
Cocci *Peptococcus* *Peptostreptococcus* Bacilli (rods) Clostridia: *Clostridium perfringens, Clostridium tetani, Clostridioides difficile* Propionibacterium

freshwater and marine. *Vibrio cholerae* (the cause of the waterborne infection cholera), *Campylobacters* (the cause of bacterial enteritis), and *Helicobacter pylori* (the cause of stomach ulcers) are common pathogens in this group.

Some Gram-negative bacilli appear so short that they often resemble cocci under the microscope. These are sometimes referred to as cocco-bacilli. This group includes members of the genera *Haemophilus* and *Acinetobacter*, the latter being a cause of hospital-acquired **(nosocomial)** infections. Other Gram-negative bacteria are very fastidious (specific) in their nutritional requirements, including members of the genus *Legionella*, which cause atypical pneumonias and Legionnaires' disease. Anaerobic Gram-negative bacilli include the genus *Bacteroides*, which causes infections of the peritoneal (abdominal) cavity and GI tract, and *Fusobacteria*, which causes periodontal (gum) infections. **Table 27-3** organizes the Gram-negative bacteria by shape, oxygen use, and enzyme-producing groups.

The next group of bacteria includes the acid-fast bacteria, which possess a waxy cell wall, and they rarely stain using the basic Gram stain technique. These bacteria are identified using a different technique of staining that requires acid and alcohol. The most pathogenic organisms in this group include *Mycobacterium tuberculosis*, which causes tuberculosis, and *Mycobacterium leprae*, which causes leprosy.

A final group of bacteria is referred to as atypical. They are smaller in size than normal bacteria. The most common pathogenic forms are those in the *Mycoplasma*, *Chlamydia*, and *Rickettsia* groups. *Mycoplasma* lack cell walls and are highly pleomorphic, meaning they can change shape. The most common pathogen is *Mycoplasma pneumoniae*, which can cause both upper and lower respiratory infections, including tracheobronchitis and atypical pneumonia. Members of the genus *Chlamydia* have cell walls and are coccoid in shape. The most common pathogen in this group is *Chlamydia trachomatis*, a cause of female reproductive problems, pelvic inflammatory disease (PID), and neonatal respiratory and eye infections. The rickettsiae appear as pleomorphic (form-changing) bacillary or coccobacillary (short rod or oval) forms. The most common pathogens in this group include *Rickettsia rickettsii*, the cause of Rocky Mountain spotted fever (transmitted by ticks), and *Rickettsia prowazekii*, the cause of epidemic typhus fever (transmitted by infected human body lice).

BACTERIAL RESISTANCE

When antibiotics first came into use in the 1930s, they were effective against most bacterial infections. Over time, many antibiotics have lost effectiveness against common bacterial infections due to the increase of antibiotic **resistance**. Bacteria may be naturally resistant to different classes of antibiotics or may acquire resistance from other bacteria through the exchange of resistant genes. Bacteria

TABLE 27-3. Classification of Common Gram-Negative Microorganisms

Aerobic Gram Negative
Cocci Neisseria: *Neisseria meningitidis, Neisseria gonorrhoeae* *Moraxella catarrhalis* Bacilli (rods) Enterobacterales: *Escherichia coli, Klebsiella, Enterobacter, Citrobacter, Proteus, Serratia, Salmonella, Shigella* *Pseudomonas* *Legionella* *Helicobacter pylori* Cocco-bacilli *Haemophilus*
Anaerobic Gram Negative
Cocci Veillonella Bacilli (rods) Bacteroides: *Bacteroides fragilis* Fusobacterium Prevotella

can be resistant to antibiotics in many ways. There are four main mechanisms by which bacteria exhibit resistance to antibiotics:

1. Inactivation or modification of the antibiotic—Bacteria produce enzymes that deactivate the antibiotic (eg, bacteria produce an enzyme called beta-lactamase that inactivates penicillins).
2. Alteration of the target site for the antibiotic—For example, penicillin binds to penicillin-binding protein (PBP) on some bacteria, but certain bacteria have altered this protein and the antibiotic cannot bind to the organism.
3. Alteration of metabolic pathways—For example, sulfonamide antibiotics work by disrupting the synthesis of folic acid by altering para-aminobenzoic acid (PABA). Some sulfonamide-resistant bacteria are able to utilize preformed folic acid and are not dependent on PABA for folic acid synthesis.
4. Reduction of drug transport across the cell wall—This occurs by genetic alterations in certain bacteria that decrease the permeability of the cell wall to the drug or increases active efflux (pumping out) of the antibiotic across the surface of the cell.

SUSCEPTIBILITY

Susceptibility refers to the sensitivity of a microorganism to a given antibiotic. Susceptibility testing is often used to determine the likelihood that a particular antibiotic regimen will be effective in eliminating or inhibiting the infection. Susceptibility testing is performed by growing the bacterial isolate in the presence of varying concentrations of several antimicrobials and then examining the amount of growth to determine which concentrations of antimicrobials inhibit the growth of the bacteria. Results are reported as susceptible (likely to inhibit the pathogenic microorganism), intermediate (may be effective at a higher-than-normal concentration), and resistant (not effective at inhibiting the growth of the organism). The organism is categorized as susceptible, intermediate, or resistant by determining the minimum inhibitory concentration (MIC) of the antibiotic. The MIC is the lowest concentration of an antibiotic that inhibits the growth of the bacteria. This information is then used to determine the best option for treating the infection. While **broad-spectrum** antibiotics are often ordered as initial therapy (to begin treatment of an apparent infection before all tests are complete), prolonged or inappropriate use of such agents can lead to antibiotic resistance, and more specific therapy is generally prescribed once the susceptibility of the infecting organisms has been determined.

PRACTICE POINT

Once the organism is identified and antibiotic sensitivities are known, antibiotic therapy should be changed, if necessary, to the narrowest-spectrum agent that will treat the infection. This way we can prevent antibiotic resistance and unnecessary side effects caused by broad-spectrum antibiotics. This is why antibiotic orders are sometimes revised after a few days of treatment.

ANTIBIOTIC MEDICATIONS

Antibiotics are the drugs of choice for the treatment of bacterial infections. The goal of antibiotic therapy is to kill invading bacteria without harming the host. Antibiotic effectiveness depends on the mechanism of action of the antibiotic, distribution of the drug to the site of infection, immune status of the host, and resistance patterns of the organism.

The first class of antibiotics discussed here are those that are categorized in the beta-lactam group (because they have a beta-lactam ring in their chemical structure). Beta-lactam antibiotics work by inhibiting cell wall synthesis of bacteria. The first antibiotic class in this group to be discovered was penicillin. It was discovered by Alexander Fleming in 1928 and developed as a treatment for human infections in the late 1930s.[3] Over the years, as a result of research prompted by bacterial resistance, the beta-lactam class has grown into several groups with various spectra of activity (ie, activity against specific types of microorganisms).

Penicillins are **bactericidal**. They kill bacteria by activating enzymes that destroy the bacterial cell wall.[3] Some organisms produce beta-lactamase, an enzyme that inactivates penicillins. This effect can be blocked by adding a beta-lactamase inhibitor (clavulanic acid, sulbactam, or tazobactam) to the penicillin. Penicillins are primarily used for Gram-positive organisms and some Gram-negative cocci. A minority of Gram-negative bacilli are also susceptible to large parenteral (intravenous, or IV) doses of penicillin.

All classes of penicillins have the same adverse effects and reaction, which include anaphylaxis, drug-fever, serum

PRACTICE POINT

Human cells do not have cell walls, so they are not susceptible to the cell wall destructive action of beta-lactam antibiotics on the walled bacterial cells.

sickness, rash, nephritis, hemolytic anemia, and leucopenia. Side effects patients may experience when taking these medications include diarrhea, colitis, nausea, and vomiting. Most of the penicillins are renally excreted and dose modifications are necessary for patients with impaired kidney function. The lists that follow detail the characteristics of the major groups of penicillin antibiotics. Pronunciations, brand names, and dosage forms for these agents are detailed in **Medication Table 27-1** (Medication Tables are located at the end of the chapter).

ALERT!

Penicillin G for injection is available in different salts (benzathine, potassium, and procaine), which are not interchangeable. Of these, only penicillin G potassium solution may be administered via the IV route; the others are long-acting suspensions for intramuscular (IM) injection.

Natural Penicillins

Penicillin G (IV) Penicillin VK (Oral) Penicillin benzathine/procaine (IM)

- Spectrum of activity
  - Gram-positive organisms (e.g., streptococci)
  - Gram-negative organisms (*Neisseria meningitides*)
- Avoid use for staphylococci infections
- Advantages: good oral absorption; inexpensive; IM formulation utilized for syphilis, as well as some respiratory tract infections and antibacterial **prophylaxis** in patients with rheumatic heart disease
- Disadvantages: frequent dosing (q 4 hr to q 6 hr) for oral and IV dosage forms; increasing resistance

Aminopenicillins

Ampicillin (IV, Oral) Amoxicillin (Oral) Ampicillin/Sulbactam (IV) Amoxicillin/Clavulanate (PO)

- Semisynthetic (chemically altered) derivatives of natural penicillins
- Are not susceptible to acid hydrolysis in the digestive tract (unlike natural penicillins)
- Spectrum of activity
  - Gram-positive organisms (enterococci, streptococci, *Listeria*)
  - Gram-negative organisms (better activity compared with natural penicillins)
- Ampicillin/sulbactam and amoxicillin/clavulanate include beta-lactamase inhibitors, which increases the spectrum of activity, including coverage against anaerobic bacteria
- Advantages: broader spectrum than natural penicillins; good tissue distribution
- Disadvantages: superinfections (an infection following a previously treated infection, typically caused by an overgrowth of bacteria that were not affected by antibiotic therapy treating the initial infection); GI intolerance more commonly seen with oral formulations that contain a beta-lactamase inhibitor.

