

Antibiotic Streamlining

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Learning Objectives

1. Discuss the benefits of antibiotic streamlining.
2. Identify the signs and symptoms associated with infection.
3. Describe the three general stages of infection and the accompanying symptoms associated with each stage.
4. Identify and interpret the basic components of a culture and susceptibility report.
5. Describe examples of situations where *in vitro* susceptibility testing does not predict therapeutic response in the clinical setting.
6. Differentiate between colonization and infection.
7. Define normal flora and list examples of normal flora in the human body.
8. Identify antibiotics used for treatment of infections caused by selected organisms.
9. Discuss patient specific factors that should be considered when dosing antimicrobials.
10. Describe the role of combination antibiotic therapy.
11. Identify antibiotics that provide duplicate therapy.

Introduction

Many antibiotics are used before an infection is confirmed. The use of antibiotics in this manner is referred to as *empiric therapy*. Empiric therapy is a “best guess” approach that takes into account the type of infection suspected and the patient’s clinical status and medication allergies. Once diagnostic test results are received, empiric therapy may not be the best choice for treating the identified infecting organism(s). In this case, antibiotics may need to be streamlined or changed to better target the infecting organism.

Antibiotic streamlining refers to the process of converting patients from one antibiotic that covers several different types of bacteria (known as *broad spectrum*) to a different antibiotic that is targeted specifically to the infecting organism (known as *narrow spectrum*). The streamlining process involves monitoring microbiology culture and susceptibility (C&S) data and using the information to evaluate the patient’s existing antibiotic therapy. If appropriate, a recommendation to streamline therapy may be made. Usually, it involves changing or reducing the number of antibiotics, but occasionally it may also mean discontinuing therapy completely. Streamlining is one of the most important ways that pharmacists can encourage appropriate antibiotic use, limit the development of bacterial resistance, and improve patient care (see Table 30-1).

Benefits associated with antibiotic streamlining include

- reducing secondary infections such as candidiasis or *Clostridium difficile* associated diarrhea (CDAD)
- decreasing morbidity and mortality¹; appropriate therapy early in the infection can improve patient outcome

TABLE 30-1. Examples of Antibiotic Streamlining

SAMPLE INTERVENTION	OUTCOME/BENEFIT
Converting from imipenem/cilastatin to cefazolin in a patient with a urinary tract infection caused by a strain of <i>Escherichia coli</i> that is susceptible to cephalosporins	Prevents the development of antimicrobial resistance and reduces the likelihood that the patient will develop secondary infections from broad spectrum antibiotic use
Discontinuing therapy for a patient who was originally started on antibiotics in the ED for respiratory distress and was subsequently diagnosed with a congestive heart failure exacerbation	Minimizes adverse drug reactions; reduces the chance that bacteria normally present in the body will develop resistance and cause a new infection
Discontinuing metronidazole when the patient is receiving piperacillin/tazobactam for a wound infection (and does not have a confirmed or suspected CDAD infection)	Avoids duplicate therapy; minimizes adverse drug reactions
Discontinuing vancomycin in a nursing home patient who is colonized with methicillin resistant <i>Staphylococcus aureus</i> (MRSA) but displays no sign of active infection	Avoids the unnecessary treatment of colonization in a patient who has no active signs of infection

- supporting the institution's infection control processes
- minimizing antimicrobial resistance
- minimizing toxicity and adverse effects
- reducing healthcare expenditures

Signs and Symptoms of Infection

The human body responds to infection by triggering a cascade of reactions to fight the invading organisms. Typically, these reactions will trigger certain physiologic responses that lead to a change in the patient's vital signs and clinical status, producing signs and symptoms of infection. By definition, signs are defined as something that can be measured or observed whereas symptoms are based on patient report. In the context of infection, measurable signs of infection include the following:

1. **Fever**—Body temperature above 38°C (100.4°F). Not all patients will present with a fever. Elderly patients may actually present with hypothermia, which is defined as a temperature less than 36°C (96.8°F).
2. **Hypotension**—Systolic blood pressure less than 90 mm Hg. Hypotension may be caused by dehydration or sepsis. Patients with less severe infection or underlying hypertension may not develop hypotension.
3. **Tachycardia**—Heart rate above 100 beats per minute. Remember that some patients may have underlying tachycardia due to cardiac sources or secondary to medication.

4. *Tachypnea*—Rapid breathing of greater than 20 breaths per minute or a PaCO₂ of less than 32 mm Hg (for patients on mechanical ventilation). Patients with infection tend to become acidotic and rapid breathing increases pH in attempt to return it to the normal range. Patients with underlying respiratory diseases (such as chronic obstructive pulmonary disease) may have a low baseline respiratory rate and their compensatory response in breathing may not result in high respiratory rate.
5. *White blood cells*—Abnormal white blood cell (WBC) count. WBC counts may begin to trend upward past the normal range (usually 4,000 to 12,000 cells/mm³). This is known as *leukocytosis*. There may also be a “left shift,” which is an increase in immature neutrophils (also known as *bands*). Remember that some medications, such as steroids, can also cause leukocytosis. Patients receiving chemotherapy may have the opposite effect and have extremely low neutrophils (a type of WBC). This is usually expressed through the term *neutropenia*. These patients are at high risk for developing an infection.
6. *Positive culture*—Isolation of the causative organism(s) from a specimen can confirm infection.

In addition to the above signs, there are additional clinical signs and symptoms for common infections found in the acute care setting (see Table 30-2). It is important to understand these signs and symptoms in any patient who has a presumed or documented infection.

Stages of Infection

Response to infection can be very individualized. However, generally, there are three stages of infection.²

1. **Stage I** is referred to as *early infection*. This typically occurs during the first few days of the illness. The patient may be clinically unstable and have leukocytosis or neutropenia. Vital signs may be abnormal and diagnostic exams suggest an infection is present. There is uncertainty as to the specific organism that is causing the infection so cultures are obtained and a preliminary result may or may not be available. Remember that the latter can be influenced by previous or current antibiotics that may have been administered.
2. In **Stage II** (usually days 4 to 6), if the correct therapy is being given, the patient should begin to stabilize. A movement of the WBC count back into the normal range may be seen. Fever may no longer be present and other vital signs may return to normal. The causative organism(s) are usually identified by this stage.
3. By **Stage III** (days 7 and on), if the appropriate therapy has been received, the patient’s vital signs and WBC count should have returned to normal, fever has resolved, and repeat diagnostic exams are normal or improving. Although antibiotic streamlining can occur anytime, the best opportunity is in Stage I or early Stage II.

Interpreting Microbiology Information

Pharmacists who are involved in the antibiotic streamlining process must understand how to interpret a culture and susceptibility report (see Figure 30-1). It is important to note that these reports may vary from institution to institution but should have similar information recorded on the final reports.

TABLE 30-2. Signs and Symptoms of Common Types of Infections

TYPE OF INFECTION (SYSTEM INVOLVED)	SIGNS	SYMPTOMS
Gastroenteritis (gastrointestinal tract)	Positive culture specifically for <i>Shigella</i> , <i>Salmonella</i> , <i>Camphylobacter</i> or <i>E. coli</i> , electrolyte disturbances	Profuse diarrhea, abdominal pain, nausea, vomiting, and/or dehydration
Meningitis (central nervous system)	Cerebrospinal fluid findings (look for glucose, total protein, WBCs, and gram stain results), positive Kernig's or Brudzinski's sign	Photophobia, headache, stiffness of the neck, rigidity, seizures, nausea, vomiting and/or blurred vision; in young children, symptoms may include irritability, altered sleep patterns, vomiting, high pitched crying, and decreased oral intake
Peritonitis (gastrointestinal)	Few or no bowel sounds, CT scan	Severe abdominal pain, rebound tenderness, nausea, vomiting, diarrhea, and/or abdominal swelling
Pneumonia (pulmonary)	Increased sputum production, decreased breath sounds, inspiratory "crackles," abnormal chest x-ray	Chest pain and productive cough. A nonproductive cough may still be present in infection; however, keep in mind that other disease states (e.g., congestive heart failure exacerbation or chronic bronchitis) or certain medications (e.g., angiotensin-converting enzyme inhibitors) may also cause cough.
Urinary Tract Infection [UTI] (urogenital)	Urinalysis results, changes in BUN and serum creatinine	Pyuria (burning) upon urination, discolored urine, and/or increased frequency of urination; patients with a more severe form of infection (<i>pyelonephritis</i>) may complain of severe lower back pain
Wound (integument/skin)	Measurement of ulcer width and/or depth, visible break in skin that is producing puss or is discolored from normal skin tone	Warmth, redness, swelling, and/or pain