PRACTICE POINT

Aminopenicillins for IV use are not compatible with all commonly used admixture solutions and are most frequently mixed in normal saline (0.9% sodium chloride) for maximum stability. Technicians should review package inserts and reference materials before reconstitution and admixture.

Oral ampicillin has poor absorption, causing increased GI side effects. Amoxicillin is preferred for oral therapy.

ALERT!

Amoxicillin is available with and without clavulanate in many oral dosage forms, including capsules, chewable tablets, extended-release tablets, and powders for suspension, and in a wide variety of strengths. With so many choices, extra care must be taken to select the correct product for dispensing.

Antistaphylococcal (Penicillinase-Resistant) Penicillins

Nafcillin (IV) Oxacillin (IV) Dicloxacillin (PO)

- Have activity against organisms (*Staphylococcus*) that produce beta-lactamase (penicillinase), which inactivates natural penicillins (no need for added beta-lactamase inhibitor)
- Spectrum of activity
  - Gram-positive organisms, staphylococci (main target)
- No Gram-negative activity
- Advantages: preferred agents for methicillin-susceptible *Staphylococcus aureus* (MSSA); no dosing adjustment needed for renal function impairment
- Disadvantages: frequent dosing (q 4 hr); no activity against methicillin-resistant *Staphylococcus aureus* (MRSA) or Gram-negative organisms

Extended-Spectrum Penicillins

Piperacillin/Tazobactam (IV)

- Activity against organisms that produce beta-lactamase, which inactivates penicillin (penicillinase)
- Spectrum of activity
  - Gram-positive organisms (streptococci, enterococci, staphylococci)
  - Gram-negative organisms; adds coverage to more resistant bacteria, including *Pseudomonas*
  - Anaerobic activity, including *Bacteroides fragilis*
- Advantages: broad spectrum of coverage, including *Pseudomonas*; good tissue distribution
- Disadvantages: formulations contain large amounts of sodium, may contribute to renal impairment

CASE?

The ER physician orders a 10-day course of ceftriaxone (Rocephin) and azithromycin (Zithromax) intravenously and admits the patient to the medical floor for community-acquired pneumonia. What additional information will the pharmacist want to know about G. F. before these medications are sent for him?

The next group of beta-lactam antibiotics is the cephalosporins, which are bactericidal, with both Gram-positive and Gram-negative activity. Like the penicillins, they inhibit cell wall synthesis. Cephalosporins penetrate well into most body fluids, especially in the presence of inflammation. Hypersensitivity reactions are the most common adverse effect of cephalosporins (urticaria and anaphylaxis are rare). Since the cephalosporins have a beta-lactam ring in the chemical structure like penicillins, some patients who have had an allergic reaction to penicillin may also react to a cephalosporin. Cross-reactivity rates between cephalosporins and penicillins is uncommon and is around 2% to 5%.[4] Cephalosporins can be given cautiously to patients with a history of delayed hypersensitivity to penicillin if necessary, but a different class of antibiotics is usually chosen if possible.

Many patients complain of pain with IM injections. Thrombophlebitis (inflammation of the vein) after IV use is possible. Most of the cephalosporins are renally excreted and dose modifications are required for patients with impaired kidney function. All cephalosporins can produce leukopenia and thrombocytopenia and prolonged use can contribute to the development of *Clostridioides difficile* (pseudomembranous) colitis. The cephalosporins are classified in *generations*,

ALERT!

Cephalosporins should not be administered to patients who have had an anaphylactic (life-threatening) reaction to penicillin. If the patient's allergic reaction to penicillin was considered minor (rash, fever), the cephalosporin is often administered or prescribed anyway. That is why information about the nature of a patient's allergic reaction is kept in the profile.

numbered first through fifth. Later generations generally have an expanded spectrum against aerobic Gram-negative bacilli. The lists that follow detail the characteristics of each generation; additional details are summarized in **Medication Table 27-2**.

First-Generation Cephalosporins

Cefazolin (IV) Cefadroxil (Oral) Cephalexin (Oral)

- Spectrum of activity
  - Gram-positive organisms (staphylococci, streptococci)
  - Gram-negative organisms (*E. coli, Proteus, Klebsiella*)
- Commonly used for surgical prophylaxis
- Advantages: inexpensive, good Gram-positive coverage, especially methicillin-susceptible *Staphylococcus aureus* (MSSA)
- Disadvantages: little Gram-negative coverage, no *Enterococcus* coverage

ALERT!

LOOK-ALIKE/SOUND-ALIKE—Both generic names and brand names of many cephalosporins begin with "cef" or "ceph" and are easily confused.

Second-Generation Cephalosporins

Cefaclor (Oral) Cefuroxime (IV, IM, Oral) Cefprozil (Oral) Cefotetan (IV) Cefoxitin (IV)

- Often used for polymicrobial infections (multiple microorganisms) involving Gram-negative bacilli and Gram-positive cocci
- Cefotetan and cefoxitin are referred to as the cephamycins; they have anaerobic activity and are, therefore, mainly used prophylactically for intra-abdominal procedures
- Advantages: better Gram-negative coverage than the first generations
- Disadvantages: Increasing resistance; no *Enterococcus* coverage

ALERT!

LOOK-ALIKE/SOUND-ALIKE—Keflex, a brand name of cephalexin, has been confused with Keppra, an anticonvulsant.

Third-Generation Cephalosporins

Cefdinir (Oral) Cefditoren (Oral) Cefixime (Oral) Cefotaxime (IV, IM) Cefpodoxime (Oral) Ceftazidime (IV, IM) Ceftibuten (Oral) Ceftriaxone (IV, IM)

- Spectrum of activity
  - Gram-positive organisms (streptococci)
  - Gram-negative organisms (adds coverage of *Neisseria meningitides* and *H. influenzae*)
    - Ceftazidime is the only third-generation cephalosporin with *Pseudomonas* activity
- Ceftriaxone and cefotaxime are used empirically (initiation of antibiotic therapy based on the most common organisms that cause the type of infection) for acute meningitis due to suspected *Streptococcus pneumoniae, H. influenzae*, or *Neisseria meningitides*
- Advantages: many therapeutic uses; used to treat nosocomial infections
- Disadvantages: relatively poor activity against Gram-positive cocci, especially methicillin-sensitive *Staphylococcus aureus* (MSSA), and no *Enterococcus* coverage

Fourth-Generation Cephalosporin

Cefepime (IV, IM)

- Spectrum of activity
  - Gram-positive organisms; maintains activity against staphylococci and streptococci
  - Gram-negative organisms; adds *Pseudomonas* activity and beta-lactamase–producing enterobacteriaceae, such as *Enterobacter*
- Advantages: broad spectrum of activity
- Disadvantage: available in IV formulations only, no *Enterococcus* activity

Fifth-Generation Cephalosporin

Ceftaroline (IV)

- Spectrum of activity
  - Gram-positive organism; activity against MRSA
  - Gram-negative organism; similar to third-generation cephalosporins (eg, Ceftriaxone)
- Advantages: approved for community-acquired pneumonia as well as skin and soft tissue infections
- Disadvantage: available in IV formulations only, no *Enterococcus* activity

Cephalosporins with Beta-lactamase Inhibitors

Ceftazidime/Avibactam (IV)
Ceftolozane/Tazobactam (IV)

Ceftazidime and Ceftolozane act like other beta-lactams by inhibiting cell wall synthesis. Avibactam and tazobactam have little antibacterial effect but instead inactivate certain enzymes, allowing for a broader spectrum of coverage. Ceftazidime/avibactam and Ceftolozane/tazobactam are utilized for complicated urinary tract infections (UTIs) and, with the addition of metronidazole, complicated intra-abdominal infections.

Ceftazidime/avibactam has activity against both carbapenem-resistant organisms and *Pseudomonas aeruginosa*. Ceftolozane/tazobactam also has activity against resistant Gram-negative bacteria and is used most commonly for resistant *Pseudomonas aeruginosa*.

- Advantages: Good tissue distribution, activity against resistant Gram-negative bacteria
- Disadvantages: Expensive; dosage may need to be adjusted for patients with impaired renal function

Cefiderocol (IV)

The newest of the cephalosporins, approved for community-acquired UTIs, as well as hospital-acquired/ventilator-associated pneumonia (HAP/VAP). Known to have good Gram-negative activity against more carbapenem-resistant organisms, along with *Pseudomonas* and *Acinetobacter*.

- Advantages: Activity against resistant Gram-negative bacteria
- Disadvantages: There is an increase in all cause mortality in patients with carbapenem-resistant Gram negative bacterial infections

Other Beta-Lactam Antibiotics

Penicillins and cephalosporins are not the only antibiotics with a beta-lactam ring incorporated into their chemical structures. Carbapenems and monobactams also have this ring and work by inhibiting bacterial wall synthesis. They differ in spectrum of action, effectiveness, and side effect profiles and are included in the beta-lactam summary in Medication Table 27-2.