FIGURE 30-1. Anatomy of a Culture and Susceptibility Report

1 Source: Sputum Ward: ER
Preliminary Gram Stain: Moderate WBCs, few epithelial cells, many gram positive cocci

01	Staphylococcus epidermis	Status	Final	2	
01	S. epidermis				
Drug	MIC	Interps	Drug	MIC	Interps
Amox/K Clav (c,d)	<=4/2	R			
Amp/Sulbactam (c,d)	<=8/4	R			
Ampicillin	9	BLAC			
Azithromycin	>4	R			
Cefazolin	<=8	R			
Cefepime	16	R			
Cefotaxime (c,e)	<=8	R			8
Cefotaxime (c,e)	>32	R			
Cephalothin	<=8	R			
Chloramphenicol	<=8	S			
Ciprofloxacin	>2	R			
Clindamycin	>2	R			
Erythromycin	>4	R			
Gentamicin	<=4	S			3 4
Imipenem (c)	<=4	R			
Levofloxacin	>4	R			
Linezolid	<=2	S			
Nitrofurantoin	<=32				
Norfloxacin	>8				
Ofloxacin	>4	R			5
Oxacillin	>2	R			
Penicillin	8	BLAC			6
Rifampin	<=1	S			
Synercid	<=1	S			
Tetracycline	<=4	S			
Trimeth/Sulfa	<=2/38	S			
Vancomycin	<=2	S			7

Culture and Susceptibility Report Key

1. This denotes the original gram stain information. Many times, semiquantitative information will be provided about the quality of the specimen before the final pathogen is known. In sputum cultures, there may be comments such as “heavy growth, many WBCs, many red blood cells (RBCs), many or few epithelial cells, etc.” A quantitative bacterial count (e.g., >100,000 cfu/mL) is typically provided when it is a urine specimen but may also be provided for other specimens on request.
2. This indicates that this is the final report. Sometimes, if the culture and susceptibility has not been confirmed, it will say “pending.”
3. This number represents the minimum inhibitory concentration (MIC) for the drug listed. In this case, the MIC is less than or equal to 4 mcg/mL which means susceptible based on national laboratory guidelines. The susceptibility definition varies based on the organism and the antibiotic being tested.

4. This is where the susceptibility results are reported. In this case, S = Susceptible, I = Intermediate, and R = Resistant.
5. Since this strain of *S. epidermidis* is oxacillin resistant, it is classified as MRSE or Methicillin resistant *S. epidermidis*.
6. BLAC—This indicates that this strain of *S. epidermidis* produces beta lactamase.
7. When two MICs are listed, this means that the MIC is different for each drug in the combination product. In this case, the MIC for trimethoprim is less than or equal to 2 mcg/mL, whereas the MIC for sulfamethoxazole is less than or equal to 38 mcg/mL.
8. These letters refer to supplemental comments on the report (not shown).

Limitations of Microbiological Testing

Testing a bacteria, virus, or fungi for susceptibility to an anti-infective in a nonphysiologic environment, such as in a test tube, is known as *in vitro* testing. One limitation of *in vitro* testing is that it only represents the susceptibility of the pathogen to a given anti-infective at a single point in time and does not take into account the different conditions that exist within the body (known as *in vivo*). When infection is present, other factors may influence the ability of an anti-infective agent to eradicate a pathogen, such as the patient's immune status (e.g., neutropenic versus non-neutropenic) or the behavior of the microbe in the patient. When evaluating a positive culture in the context of the reported bacterial susceptibilities, keep in mind that there are some exceptions in which an *in vitro* test result does not necessarily predict a therapeutic response *in vivo* and, therefore, the respective antibiotic should not be used. Some examples include the following:

- *An extended spectrum beta lactamase (ESBL) producing organism (usually E. coli or Klebsiella spp.) that is susceptible to cefoxitin*—Cefoxitin is stable to breakdown by ESBLs *in vitro*. However, there have been clinical failures reported and it should not be used for treatment. Other antibiotics that should not be used to treat a documented ESBL infection include any cephalosporin, including cefepime, extended spectrum penicillins, and aztreonam. In some cases, fluoroquinolones may have *in vitro* activity. However clinical failure can also occur with these agents. The primary treatment of choice for an infection caused by an ESBL producing organism is typically a carbapenem.
- *A MRSA susceptible to sulfamethoxazole/trimethoprim*—It is very common for a MRSA strain to be listed as susceptible to sulfamethoxazole/trimethoprim on the C&S report. The site of infection should be considered in this case, along with whether or not the strain is community acquired (typically resistant to beta lactams only) or hospital acquired (typically resistant to multiple classes of antibiotics). For example, this antibiotic may be appropriate to treat a community acquired MRSA skin and soft tissue infection but would not be the ideal treatment choice for an ICU patient with MRSA bacteremia.
- *An Enterococcus spp. that is susceptible to cephalosporins*—Cephalosporins may appear to be effective against these organisms based on laboratory results, but clinically they are not effective in treating enterococcal infections. The combination of trimethoprim/sulfamethoxazole also may appear effective against these organisms in the laboratory but will not be effective in a patient. In general, susceptibility testing for these organisms can be misleading. Infections due to enterococcus are commonly treated with ampicillin or vancomycin, often combined with gentamicin.

General Guidelines for Microbiological Testing

Knowing how the microbiology laboratory does its testing can help when interpreting C&S results. For each culture, there is usually a preliminary report, as well as a final report that is posted in the patient's chart. A culture with no growth is considered to be a *negative culture*. A culture with growth identified is called a *positive culture*.

Antimicrobial susceptibilities are not reported for every drug and are based on national laboratory standards and expert rule systems that are built into the automated testing systems. Only appropriate drug-microorganism combinations are reported. For example, ciprofloxacin susceptibility will not be reported for a positive *Streptococcus pneumoniae* culture. Ciprofloxacin is never the drug of choice to treat *S. pneumoniae* because of the ease in which resistance can develop.

Individual hospital testing practices may vary, but generally susceptibility testing is performed on all routine bacterial cultures that are deemed to be positive. However, in most hospitals susceptibility testing is not routinely performed on the following:

1. Anaerobes
2. Yeast/molds
3. *Lactobacillus spp.*
4. Diptheroid/*Corynebacteria spp.*
5. *Neisseria spp.* and *Moraxella spp.*
6. Some species of viridans streptococci
7. Organisms that are rare, unusual, or do not have standardized methods of testing
8. Cultures with growth that may be reported with normal flora statements:
 - Normal respiratory flora
 - Normal skin flora
 - Normal genital/vaginal flora
 - Normal oral flora
 - Normal upper respiratory flora
 - No *Salmonella*, *Shigella*, or *Campylobacter* isolated
9. Cultures with growth that may be reported as contaminated or insignificant:
 - Polymicrobial growth—skin flora
 - Polymicrobial growth—fecal flora
 - Random urine cultures with less than 10,000 cfu/mL

Positive cultures are typically reported to the facility's infection control program for some significant pathogens including the following:

1. MRSA (methicillin [oxacillin] resistant *Staphylococcus aureus*)
2. VRE (vancomycin resistant enterococcus)
3. ESBL (extended beta-lactamase producer)
4. Positive smears for acid-fast bacilli (AFB)
5. Positive *Clostridium difficile* toxin A/B tests
6. Positive respiratory syncytial virus (RSV) test
7. Positive influenza A/B test

Colonization versus Infection

Having an awareness of the difference between colonization and infection is very important in determining whether or not therapy is warranted. The human body can have a symbiotic relationship with certain types of bacteria and fungi. In the absence of clinical symptoms, this relationship is referred to as *colonization*. When a host's immune system is compromised, or is introduced to variant strains or foreign pathogens, then infection occurs. Questions should be asked to determine whether or not treatment is necessary (see Table 30-3).

TABLE 30-3. To Treat or Not to Treat?