Carbapenems

Imipenem-Cilastin (IV) Meropenem (IV)
Ertapenem (IV, IM) Doripenem (IV)

The carbapenems are bactericidal drugs that have an extremely broad spectrum of activity. All the carbapenems can cause GI disorders, rash, phlebitis, and headache. In rare cases they may cause hypotension (decreases in blood pressure). Imipenem-cilastin can also increase seizure risk. Carbapenem doses must be adjusted in patients with impaired kidney function. There is a possible cross-reaction with penicillins and these drugs should therefore be avoided in severe allergies.

- Spectrum of activity
  - Gram-positive organisms; broad coverage including enterococci, except ertapenem
  - Gram-negative organisms; broad coverage including *Pseudomonas*, except ertapenem
  - Anaerobic activity
- Advantages: broad spectrum of activity
- Disadvantages: more serious adverse reactions than penicillins and cephalosporins

Meropenem/Vaborbactam (IV)

The first carbapenem with a beta-lactamase inhibitor approved by the U.S. Food and Drug Administration (FDA). Vaborbactam inhibits the degradation of meropenem from bacterial enzymes, allowing for activity against carbapenem-resistant enterobacteriaceae (CRE). Meropenem-vaborbactam is approved for UTI, including pyelonephritis. Known for its broad Gram-negative coverage.

ALERT!

LOOK-ALIKE/SOUND-ALIKE—Doribax, the brand name for doripenem, has been confused with Zovirax, an antiviral injection, and Invanz, the brand name for ertapenem, has been mistaken for Avinza, an oral morphine preparation.

Imipenem-Cilastin-Relebactam (IV)

This is the newest carbapenem with a beta-lactamase inhibitor. The purpose of relebactam is to restore the activity of resistant organisms to imipenem-cilastin. This includes carbapenem-resistant *Klebsiella* and *Pseudomonas*. Imipenem-cilastin-relebactam is approved for complicated UTIs and intra-abdominal infections.

Monobactams

Aztreonam (IV, IM, Inhalation)

The monobactams are cell wall–inhibiting bactericidals. They can cause similar side effects to carbapenems and must be dose-adjusted in patients with impaired kidney function. The only agent in this group currently available in the United States is aztreonam and this antibiotic only has Gram-negative activity, including *Pseudomonas*.

- Advantages: excellent safety profile; can be used safely in penicillin-allergic patients
- Disadvantages: no Gram-positive or anaerobic coverage, increasing resistance in *Pseudomonas* sp.

Non-Beta-Lactam Antibiotics

Fluoroquinolones

Levofloxacin (IV, Oral) Ciprofloxacin (IV, Oral, Otic, Ophthalmic) Moxifloxacin (IV, Oral) Ofloxacin (Oral, Otic, Ophthalmic) Delafloxacin (IV, Oral)

The fluoroquinolones (often called *quinolones* for short) are bactericidal and act by inhibiting the activity of enzymes essential for bacterial DNA replication. Fluoroquinolone doses must be adjusted for patients with impaired kidney function. They can cause nausea, vomiting, and diarrhea, as well as altered mental status and confusion when not properly adjusted for renal function. They can cause cardiac dysfunction in patients with cardiac conduction problems or when used in combination with other medications that have cardiac effects, which can predispose patients to ventricular tachyarrhythmia. Another downside to these antibiotics is the concern for tendon rupture. Characteristics of the fluoroquinolones are listed below; additional details are summarized in **Medication Table 27-3**.

- Spectrum of activity
  - Gram-positive organisms; Moxifloxacin and Levofloxacin overall have good activity against streptococci infections
  - Gram-negative organisms; Levofloxacin and Ciprofloxacin have *Pseudomonas* activity
  - Adds atypical coverage (*Mycoplasma* spp., *Chlamydophilia* spp., *Mycobacterium*)
  - Anaerobic activity with Moxifloxacin (only one in its class)
  - Delafloxacin has activity against *Pseudomonas* and MRSA (only one in its class)
- Advantages: convenient dosing (q 12 hr, q 24 hr), good tissue distribution
- Disadvantages: should not be administered to children younger than 16 years (cartilage dysfunction); some serious side effects

PRACTICE POINT

The oral fluoroquinolones should not be administered at the same time as preparations containing aluminum, calcium, magnesium, and iron, such as antacids or dietary supplements.

Aminoglycosides

Amikacin (IV, IM) Gentamicin (IV, IM, Ophthalmic) Neomycin (Oral) Paromomycin (Oral) Plazomicin (IV) Streptomycin (IV, IM) Tobramycin (IV, IM, Inhalation, Ophthalmic)

The aminoglycosides are bactericidal and work by inhibiting bacterial protein synthesis. Aminoglycosides are poorly absorbed orally and are administered by inhalation, intravenously, topically, and in the eye and ear. Oral dosage forms are indicated only for intestinal infections and for the treatment and prevention of hepatic encephalopathy (see Chapter 23).

The aminoglycosides have a narrow *therapeutic range*, meaning that, while a minimum concentration is necessary

ALERT!

IV doses of the fluoroquinolones should be infused over at least 60 minutes, regardless of the volume or dose; longer infusion times may be required for higher doses.

for bactericidal action, at higher concentrations they can cause serious adverse effects. These adverse events include nephrotoxicity (kidney damage), which in most cases is reversible, and ototoxicity (hearing loss/impairment), which is often irreversible. To prevent these adverse events from occurring, clinicians must base the dose of these medications on several pharmacokinetic parameters, including patient weight, site of infection, and renal function. Pharmacokinetic equations (of the type introduced in Chapter 2) are used to determine the proper dose and dosing interval to achieve therapeutic drug levels, to ensure eradication of the infecting organism without causing harm to the patient. *Peak levels* are determined within 30–60 minutes after a dose has been administered and are presumed to be the highest blood concentration of antibiotic that is achieved. *Trough levels* are determined shortly before the next scheduled dose is given and are presumed to be the lowest level to which antibiotic concentrations fall in a specific treatment regimen. Characteristics of the aminoglycosides are listed below; additional details are summarized in Medication Table 27-3.

ALERT!

LOOK-ALIKE/SOUND-ALIKE—Gentamicin has been involved in medication mix-ups with gentian violet, a topical antiseptic.

- Spectrum of activity
  - Gram-positive; only in combination with cell wall inhibitors (eg, beta-lactams) for synergy
  - Gram-negative; can be used alone or, for serious infections, in combination with other antibiotics
- Advantages: excellent Gram-negative coverage; provides synergistic activity for Gram-positive infections
- Disadvantages: nephrotoxicity, ototoxicity, cost of monitoring when used systemically

PRACTICE POINT

During systemic therapy with aminoglycosides, patient blood samples are sent to the lab to confirm that antibiotic concentrations are within the therapeutic window.

Macrolides

Azithromycin (IV, Oral) Clarithromycin (Oral) Erythromycin (IV, Oral, Ophthalmic, Topical) Fidaxomicin (Oral)

Unlike the groups discussed above, the macrolide antibiotics are primarily **bacteriostatic**. They kill bacterial cells by inhibiting protein synthesis and, thus, suppress bacterial replication.

Erythromycin, the prototype macrolide, has peristalsis activity, therefore causing GI disturbances, including nausea, vomiting, abdominal cramps, and diarrhea. These side effects are less common with clarithromycin and azithromycin, which were developed later. Erythromycin may cause dose-related tinnitus (ringing of the ears), dizziness, and reversible hearing loss. Erythromycin has numerous drug interactions because it inhibits hepatic metabolism through the cytochrome P-450 system, so it can increase drug levels of other medications that are metabolized through the same pathway. This interaction can lead to toxic drug levels that predispose patients to adverse drug reactions and side effects. The macrolides can cause cardiac dysfunction in patients with cardiac conduction problems or when used in combination with other medications that have certain cardiac effects. This may then predispose a patient to ventricular tachyarrhythmia. Erythromycin and clarithromycin can further elevate the PT/INR (prothrombin time/international normalized ratio) when taken with warfarin. Azithromycin has the lowest tendency of the macrolides to cause drug interactions. Characteristics of the macrolides are listed below; additional details are summarized in Medication Table 27-3.

- Spectrum of activity
  - Gram-positive organisms (streptococci)
  - Gram-negative organisms (limited activity)
  - Atypical bacteria: *Mycoplasma pneumoniae*, *Chlamydia trachomatis*, *Chlamydophila pneumoniae*, *Legionella sp.*, *Corynebacterium diphtheriae*, *Campylobacter, Treponema pallidum, Propionibacterium acnes*, and *Borrelia burgdorferi*
  - Clarithromycin is used for *Helicobacter pylori*

- Fidaxomicin's only place in therapy is for *Clostridiodes difficile* colitis
- Advantages: good for community-acquired infections, convenient dosing (azithromycin), dosage not adjusted for renal impairment (exception clarithromycin)
- Disadvantages: high side effect profile; many drug interactions with other medications that have cardiac effects (QT prolongation) and predisposes to ventricular tachyarrhythmia; increased resistance

Tetracyclines

Doxycycline (IV, Oral) Minocycline (IV, Oral)
Tetracycline (Oral) Tigecycline (IV)
Omadacycline (IV, Oral) Eravacycline (IV)

The tetracyclines are bacteriostatic antibiotics that slow bacterial growth by inhibiting bacterial protein synthesis. Because tetracycline absorption is decreased by metallic cations such as aluminum, calcium, magnesium, and iron, preparations containing these ions should not be taken with this class of antibiotics. All tetracyclines can cause nausea, vomiting, and diarrhea. They can also exacerbate gastroesophageal reflux disease (GERD, discussed in Chapter 20). Tetracyclines can cause photosensitivity (increased incidence of sunburns when exposed to the sun). They can cause staining of teeth, hypoplasia (defects) of dental enamel, and abnormal bone growth in children.