QUESTION	ANSWER
Is the positive culture from a nonsterile site?	A positive culture from a nonsterile site may or may not be indicative of an infection and needs to be reviewed in the context of the patient's clinical presentation. Pulmonary secretions and sputum cultures represent the biggest challenges in treating a patient for infection. Sputum is not considered to be a sterile body fluid. Cultures that are obtained from the patient coughing up sputum or tracheal secretions from the upper part of an endotracheal tube (ET) may be contaminated with oral flora and are typically not optimal for use in diagnosing infection. These cultures may falsely grow bacteria and fungus that are not the true infecting pathogens. Sputum samples obtained from a bronchoscopy (deep into the lungs) are more accurate in terms of diagnosis.
Is the positive culture from a normally sterile site?	A sterile site is an area of the body where bacterial or fungal organisms are not likely to be found. Examples include blood, spinal fluid, and internal organs. A positive culture from these sites may be highly suggestive of an infection, unless contamination of the specimen is suspected. A positive culture should always be evaluated in conjunction with clinical symptoms and other diagnostic results.
What risk factors are present that predispose the patient to developing an infection?	Infections can occur when the host's immune system or natural defenses are compromised. Burn patients are at high risk for developing systemic candidiasis because their damaged skin serves as portal of entry for bacteria and fungus into the blood. Neutropenic cancer patients and HIV positive patients are also at high risk for infections, due to their compromised immune systems. In these patients, bacteria or fungus may not grow from all cultures and therefore, the majority of therapy will be empiric.
Is the pathogen in question normally present in healthy individuals?	A pathogen that is typically present in the human body may represent the patient's normal flora. The next section discusses normal flora and reviews those organisms that typically reside in the normal human body.
Does the patient have other signs and symptoms of infection present?	Refer to the previous section on clinical signs and symptoms of infection for more information.

TABLE 30-4. Normal Flora in the Human Body

BODY SITE	NORMAL FLORA
Skin	Diphtheroids (e.g., <i>Corynebacterium</i> spp.), <i>Propionobacteria</i> , Staphylococci (especially <i>Staphylococcus epidermidis</i>)
Gastrointestinal tract	<i>Bacteroides</i> spp., <i>Clostridium</i> spp. (some species), Diphtheroids, Enterobacteriaceae (e.g., <i>E.coli</i> , <i>Klebsiella</i> spp.), Enterococcus, <i>Candida</i> spp. (usually <i>C. albicans</i>)
Upper respiratory tract	<i>Haemophilus</i> spp., <i>Neisseria</i> spp., <i>Viridans streptococci</i> , <i>Streptococcus pneumoniae</i> , Staphylococci, Diphtheroids
Genital tract	<i>Corynebacterium</i> spp., Enterobacteriaceae, <i>Lactobacillus</i> spp., <i>Mycoplasma</i> spp., Staphylococci, Streptococci, <i>Candida</i> spp. (usually <i>C. albicans</i>)

Normal Flora

In a healthy human, the internal tissues (e.g., blood, brain, muscle, bone, and other internal organs) are normally free of microorganisms. On the other hand, the surface tissues (e.g., skin and mucous membranes) are constantly in contact with environmental organisms and become readily colonized by certain microbial species. The mixture of organisms regularly found at any anatomical site is referred to as the *normal flora*.

The normal flora of humans is complex and consists of more than 200 species of bacteria and yeasts. The makeup of the normal flora depends upon various factors, including genetics, age, sex, stress, nutrition and diet of the individual. Table 30-4 lists examples of some of the bacterial species that occur as normal flora of humans.

Common Bacteria, Their Infection Sites, and Treatment

Understanding the different bacteria that can cause infection and the medications that treat infections with these organisms is imperative in antibiotic streamlining. One factor that increases the complexity of this process is that there are a number of antibiotics that can be used to treat these organisms (see Table 30-5).

Patient Specific Factors

It is important to be aware of patient specific, or “host” factors that can either change the way a patient responds to a medication or can influence the medication selection. After a patient has been identified for antibiotic streamlining, the following patient specific factors should be taken into consideration before an alternative therapy is recommended. These factors include the following:

1. Age—Neonates have different metabolic capabilities and may not be able to tolerate certain antimicrobials, such as sulfonamides and ceftriaxone. Fluoroquinolones have also historically been avoided in pediatrics due to concerns about skeletal muscle toxicity identified in early animal studies.