Tigecycline, a derivative of tetracycline designed to overcome bacterial resistance, exhibits activity against community-acquired pneumonia, complicated intra-abdominal infections, and complicated skin and skin structure infections caused by susceptible organisms. This includes MRSA and vancomycin-sensitive *Enterococcus faecalis*. It is only administered intravenously.

Eravacycline is a fluorocycline that is structurally similar to tigecycline, with slight modifications. It is a newer drug in this class, typically used for complicated intra-abdominal infections. It is typically reserved for use against drug-resistant bacteria. It has activity against vancomycin-resistant *Enterococcus* (VRE), MRSA, anaerobes, and resistant enterobacterales. It is only administered intravenously.

Omadacycline, a semisynthetic tetracycline derivative, is also a newer drug in this class, with activity against community-acquired pneumonia and complicated skin and skin structure infections by susceptible organisms, including MRSA, *Enterococcus faecalis*, and *Enterobacter*. In addition to the intravenous form, it is available as an oral tablet. Patients taking omadacycline by mouth should follow the same precautions mentioned for the older tetracyclines.

PRACTICE POINT

While it penetrates tissues very well, tigecycline cannot be used to treat bloodstream infections because it does not reach high enough concentrations there. It is also very expensive; thus, it is reserved for infections that cannot be treated effectively by other antibiotics.

ALERT!

Because of their interactions with bone and dental enamel, tetracyclines should be avoided after the first trimester of pregnancy and in mothers who are breastfeeding, as well as in children below the age of 8.

Characteristics of the tetracyclines are listed below; additional details are summarized in Medication Table 27-3.

- Spectrum of activity
  - Gram-positive (community-acquired MRSA coverage)
  - Gram-negative (*Neisseria gonorrhea* and *Helicobacter pylori*)
  - Atypical (rickettsia, spirochetes [*Treponema pallidum*, *Borrelia burgdorferi*], *Vibrio* sp., *Brucella* sp., *Bacillus anthracis*, *Mycoplasma*, and *Chlamydia*)
- Advantages: activity against community-acquired MRSA; inexpensive, not adjusted for impaired renal function
- Disadvantages: high side effect profile; increasing resistance

PRACTICE POINT

Patients taking tetracyclines and related agents should avoid direct sunlight as well as tanning beds and use a sunblock of SPF 15 or higher on areas exposed to the sun (including the lips).

Glycopeptides

**Vancomycin (IV, Oral) Telavancin (IV)
Dalbavancin (IV) Oritavancin (IV)**

Glycopeptides are bactericidal antibiotics that inhibit cell wall synthesis. Vancomycin can be associated with ototoxicity and nephrotoxicity if drug concentrations in the body become too high. As with the aminoglycosides, several pharmacokinetic parameters must be considered by doctors and pharmacists deciding on dose and frequency of administration. Patients at the highest risk for drug accumulation are the elderly and those with impaired kidney function. The oral formulation of vancomycin is not systemically absorbed and is only effective for treating *Clostridioides difficile* colitis (a local effect in the GI tract). Vancomycin intended for use in treating systemic infections must be infused intravenously over at least 60 minutes. Telavancin is a synthetic derivative of vancomycin indicated only for skin and skin structure infections by certain Gram-positive cocci. It is administered only by IV infusion, over at least 60 minutes. Dalbavancin and oritavancin, like telavancin, are semisynthetic derivatives.

PRACTICE POINT

IV vancomycin doses should be limited to concentrations of 5 mg/mL, unless patients are fluid-restricted, and infused at rates not to exceed 10 mg/min.

PRACTICE POINT

The FDA requires distribution of a medication guide to patients receiving telavancin.

ALERT!

Glycopeptides can cause a dangerous reaction termed "red man syndrome" that is characterized by redness, flushing, and itching. This is not an allergic reaction; it occurs when IV infusion of the drug is too rapid. Glycopeptides can still be used but the infusion needs to be slowed down.

Oritavancin can be given as a single dose, whereas dalbavancin can be given in either one to two doses. Both are indicated for skin and skin structure infections for Gram-positive organisms. Oritavancin is administered only by IV, over at least 3 hours, whereas dalbavancin can be administered over 30 minutes.

- Spectrum of activity
  - Only covers Gram-positive bacteria
  - Gram-positive cocci (staphylococci including MRSA, streptococci, enterococci) and Gram-positive bacilli
  - Oral vancomycin only used for *Clostridioides difficile*
- Advantages: very effective against penicillin and cephalosporin-resistant strains of Gram-positive organisms; vancomycin is the drug of choice for MRSA; dalbavancin and oritavancin only require one or two doses
- Disadvantages: Vancomycin and telavancin can accumulate in patients with impaired kidney function leading to increased drug concentrations and incidence of toxicity

ALERT!

Vancomycin injection is very irritating and is never administered via the IM route.

Sulfonamides

Co-trimoxazole (IV, Oral) Sulfacetamide (Topical, Ophthalmic) Sulfadiazine (Topical, Oral)

The sulfonamides, sometimes called *sulfa drugs* or *sulfas*, were the earliest antibiotics marketed for human therapy.[3] First used in 1932, they represented a dramatic change in the way infections were treated. Although the penicillins and newer antibiotics, along with the widespread emergence of bacterial resistance to them, have reduced the importance of this class, several are still in use today.

Sulfonamides are bacteriostatic; they inhibit bacterial replication by interfering with folic acid synthesis in bacteria unable to utilize preformed folate for cellular processes. Since the introduction of sulfonamides, many bacterial strains have acquired the ability to skip the metabolic step blocked by sulfonamides and incorporate absorbed folate

into their metabolism, so they have become resistant to these antibiotics.

PRACTICE POINT

Human cells are unable to make their own folic acid and always use preformed folate, characterized as an essential vitamin (see Chapter 24) for their body processes, so sulfonamides are not toxic to them the way they are to bacterial cells.

Sulfonamides were named because their chemical structure includes an altered version of the folic acid precursor PABA (the one used by bacteria to make folic acid) that has a sulfate molecule attached.[3] A similar structure is also found in other medications, including thiazide diuretics and some diabetes medications.

ALERT!

Patients who have had a hypersensitivity reaction to a "sulfa" drug, for instance, a sulfonamide antibiotic, are more likely to react adversely to other sulfas, such as thiazide diuretics or sulfonylurea diabetes agents. However, this does not preclude the use of a diuretic.

PRACTICE POINT

A sulfa allergy is not the same as a sulfur allergy. Sulfa refers to the sulfonamide chemical structure found in these antibiotics and some other drugs. Sulfur is a chemical element that is part of many nonsulfa medications and included in many bodily substances.

Co-trimoxazole, a combination of the sulfonamide antibiotic sulfamethoxazole and another agent, trimethoprim (which also interferes with bacterial folic acid production), is the most commonly used sulfa anti-infective. It is active against a wide variety of Gram-positive and Gram-negative organisms and is prescribed for the treatment of bacterial infections of the ears (otitis media), GI tract (travelers' diarrhea), respiratory system, and urinary tract. Co-trimoxazole has also been found to be an effective prophylaxis and treatment for pneumonia caused by the organism *Pneumocystis jiroveci*, a fungal infection (PJP) that affects immunosuppressed patients, especially HIV-infected individuals. It appears to be effective against toxoplasmosis, a protozoal parasite, as well. Important to note if giving the IV formulation of sulfamethoxazole/trimethoprim, the weight-based dosing is determined using the trimethoprim component.

PRACTICE POINT

The U.S. Department of Health and Human Services recommends oral co-trimoxazole as the drug of choice for primary prophylaxis of Pneumocystis *pneumonia in HIV-infected individuals.*[2]

Other sulfa antibiotics include sulfadiazine (used orally for bacterial infections and topically as silver sulfadiazine, for burns), sulfacetamide (used only for ophthalmic infections), sulfasalazine (used in the management of ulcerative colitis—see Chapter 22), and sulfisoxazole (available in combination with erythromycin for the treatment of ear infections). Facts to remember about sulfonamide antibiotics are listed below; additional information is included in Medication Table 27-3.

ALERT!

LOOK-ALIKE/SOUND-ALIKE—The sulfonamide antibiotics have similar names, and pharmacy personnel have reported errors that occurred when sulfadiazine was confused with sulfisoxazole.

- Spectrum of activity
  - Co-trimoxazole, wide range of activity
  - Susceptible enterobacterales
  - *Pneumocystis jiroveci* pneumonia
  - *Toxoplasma gondii*
  - *Listeria monocytogenes*
  - Community-acquired MRSA
  - *Stenotrophomonas maltophilia*

- Advantages: inexpensive; useful for less common bacterial infections
- Disadvantages: allergic/hypersensitivity reactions; increasing resistance; drug interactions (eg, warfarin); monitor for hyperkalemia

Miscellaneous Antibiotics

A number of antibiotics are not classified in groups and are discussed here as miscellaneous. They are listed below with their most prominent characteristics (see also Medication Table 27-3).