TABLE 30-5. Common Bacteria and Antibiotic Treatment Options

BACTERIA	SELECTED ANTIBIOTICS WITH ACTIVITY AGAINST THIS BACTERIA ^{a,b}	TYPES OF INFECTIONS CAUSED BY THIS BACTERIA
GRAM POSITIVE		
<i>Enterococcus spp.</i>	<i>Vancomycin susceptible</i> — Amoxicillin, ^c ampicillin, ^c nitrofurantoin (urine isolates only), penicillin, or vancomycin. Gentamicin or streptomycin have activity in combination with a beta lactam. <i>VRE</i> —Daptomycin or linezolid	Peritonitis, pelvic infections, UTI, pyelonephritis, endocarditis, bacteremia, complicated skin and soft-tissue infections (CSSI)
<i>Staphylococcus aureus</i>	<i>Methicillin susceptible</i> — Amoxicillin, ^c ampicillin, ^c cefazolin, clindamycin, dicloxacillin, doxycycline, minocycline, nafcillin, oxacillin, or trimethoprim/sulfamethoxazole. Rifampin or gentamicin may be used in combination with a second drug. <i>MRSA</i> —Daptomycin, linezolid, tigecycline, or vancomycin	Endocarditis, bacteremia, meningitis, pneumonia, CSSI, osteomyelitis
<i>Staphylococcus epidermidis</i> (in most cases, this will be methicillin resistant)	<i>Methicillin susceptible</i> — Dicloxacillin, nafcillin, oxacillin, or ampicillin ^c <i>MRSE</i> —Daptomycin, linezolid, or vancomycin	Endocarditis, bacteremia, CSSI
<i>Streptococcus pneumoniae</i> (<i>penicillin susceptible</i>)	Amoxicillin, ^c azithromycin, ceftriaxone, cefotaxime, clarithromycin, doxycycline, gemifloxacin, levofloxacin, moxifloxacin, penicillin, or sulfamethoxazole/trimethoprim	Meningitis, otitis media, pharyngitis, pneumonia, sinusitis
<i>Streptococcus pyogenes</i>	Amoxicillin, ^c ampicillin, ^c or penicillin	Pharyngitis, SSTI, necrotizing fasciitis (rare)
<i>Listeria monocytogenes</i> (Gram-positive rod)	Ampicillin (+/- gentamicin) or sulfamethoxazole/trimethoprim	Meningitis (pediatric and elderly population)
GRAM NEGATIVE		
<i>Acinetobacter baumannii</i>	Varies; refer to individual C&S or hospital susceptibility patterns	Bacteremia, pneumonia, CSSI (<i>Note: Usually hospital acquired; implicated in ICU outbreaks.</i>)

TABLE 30-5. Common Bacteria and Antibiotic Treatment Options (Continued)

BACTERIA	SELECTED ANTIBIOTICS WITH ACTIVITY AGAINST THIS BACTERIA ^{a,b}	TYPES OF INFECTIONS CAUSED BY THIS BACTERIA
<i>Citrobacter freundii</i> (part of the genera Enterobacteriaceae)	Aztreonam, ciprofloxacin, ertapenem, gentamicin, imipenem/cilastatin, levofloxacin, meropenem, piperacillin, ^c ticarcillin, ^c or tobramycin	Bacteremia, pneumonia, intra-abdominal infections, CSSI, UTI (<i>Note: Usually hospital acquired.</i>)
<i>Enterobacter cloacae</i> (part of the genera Enterobacteriaceae)	Aztreonam, ciprofloxacin, ertapenem, gentamicin, imipenem/cilastatin, levofloxacin, meropenem, piperacillin, ^c ticarcillin, ^c or tobramycin	Bacteremia, pneumonia, CSSI, UTI (<i>Note: Usually hospital acquired.</i>)
<i>Escherichia coli</i> (part of the genera Enterobacteriaceae)	Amoxicillin, ^c ampicillin, ^c aztreonam, cefazolin, cefotaxime, ceftriaxone, ciprofloxacin, gentamicin, levofloxacin, moxifloxacin (nonurinary infections), piperacillin, ^c sulfamethoxazole/trimethoprim, ticarcillin, ^c or tobramycin	Gastroenteritis, intra-abdominal infections, UTI, genitourinary, bacteremia, CSSI
<i>Haemophilus influenzae</i>	Amoxicillin, ^c azithromycin, cefotaxime, ceftriaxone, clarithromycin, doxycycline, gemifloxacin, levofloxacin, moxifloxacin, or sulfamethoxazole/trimethoprim	Meningitis, pharyngitis, pneumonia, sinusitis
<i>Klebsiella pneumoniae</i> (part of the genera Enterobacteriaceae)	Amoxicillin, ^c azithromycin, cefotaxime, ceftriaxone, clarithromycin, gemifloxacin, levofloxacin, moxifloxacin, or sulfamethoxazole/trimethoprim	Pneumonia, UTI, CSSI, bacteremia
<i>Legionella pneumophila</i>	Azithromycin, clarithromycin, gemifloxacin, levofloxacin, or moxifloxacin	Pneumonia (also called <i>Legionnaires' disease</i>)
<i>Moraxella catarrhalis</i>	Amoxicillin/clavulanate, azithromycin, cefotaxime, ceftriaxone, clarithromycin, gemifloxacin, levofloxacin, moxifloxacin, or sulfamethoxazole/trimethoprim	Pharyngitis, pneumonia (community acquired), sinusitis