Chloramphenicol (IV)

Like many of the other antibiotics, chloramphenicol exerts its antimicrobial action by inhibiting protein synthesis. It is bacteriostatic for a wide variety of microorganisms but is considered bactericidal for *H. influenzae*, *Neisseria meningitidis*, and *S. pneumoniae*.[3] Chloramphenicol is an older antibiotic and resistant strains of some pathogens are common.

Unfortunately, chloramphenicol's protein synthesis inhibition is not limited to microorganisms.[3] Some human cells, particularly those of the blood-forming system, are also affected by its action, and it has been known to cause serious, even fatal, blood disorders. For this reason, use of chloramphenicol is limited to serious infections by pathogens with documented sensitivity to the drug and only when less dangerous drugs cannot be used (because of resistance or patient factors such as allergy).

- Broad spectrum of activity against a wide variety of organisms
- Used infrequently in the treatment of typhoid fever, meningitis, Rocky Mountain spotted fever, and anthrax when other drugs cannot be used
- Advantages: broad spectrum, good penetration of spinal fluid for central nervous system infections such as meningitis
- Disadvantages: resistant organisms; life-threatening adverse reactions; allergic/hypersensitivity reactions

Clindamycin (IV, Oral, Vaginal, Topical)

Clindamycin is classified as lincosamide, which is bacteriostatic by inhibiting protein synthesis of bacteria.

- Spectrum of activity
  - Activity against anaerobic organisms (above the diaphragm)
  - Community acquired MRSA infections
- Advantages: option for patients with severe penicillin allergies; renal function dose adjustments are not necessary
- Disadvantages: high rate of *Clostridioides difficile* colitis with use

Daptomycin (IV)

Daptomycin is classified as a lipopeptide that is bactericidal by disrupting multiple aspects of bacterial cell membrane function and inhibition of protein, DNA, and RNA synthesis, which results in bacterial cell death.

- Spectrum of activity
  - Gram-positive cocci (staphylococci, including MRSA, streptococci, enterococci, including vancomycin-resistant *Enterococcus* [VRE]) and Gram-positive bacilli
- Advantages: excellent activity for resistant Gram-positive organisms
- Disadvantages: expensive; cannot be used for pneumonia due to inactivation by lung surfactant; weekly monitoring of creatinine kinase levels

ALERT!

LOOK-ALIKE/SOUND-ALIKE—Daptomycin has been confused with dactinomycin, a cancer chemotherapy.

Linezolid (IV, Oral)

Linezolid is classified as an oxazolidinone that is bacteriostatic by inhibiting bacterial replication. However, it does display some bactericidal activity against certain bacteria.

- Spectrum of activity
  - Gram-positive cocci (staphylococci, including MRSA, streptococci, enterococci, including vancomycin-resistant *Enterococcus* [VRE]) and Gram-positive bacilli
- Advantages: available in IV and oral formulations; excellent tissue penetration; dose not adjusted for renal function
- Disadvantages: thrombocytopenia and neuropathies with prolonged use; monoamine oxidase inhibitor drug interactions

ALERT!

LOOK-ALIKE/SOUND-ALIKE—Zyvox, the brand name for linezolid, looks and sounds like Zovirax, a brand-name antiviral agent.

Metronidazole (IV, Oral, Topical, Vaginal)

Metronidazole demonstrates bacteriostatic action by disrupting bacterial DNA structure, resulting in inhibition of protein synthesis.

- Spectrum of activity
  - Excellent activity against anaerobic bacterial (below the diaphragm) and protozoal infections
- Advantages: available in IV, oral, and topical formulations; does not require renal function dose adjustments
- Disadvantages: patients have to avoid alcohol while taking medication due to disulfiram-like reaction (severe nausea and vomiting); drug interactions (eg, warfarin)

ALERT!

LOOK-ALIKE/SOUND-ALIKE—Metronidazole looks and sounds like metformin, an agent for the treatment of diabetes, which has a similar dosing range and some same-strength oral tablets.

Rifaximin

Rifaximin works by inhibiting bacterial RNA synthesis. It is used for travelers' diarrhea and as an alternative for treatment of *Clostridioides difficile*-associated diarrhea.

- Activity against *Escherichia coli, Acinetobacter, Bacteroides, Enterobacter cloacae*, and various other organisms that reside in the GI tract
- Advantages: low resistance rates; available in oral formulation
- Disadvantages: superinfections; not for use in children younger than 12 years

Quinupristin/Dalfopristin (IV)

Quinupristin/dalfopristin is classified as a streptogramin, an antibiotic that is bacteriostatic by inhibiting bacterial protein synthesis.

- Activity against vancomycin-resistant *Enterococcus faecium* bacteremia; treatment of complicated skin and skin structure infections caused by methicillin-susceptible *Staphylococcus aureus* or *Streptococcus pyogenes*
- Advantages: good activity against resistant Gram-positive organisms
- Disadvantages: may cause arthralgias and/or myalgias with use and can cause hyperbilirubinemia

Colistimethate (IV, IM, Inhaled)

Colistimethate has bacteriostatic activity by acting as a cationic detergent, which damages the bacterial cytoplasmic membrane, causing leaking of intracellular substances and cell death.

- Has activity against resistant strains of Gram-negative bacilli (*Pseudomonas aeruginosa, Enterobacter aerogenes, Escherichia coli*, and *Klebsiella pneumoniae*)
- Advantages: active against resistant organisms; may be used as inhalation therapy to treat lung infections
- Disadvantages: must be dose adjusted in patients with impaired kidney function

Nitrofurantoin (Oral)

Nitrofurantoin is a bactericidal antibiotic with a unique mechanism of action. It is chemically changed by bacteria to a product that inactivates or alters bacterial ribosomal proteins and other macromolecules, inhibiting energy metabolism and DNA synthesis.

- Only indicated for urinary tract infections
- Spectrum of activity
  - Common urinary organisms (eg, *E. coli*, *Klebsiella*, *Proteus*, *Enterococcus*) if susceptible
- Advantages: inexpensive
- Disadvantages: should not be used in patients with impaired renal function; avoid for pyelonephritis

Fosfomycin (Oral)

- Only indicated for urinary tract infections
- Spectrum of activity
  - Common urinary organisms (eg, *E. coli*, *Klebsiella*, *Proteus*, *Enterococcus*) if susceptible
- Advantages: one-time dose
- Disadvantages: avoid for pyelonephritis

Antimycobacterials/Antituberculosis Antibiotics

These agents are used in the treatment of tuberculosis and other infections caused by the organisms from the genus *Mycobacterium*. Because the mycobacteria are slow-growing organisms, tuberculosis infection may be active or latent (not causing signs and symptoms of active infection) in the host. At any time, the latent infection can develop into an active disease. The treatment of these infections is complex due to the multidrug-resistant strains of *Mycobacterium*. Many of the antibiotics used to treat these infections have severe side effects and patient compliance or adherence to treatment regimens is often poor. This has led to bacterial resistance and the need for multiple medication combinations to overcome resistance patterns. A single drug may be given for 4–6 months upon discovery of a latent infection without symptoms, but treatment of active disease usually involves a regimen of two to four drugs, chosen based on the tested sensitivity of the infecting organism.[2] Treatment with these drug combinations can range from 18 weeks up to 18 months.

Rifampin (IV, Oral)

Rifampin is a bactericidal antibiotic that inhibits bacterial RNA synthesis by preventing attachment of an enzyme to DNA, thus blocking initiation of RNA transcription.

- Activity against tuberculosis in combination with other agents; also has activity against *Haemophilus influenzae*, *Legionella* pneumonia; used in combination with other anti-infectives in the treatment of staphylococcal and *M. leprae* infections
- Disadvantages/considerations: may permanently discolor soft contact lenses; causes red–orange discoloration of urine, feces, saliva, sweat, and tears. There is an increase in bacterial resistance; multiple drug interactions; hepatic dysfunction

ALERT!

LOOK-ALIKE/SOUND-ALIKE—Rifampin looks and sounds like rifaximin, an antibiotic that is not indicated for the treatment of tuberculosis.

Ethambutol (Oral)

Ethambutol is a bacteriostatic antibiotic that interferes with cellular metabolism, resulting in the impairment of bacteria replication and cell death.

- Used in combination with other antibiotics to treat tuberculosis; has activity against *Mycobacterium avium complex* (MAC) and *Mycobacterium tuberculosis*
- Disadvantages: many side effects, including optic neuritis with decreased visual acuity, dermatitis, pruritus, headache, fever, and mental confusion

Cycloserine (Oral)

Cycloserine may be bactericidal or bacteriostatic, depending on its concentration at the site of infection and the susceptibility of the organism. It interferes with bacterial cell wall synthesis.

- Used in combination with other antibiotics to treat tuberculosis; has activity against strains of *E. coli* and *Enterobacter* for the treatment of urinary tract infections
- Disadvantages: many side effects, including drowsiness, somnolence, headache, dizziness, anxiety, nervousness, vertigo, and confusion; dose must be adjusted in patients with altered kidney function

Isoniazid (IM, Oral)

Isoniazid is a bactericidal antibiotic with activity against many types of mycobacteria, primarily those that are actively dividing. Its exact mechanism of action is not known, but it may be related to the inhibition of mycolic acid synthesis and disruption of the cell wall.

- Used in monotherapy or in combination with other antibiotics to treat tuberculosis, as well as in the treatment of both latent and active tuberculosis; has activity against *Mycobacterium bovis*, *M. tuberculosis*, and *M. kansasii*

- Disadvantages: many side effects; U.S. Black Box Warning: severe and sometimes fatal hepatitis may occur, usually within the first 3 months of treatment, although may develop even after many months of treatment; peripheral neuropathies (tingling, numbness in toes/fingers); vitamin B_6 depletion

Pyrazinamide (Oral)

Pyrazinamide may be bacteriostatic or bactericidal, depending on its concentration and the susceptibility of the organism. The exact mechanism of action is unknown but is partially related to the conversion of medication to pyrazinoic acid, which lowers the pH of the environment, leading to the suppression of bacterial growth.

- Used in combination with other antibiotics to treat tuberculosis; has activity only against *Mycobacterium tuberculosis*
- Disadvantages: many side effects; liver toxicity; dosage must be reduced in patients with renal dysfunction, myalgia, nausea, and vomiting

PRACTICE POINT

Some of the antituberculosis antibiotics are supplied as packages that include the multiple drugs included in a given regimen. These include Rifater (pyrazinamide, isoniazid, and rifampin) and Rifamate (isoniazid and rifampin).

Other antimycobacterial drugs include aminosalicylic acid, capreomycin, ethionamide, rifabutin, and rifapentine. These are used infrequently in cases of resistant disease or patients who do not respond to other therapies. Their pronunciations, brand names, routes of administration, and dosage forms are included in Medication Table 27-3 along with those of the antituberculosis drugs described above. Table 27-4 summarizes types of infection, likely organisms, and first- and second-line antibiotic choices.

TABLE 27-4. Empiric Treatment of Common Infections

Site of Infection	Likely Organism	First-Line Agent	Second-Line Agent
Skin infection	*Staphylococcus* sp., *Streptococcus* sp.	Antistaphylococcal penicillins (PCNs), 1st-generation cephalosporin	Vancomycin (if methicillin-resistant *Staphylococcus aureus* [MRSA] is suspected or severe allergy to PCN)
Urinary tract	*Escherichia coli*, *Proteus*, *Klebsiella*, *Enterococcus*	Nitrofurantoin, fosfomycin, sulfamethoxazole/trimethoprim	Fluoroquinolone (levofloxacin and ciprofloxacin) Beta-lactam (amoxicillin/clavulanate, ampicillin/sulbactam, cefdinir cefaclor, cefpodoxime, cephalexin)
Respiratory	Atypical, *Streptococcus pneumoniae*, *Haemophilus influenzae* (community acquired), MRSA, *Pseudomonas* (hospital-acquired)	**Community**: azithromycin, fluoroquinolone (levofloxacin, moxifloxacin), amoxicillin, doxycycline, amoxicillin/clavulanate, 3rd-generation cephalosporin (ceftriaxone, cefpodoxime, cefotaxime), ceftaroline **Hospital**: Vancomycin, linezolid, piperacillin/tazobactam, cefepime, ceftazidime, meropenem, imipenem, fluoroquinolone (levofloxacin, ciprofloxacin), aminoglycosides	
Intra-abdominal	Anaerobes, *E. coli*	**Community**: 2nd-generation cephalosporin, ertapenem, moxifloxacin, tigecycline, piperacillin-tazobactam; combination options are cefazolin, cefuroxime, ceftriaxone, cefepime, levofloxacin with metronidazole **Hospital**: Meropenem, piperacillin-tazobactam. Combination options are levofloxacin or cefepime with metronidazole	

ANTIBIOTIC SELECTION

Several factors must be considered for antibiotic selection. First, the clinician must determine the goal of therapy. In some cases, this will be to prevent an infection following surgery or another procedure. This is known as surgical prophylaxis. Not all surgeries or procedures require the patient to receive antibiotic therapy. Treatment with antibiotics is recommended for patients with valvular heart disorders or artificial joints, as well as those who are immunosuppressed, or otherwise at high risk for infection. Procedures carrying a higher risk of bacterial infections are those performed in the mouth, GI tract, and genitourinary tract. If **prophylactic** antibiotic therapy is indicated, antibiotic selection is based on the normal flora that resides in the location of the procedure. For example, a patient at risk for endocarditis (infection of the heart valves or lining of the heart) who is scheduled for a dental procedure would receive amoxicillin 2,000 mg orally 30–60 minutes prior to the procedure. Amoxicillin has activity against those organisms that inhabit the oral cavity. The goal of using amoxicillin in this patient is to prevent the bacteria that enter the bloodstream (from the dental procedure) from causing an infection in the heart. As stated earlier, not all patients need antibiotic prophylaxis; it is routinely used for those with risk factors for infectious processes. There are several guidelines available for prophylactic antibiotic dosing for various procedures.

In other cases, the goal of therapy will be to treat an infection that has already developed. Regardless of the goal, antibiotic selection is determined by the most likely organism to cause an infection based on the location of the infectious process or type of surgery performed. Empiric therapy refers to the selection of an antibiotic based on the organisms most commonly encountered at the site of the infection prior to obtaining culture results. Finally, definitive treatment refers to antibiotic selection that has activity toward a known pathogen based on the results of culture and sensitivity testing. In addition, the following factors must be considered for antibiotic selection.

- Allergies or history of adverse drug reactions to certain antibiotics (cross-sensitivity of antibiotic class)
- Patient's age (FDA approval for specified ages or known toxicity within certain age groups)
- Genetic or metabolic abnormalities (drug accumulation/toxicity)
- Renal (kidney) function (dose adjustment if renally excreted)
- Hepatic (liver) function (dose adjustment if hepatically metabolized)
- Site of infection (drug distribution/tissue penetration)
- Pregnancy/lactation (safe use in pregnancy or lactation)
- Concomitant drug therapy (drug interactions)
- Concomitant disease states (drug/disease interaction)
- Antibiogram (hospital-specific susceptibility and resistance patterns)
- Resistance patterns

COMBINATION THERAPY

Combination therapy refers to the use of more than one antibiotic to treat an infection. The concept behind combination therapy is to achieve one of the following: broaden antimicrobial coverage for a suspected organism or multiple organisms, improve efficacy though synergistic activity, and help overcome bacterial resistance. Many infections, such as pneumonia and hospital-acquired (nosocomial) infections, are treated with combination therapy for the reasons listed earlier. In addition, when patients are started on empiric therapy and the organism is yet to be identified, they may be placed on multiple antibiotics until the cultures and sensitivities are reported. At that time, the clinician may narrow down the antibiotic regimen based on the results and patient response.

CASE?

Why do you think G. F. was started on both ceftriaxone and azithromycin?

PATIENT MONITORING

Patient monitoring begins once antibiotic therapy is initiated. This includes monitoring the patient for safety, efficacy, response, and completion of therapy. Safety monitoring includes watching for both allergic reactions and adverse drug events associated with the selected antibiotic(s). As with all medications, the patient's allergies must be reviewed prior to any medication being dispensed. Antibiotic allergies range from nausea to anaphylaxis. If a patient is allergic to

penicillin, there is a small chance of cross allergy to other antibiotics in the beta-lactam class. For mild reactions to penicillins, such as nausea or a mild rash, most clinicians will confidently dispense an antibiotic in a different beta-lactam group, such as a cephalosporin. If the patient reports an incident of anaphylactic reaction to penicillin, an antibiotic from a different class altogether (ie, fluoroquinolone) should be used to ensure patient safety. Allergies are often a class effect and antibiotics from a different class should be used for severe allergies to avoid additional reactions.

In addition to allergies, patients should be monitored for adverse drug reactions. It is important for clinicians to be familiar with the common side effects of different antibiotic classes to be able to properly monitor the patient. Adverse reactions to antibiotics include the side effects one may experience while taking the medication. They can also be the result of a drug interaction that increases the chance of a known adverse reaction or unwanted effect due to altered drug absorption, distribution, and elimination.

It is important for clinicians to monitor patients for response to antibiotic therapy, ensuring efficacy of the antibiotic(s) selected to treat the infection. As mentioned earlier, cultures are obtained to help identify the pathogenic organism(s). These cultures are monitored for growth, identification, and sensitivity of the organism to specific antibiotics. Commonly, cultures may remain negative and no organism(s) grow in the culture obtained. If this is the case, the patient's laboratory and physical condition will be monitored to determine the efficacy of the selected therapy. In cases where cultures do grow, the clinician will review the identified organism(s) and compare it to the antibiotic regimen the patient is receiving to ensure proper antimicrobial coverage. If sensitivities are reported, the clinician may modify the regimen to an antibiotic that is more effective against the specific pathogen. Whenever possible, therapy is adjusted to provide coverage for only those organisms isolated or suspected. This is an important factor in reducing the possible development of resistant organisms.