TABLE 30-5. Common Bacteria and Antibiotic Treatment Options (Continued)

BACTERIA	SELECTED ANTIBIOTICS WITH ACTIVITY AGAINST THIS BACTERIA ^{a,b}	TYPES OF INFECTIONS CAUSED BY THIS BACTERIA
<i>Neisseria gonorrhoeae</i>	Cefotaxime, cefixime, cefpodoxime, ceftriaxone, ciprofloxacin, or levofloxacin	Pelvic inflammatory disease, urethritis, oral and anal infections
<i>Neisseria meningitidis</i>	Cefotaxime, ceftriaxone, cefuroxime, or penicillin	Meningitis
<i>Proteus mirabilis</i> (part of the genera Enterobacteriaceae)	Amoxicillin, ^c ampicillin, ^c aztreonam, ceftazidime, cefotaxime, ceftriaxone, ciprofloxacin, gentamicin, levofloxacin, moxifloxacin (nonurinary infections), piperacillin, ^c sulfamethoxazole/trimethoprim, ticarcillin, ^c or tobramycin	Intra-abdominal, pneumonia, UTI, CSSI, bacteremia, prosthetic device infections
<i>Pseudomonas aeruginosa</i>	Amikacin, aztreonam, ceftazidime, ciprofloxacin, imipenem/cilastatin, levofloxacin, meropenem, piperacillin, ^c or tobramycin (Note: Combination therapy required for nonurinary infections.)	CSSI, osteomyelitis, bacteremia, pneumonia, UTI, prostatitis, intra-abdominal (Note: Usually hospital acquired.)
<i>Serratia marcescens</i> (part of the genera Enterobacteriaceae)	Aztreonam, ceftazidime, cefotaxime, ceftriaxone, ciprofloxacin, ertapenem, gentamicin, imipenem/cilastatin, levofloxacin, or tobramycin	Pneumonia, UTI, catheter related infections, bacteremia, CSSI
MISCELLANEOUS		
<i>Chlamydia pneumoniae</i>	Azithromycin, clarithromycin, doxycycline, gemifloxacin, levofloxacin, or moxifloxacin	Pneumonia, sinusitis, otitis media
<i>Mycoplasma pneumoniae</i>	Azithromycin, clarithromycin, doxycycline, gemifloxacin, levofloxacin or moxifloxacin	Pneumonia (also called walking pneumonia)
ANAEROBES^d		
<i>Bacteroides fragilis</i>	Metronidazole	Intra-abdominal, pelvic, CSSI
<i>Clostridium difficile</i>	Metronidazole or vancomycin	Pseudomembranous colitis
<i>Clostridium perfringens</i>	Penicillin G or clindamycin	Intra-abdominal, necrotizing skin infections

^aGilbert DN, Moellering RC, Eliopoulos GM, et al., eds. *The Sanford Guide to Antimicrobial Therapy*. 37th ed. Hyde Park, VT: Antimicrobial Therapy Inc; 2007.

^bBased on *in vitro* or *in vivo* testing. Assumes organism is pansensitive unless indicated. Listing of antibiotics is not all inclusive and order does not necessarily reflect treatment preference.