Patient-specific values, such as the WBC count and temperature, are monitored closely to determine if the patient is responding to antibiotic therapy. A baseline WBC count is obtained and monitored closely thereafter. If the WBC count trends downward, it is a good indication the patient is responding to antibiotic therapy and improving. If the patient's WBC count increases or continues to increase despite antibiotic therapy, it may be a sign of treatment failure. A patient's temperature is also monitored for response to therapy. Like the WBC count, if the temperature was elevated at baseline and the patient becomes afebrile and maintains an afebrile state, it is a good indication that the patient is responding to therapy. Alternatively, if the temperature remains elevated or spikes, it may be a sign of treatment failure.

Finally, other diagnostic tests may be reordered to evaluate for continued or worsening infection. A repeat chest x-ray can be obtained for patients who are worsening on therapy to determine if the initial infection has not responded or if there may be a new infection that may warrant a change in therapy. Clinicians must also determine duration of therapy for antibiotic use based on the type and severity of infection being treated. There are several guidelines available for various infections that serve as treatment suggestions for both selection of antibiotic therapy and duration of treatment. Although these guidelines provide recommendations for duration of therapy, it is important to also evaluate the clinical response of the patient and adjust the duration based on response. In some cases, a longer duration of therapy may be warranted.

Duration of treatment is not only important to prevent treatment failure but also to help prevent antibiotic resistance. Often patients start to feel better and do not finish their course of antibiotics. This may lead to bacterial resistance as the pathogenic organism(s) may not be completely eradicated.

PRACTICE POINT

Antibiotic treatment often continues after the symptoms of an infection have disappeared. It is important that patients complete the full prescribed course of an antibiotic treatment, even if they feel cured, to prevent recurrence of the infection and the development of resistant strains.

CASE?

After 48 hours of IV antibiotics, G. F.'s breathing has improved and his WBC count has become lower. Does this mean it is time to discontinue therapy and send him home?

Prevention of infection is the best and most effective medicine. Handwashing is the most important and effective way to limit the spread of infectious organism(s). In hospital settings, many measures are in place to limit the number of hospital-acquired infections. These include the proper use of hand sanitizer, surveillance of employee handwashing,

limiting contact with patients with highly contagious organisms (known as isolation), and monitoring of patients' IV and urinary catheters, which can increase the risk of patients getting a hospital-acquired infection.

SUMMARY

Bacteria live among us and reside in our bodies as normal flora that helps us fight off other invading organisms and assist with many important functions in various organ systems. Our bodies have various natural defenses that assist normal flora in providing protection against invading organisms. When these natural defenses fail or breakdown, normal flora can become pathogenic and cause infection. Once an infection occurs, the body's immune system starts the process of attacking the pathogen and inhibiting the replication of the pathogen. Every system in the body is susceptible to infection. In most cases, patients are febrile and have elevated WBCs that are consistent with infection. The location of the infection determines the type of disease or illness that occurs. The patient usually exhibits signs and symptoms that are specific to the type of infection. The signs and symptoms of the infection can guide the clinician regarding the most likely organism causing the infection. Depending on the type of infection and patient history, empiric antibiotic therapy is initiated. If bacterial resistance is suspected, broader coverage may be initiated. Risk factors for bacterial resistance include recent prior antibiotic use, and history of prior resistant organisms. Samples from the patient are usually cultured in hopes of identifying the offending organism and also to determine the susceptibility of that organism to various antibiotics. When the cultures reveal the infecting organism(s), the initial empiric therapy can be changed, if necessary, to agents chosen to treat the specific infection.

There are several antibiotic classes that cover specific organisms and each has specific indications for use. Once antibiotic therapy is initiated, patients are monitored for safety and for efficacy. Safety includes monitoring for allergic reactions and adverse reactions or side effects. Efficacy refers to signs of improvement and eradication of the organism(s). Monitoring cultures and sensitivities allows the clinician to modify empiric therapy to target the specific organism(s) identified and use the most effective agent based on sensitivities. A patient's vital signs and laboratory values allow the clinician to determine if a patient is improving.

Over the years, bacteria have "learned" many methods to become resistant to antibiotics. Every year new antibiotics are developed to combat resistant organisms but not at the rate of bacterial resistance that is occurring. One way to slow the development of resistance is with the proper use of antibiotic regimens, with clinicians choosing an agent with the narrowest spectrum that includes the infecting organism and treating the infection for the optimal length of time.

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CHAPTER RESOURCE

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REVIEW QUESTIONS

1. What are some ways that bacteria become resistant to antibiotics?
2. What factors should be considered when selecting an antibiotic to treat an infection?
3. Describe the difference between using antibiotics for surgical prophylaxis and empiric treatment of an infection.
4. Why is it important for patients to finish their full prescribed course of antibiotics even if it extends for several days after they feel completely better?
5. Why are beta-lactamase inhibitors added to penicillins but not to fluoroquinolones?

MEDICATION TABLES

MEDICATION TABLE 27-1. The Penicillins[a]

Agent (pronunciation)	Brand Name	Dosage Form	Route
Natural			
Penicillin G benzathine (pen i SILL in) (BENZ a theen)	Bicillin L-A	Suspension	Intramuscular (IM)
Penicillin G potassium (pen i SILL in) (poe TAS ee um)	Pfizerpen-G	Solution	Injection
Penicillin G procaine (pen i SILL in) (PROE kane)	—	Suspension	IM
Penicillin V potassium (pen i SILL in) (poe TAS ee um)	—	Tablet, solution	Oral
Aminopenicillins			
Amoxicillin (a mox i SIL in)	—	Tablet, capsule, suspension	Oral
	Moxatag	Extended-release tablet	Oral
Amoxicillin/clavulanate (a mox i SIL in) (KLAV yoo la nate)	Augmentin	Tablet, suspension	Oral
Ampicillin (am pi SILL in)	—	Capsule, suspension	Oral
	—	Solution	Injection
Ampicillin/sulbactam (am pi SILL in) (sul BAK tam)	Unasyn	Solution	Injection
Penicillinase-Resistant (antistaphylococcal)			
Dicloxacillin (dye klox a SILL in)	—	Capsule	Oral
Nafcillin (naf SILL in)	Nallpen	Solution	Injection
Oxacillin (ox a SILL in)	Bactocill	Solution	Injection
Extended Spectrum			
Piperacillin/tazobactam (pi PER a sil in) (ta zoe BAK tam)	Zosyn	Solution	Injection

[a] Pronunciations have been adapted with permission from USP Dictionary of USAN and International Drug Names (USP Dictionary) © 2022.

MEDICATION TABLE 27-2. Cephalosporins and Beta-Lactam Antibiotics[a]

Agent (pronunciation)	Brand Name	Dosage Form	Route
First Generation			
Cefazolin (sef A zoe lin)	Kefzol	Premixed solution, powder for reconstitution	Intravenous (IV), intramuscular (IM)
Cefadroxil (sef a DROX il)	Duricef	Capsule, tablet (as hemihydrate and monohydrate); suspension	Oral
Cephalexin (sef a LEX in)	Keflex	Capsule, suspension, tablet	Oral
Second Generation			
Cefaclor (SEF a klor)	—	Capsule, powder for suspension, extended-release tablet	Oral
Cefuroxime (se fyoor OX eem)	Zinacef	Premixed solution; powder for reconstitution	IV
	Ceftin	Suspension, tablet	Oral
Cefprozil (sef PROE zil)	—	Suspension, tablet	Oral
Cefotetan (SEF oh tee tan)	Cefotan	Powder for reconstitution	IV, IM
Cefoxitin (se FOX i tin)	Mefoxin	Premixed solution, powder for reconstitution	IV, IM
Third Generation			
Cefdinir (SEF di ner)	Omnicef	Capsule, suspension	Oral
Cefditoren (sef DIT or in)	Spectracef	Tablet	Oral
Cefixime (sef IX eem)	Suprax	Suspension, capsule, tablet	Oral
Cefotaxime (sef oh TAKS eem)	Claforan	Premixed solution, powder for reconstitution	IV, IM
Cefpodoxime proxetil (sef pode OX eem)	—	Suspension, tablet	Oral
Ceftazidime (SEF tay zi deem)	Fortaz, Tazicef	Premixed solution, powder for reconstitution	IV, IM
Ceftibuten (sef TYE byoo ten)	Cedax	Capsule, suspension	Oral
Ceftriaxone (sef trye AX one)	Rocephin	Premixed solution, powder for reconstitution	IV, IM
Fourth Generation			
Cefepime (SEF e peem)	Maxipime	Premixed solution, powder for reconstitution	IV, IM

Continued next page

MEDICATION TABLE 27-2. Cephalosporins and Beta-Lactam Antibiotics[a] *(Continued)*

Agent (pronunciation)	Brand Name	Dosage Form	Route
Fifth Generation			
Ceftaroline fosamil (sef TAR oh line) (FOS a mil)	Teflaro	Powder for reconstitution	IV
Cepahlosporin/Beta-Lactamase Combination			
Ceftazidime/Avibactam (SEF tay zi deem) (a vi BAK tam)	Avycaz	Powder for reconstitution	IV
Ceftolozane/Tazobactam (sef TOL oh zane) (taz oh BAK tam)	Zerbaxa	Powder for reconstitution	IV
Siderophere Cephalosporin			
Cefiderocol (SEF I DER oh kol)	Fetroja	Powder for reconstitution	IV
Carbapenems			
Doripenem (dor i PEN em)	Doribax	Powder for reconstitution	IV
Ertapenem (er ta PEN em)	Invanz	Powder for reconstitution	IV, IM
Imipenem/cilastatin (i mi PEN em) (sye la STAT in)	Primaxin	Powder for reconstitution	IV
Meropenem (mer oh PEN em)	Merrem	Powder for reconstitution	IV
Carbapenem/Beta-Lactamase Combination			
Meropenem/Vaborbactam (mer oh PEN em) (va bor BAK tam)	Vabomere	Powder for reconstitution	IV
Imipenem/cilastin/relebactam (i mi PEN em) (sye la STAT in) (REL e BAK tam)	Recarbrio	Powder for reconstitution	IV
Monobactam			
Aztreonam (AS tree oh nam)	Azactam	Premixed solution, powder for reconstitution	IV, IM
	Cayston	Powder for reconstitution (nebulizer solution)	Inhalation

[a] Pronunciations have been adapted with permission from USP Dictionary of USAN and International Drug Names (USP Dictionary) © 2022.

MEDICATION TABLE 27-3. Additional Anti-infective Classes[a]

Agent (pronunciation)	Brand Name	Dosage Form	Route
Fluoroquinolones			
Ciprofloxacin (sip roe FLOX a sin)	Ceftraxal	Solution	Otic
	Otiprio	Suspension	Otic
	Ciloxan	Solution, ointment	Ophthalmic
	Cipro	Solution	IV
	Cipro	Tablet	Oral
	ProQuin XR	Extended-release tablet	Oral
Levofloxacin (lee voe FLOX a sin)	Levaquin	Premixed solution, injection solution, oral solution, oral tablet	IV, oral
	Iquix, Quixin	Solution	Ophthalmic
Moxifloxacin (mox i FLOX a sin)	Avelox IV	Premixed solution	IV
	Avelox IV	Tablet	Oral
	Avelox ABC Pack	Tablet	Oral
Ofloxacin (oh FLOX a sin)		Tablet, solution	Oral, otic
	Ocuflox	Solution	Ophthalmic
Delafloxacin (del a FLOX a sin)	Baxdela	Powder for reconstitution	IV
	Baxdela	Tablet	Oral
Aminoglycosides			
Amikacin (am i KAY sin)	—	Solution	IM, IV
Gentamicin (jen ta MYE sin)	—	Solution (concentrated and premixed in NS)	IM, IV, ophthalmic
Neomycin (nee oh MYE sin)	Neo-Fradin	Solution, tablet	Oral
Streptomycin (strep toe MYE sin)	—	Powder for reconstitution	IM, IV
Tobramycin (toe bra MYE sin)	—	Premixed solution, powder for reconstitution, injection solution	IM, IV, ophthalmic
	Tobi	Solution for nebulization	Inhalation
Plazomicin (pla zoe MYE sin)	Zemdri	Solution	IV
Macrolides			
Azithromycin (as ith roe MYE sin)	Zithromax	Powder for reconstitution, powder for oral suspension, tablet	IV, oral
	Zmax	Extended-release microspheres for suspension	Oral
	Zithromax TRI-PAK, Zithromax Z-PAK	Tablet (dose pack)	Oral
Clarithromycin (kla RITH roe mye sin)	Biaxin, Biaxin XL	Tablet, extended-release tablet, suspension	Oral

Continued next page

MEDICATION TABLE 27-3. Additional Anti-infective Classes[a] *(Continued)*

Agent (pronunciation)	Brand Name	Dosage Form	Route
Erythromycin (er ith roe MYE sin)	E.E.S., EryPed, Ery-Tab, PCE	Delayed-release capsule, granules for suspension, powder for suspension, tablet, delayed-release tablet	Oral
	Erythrocin Lactobionate-IV	Powder for reconstitution	IV
	Ilotycin	Ointment	Ophthalmic
	Erythro-RX (USP 100%)	Powder for prescription compounding	RX formulations
	Akne-mycin, Ery	Gel, pads, solution	Topical
Fidaxomicin (fye DAX oh mye sin)	Dificid	Tablet	Oral
Tetracyclines			
Doxycycline (doks i SYE kleen)	Oracea	Capsule, delayed release	Oral
	Ocudox, Oraxyl, Vibramycin	Capsule (hyclate), powder for suspension, syrup	Oral
	Adoxa, Monodox	Capsule, tablet (monohydrate)	Oral
	Doxy 100	Powder for reconstitution	IV
	Alodox, Periostat	Tablet	Oral
	Doryx	Delayed-release tablet	Oral
	Atridox	Extended-release liquid	Subgingival
Minocycline (mi noe SYE kleen)	Minocin	Capsule, powder for reconstitution	Oral, IV
	Dynacin	Tablet	Oral
	Solodyn	Extended-release tablet	Oral
	Arestin	Sustained-release microspheres (powder)	Subgingival
Tetracycline (tet ra SYE kleen)		Capsule	Oral
Tigecycline (tye ge SYE kleen)	Tygacil	Powder for reconstitution	IV
Omadacycline (oh MAD a SYE kleen)	Nuzyra	Tablet, powder for reconstitution	Oral, IV
Eravacycline (ER a va SYE kleen)	Xerava	Powder for reconstitution	IV
Glycopeptides			
Telavancin (tel a VAN sin)	Vibativ	Powder for reconstitution	IV
Vancomycin (van koe MYE sin)	Vancocin	Capsule, premixed solution, powder for reconstitution	Oral, IV
Dalbavancin (dal ba VAN sin)	Dalvance	Powder for reconstitution	IV
Oritavancin (or it a VAN sin)	Orbactiv	Powder for reconstitution	IV

Continued next page

MEDICATION TABLE 27-3. Additional Anti-infective Classes[a] *(Continued)*

Agent (pronunciation)	Brand Name	Dosage Form	Route
Sulfonamides			
Co-trimoxazole (sulfamethoxazole with trimethoprim) (coe try MOX a zole)	—	Injection solution, oral suspension	IV, oral
	Bactrim, Septra	Tablet	Oral
	Bactrim DS, Septra DS	Tablet, double strength	Oral
Sulfacetamide (sul fa SEE ta mide)	Bleph-10, Sulfamide	Solution	Ophthalmic
	Carmol Scalp Treatment, Klaron, Ovace, Rosula, Seb-Prev	Foam, cream, gel, lotion, pad, soap, suspension, shampoo, emulsion, ointment	Topical
Sulfadiazine (sul fa DYE a zeen)	—	Tablet, cream	Oral, Topical
Erythromycin and Sulfisoxazole (er ith roe MYE sin) (sul fi SOX a zole)	E.S.P.	Powder for suspension	Oral
Antimycobacterials			
Clofazamine (kloe FAZ i meen)	Lamprene	Capsule	Oral
Dapsone (DAP sone)	—	Tablet	Oral
Antituberculosis			
Aminosalicylic acid (a mee noe sal i SIL ik) (AS id)	Paser	Delayed-release granules	Oral
Capreomycin (kap ree oh MYE sin)	Capastat	Powder for reconstitution	IV, IM
Cycloserine (sye kloe SER een)	Seromycin	Capsule	Oral
Ethambutol (e THAM byoo tole)	Myambutol	Tablet	Oral
Ethionamide (e thye on A mide)	Trecator	Tablet	Oral
Isoniazid (eye soe NYE a zid)	—	Injection solution, oral solution, tablet, syrup	IM, oral
Pyrazinamide (peer a ZIN a mide)	—	Tablets	Oral
Rifabutin (RIF a byoo tin)	Mycobutin	Capsule	Oral
Rifampin (RIF am pin)	Rifadin	Capsule, powder for reconstitution	Oral, IV
Rifapentine (RIF a pen teen)	Priftin	Tablet	Oral

Continued next page

MEDICATION TABLE 27-3. Additional Anti-infective Classes[a] *(Continued)*

Agent (pronunciation)	Brand Name	Dosage Form	Route
Miscellaneous			
Chloramphenicol (klor am FEN i kol)	—	Powder for reconstitution	IV
Clindamycin (klin da MYE sin)	Cleocin HCl	Capsule	Oral
	Cleocin Pediatric	Granules for solution	Oral
	Cleocin Phosphate	Premixed solution, injection solution, vaginal cream	IV, Topical
Daptomycin (dap toe MYE sin)	Cubicin	Powder for reconstitution	IV
Linezolid (li NE zoh lid)	Zyvox	Premixed solution, powder for oral suspension, tablet	Oral, IV
Tedizolid (ted eye ZOE lid)	Sivextro	Powder for reconstitution, tablet	Oral, IV
Metronidazole (me troe NI da zole)	Flagyl	Capsule, premixed solution, tablet, cream, gel, lotion	Oral, IV, Topical
	Flagyl ER	Extended-release tablet	Oral
Rifaximin (ri FAX i men)	Xifaxan	Tablet	Oral
Quinupristin-dalfopristin (kwi NYOO pris tin) (dal FOE pris tin)	Synercid	Powder for reconstitution	IV
Colistimethate (koe lis ti METH ate)	Coly-Mycin M	Powder for reconstitution	IM, IV
Nitrofurantoin (nye troe fyoor AN toyn)	Furadantin	Capsule	Oral
	Macrobid	Capsule	Oral
	Macrodantin	Suspension	Oral
Fosfomycin (fos foe MYE sin)	Monurol	Packet, powder for reconstitution	Oral, IV
Lefamulin (le FAM ue lin)	Xenleta	Solution, tablet	Oral, IV

IM = intramuscular; IV = intravenous; NS = normal saline.

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