^cMay be used in combination with an enzyme inhibitor (e.g., clavulanate or tazobactam) depending on the organism.

^dAnaerobic bacteria can also be classified as gram negative or gram positive.

2. *Medication allergies*—Penicillin and sulfonamide allergies are the most common.
3. *Hepatic function*—Patients with mild to severe hepatic dysfunction may not be able to metabolize medications appropriately. Doses of some antibiotics must be reduced in liver disease or avoided in severe impairment (particularly some of the antifungals).
4. *Pregnancy*—All medications should be evaluated for teratogenicity.
5. *Renal function*—Doses of medications should be adjusted based on patient’s creatinine clearance. In some cases, the medications may need to be avoided all together.
6. *Drug interactions*—Medication interactions should be reviewed before suggesting an alternative therapy.
7. *Site of action*—Certain types of infections require high concentrations of antibiotics in order to reach the site of infection. For example, significantly higher doses of antibiotics are used to treat meningitis because they have to be able to cross the blood brain barrier.

Combination Antibiotic Therapy

Combining two or more antibiotics may be necessary when treating certain types of infections. When combined, some antibiotics work synergistically to treat certain types of infections. Others are combined because a broader spectrum of coverage is needed in polymicrobial infections. For example, gentamicin is typically added to a beta lactam antibiotic for the treatment of gram positive endocarditis. Rifampin may be added to oxacillin or vancomycin to reduce the number of *S. aureus* colonies. Infections caused by *Pseudomonas aeruginosa* are generally treated with a two-drug combination that includes an antipseudomonal beta lactam (e.g., piperacillin/tazobactam) plus either an aminoglycoside, ciprofloxacin, or levofloxacin.

Duplicate Therapy

There are combinations of drugs that *may* represent unnecessary overlap in antimicrobial spectra and may require an intervention (see Table 30-6). Keep in mind that this is not a “hard and fast” rule in all situations so if you are unsure, it is best to check with another clinician prior to making an intervention. For example, piperacillin/tazobactam with intravenous metronidazole to treat a CSSI would generally be duplicate therapy. However, piperacillin/tazobactam together with oral metronidazole for *C. difficile* infection would be appropriate.

TABLE 30-6. Duplicate Therapy

ANTIBIOTIC	PLUS SECOND ANTIBIOTIC	GENERAL CATEGORY OF DUPLICATE COVERAGE
Metronidazole	Amoxicillin/clavulanate Ampicillin/sulbactam Cefoxitin Clindamycin Piperacillin/tazobactam	Anaerobic
Clindamycin	Amoxicillin/clavulanate Ampicillin/sulbactam Cefoxitin	Gram positive and anaerobes
Clindamycin	Cefazolin Oxacillin Penicillin Amoxicillin Ampicillin Vancomycin	Gram positive (but not anaerobes)
Cefazolin	Ampicillin/sulbactam Clindamycin Dicloxacillin Oxacillin Penicillin Piperacillin/tazobactam Vancomycin Linezolid Other cephalosporins	Gram positive, some gram negative (ampicillin/sulbactam, piperacillin/tazobactam, other cephalosporins)
Levofloxacin	Amoxicillin/clavulanate Ceftazidime Cefepime Ceftriaxone Ciprofloxacin Ertapenem Imipenem/cilastatin Moxifloxacin Piperacillin/tazobactam	Gram negative, gram positive
Oxacillin/Nafcillin	Cefazolin Clindamycin Dicloxacillin Linezolid Vancomycin	Gram positive

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Antibiotic Streamlining

Name: _____ **Date:** _____

KNOWLEDGE AND SKILLS	YES	NO
Demonstrates knowledge of the benefits associated with antibiotic streamlining.		
Demonstrates knowledge of the most common signs associated with an infection.		
Demonstrates knowledge of the three stages of infection.		
Identifies and interprets the primary components of the culture and susceptibility report.		
Demonstrates knowledge of organisms that generally do not undergo additional susceptibility testing after identification.		
Explains the difference between colonization and infection.		
Defines normal flora and lists examples of organisms that make up the normal flora at specific body sites.		
Identifies antibiotics that can be used to treat bacterial pathogens commonly found in the healthcare setting.		
Demonstrates knowledge of patient specific factors that can influence antimicrobial medication selection. Considers these factors when making recommendations for antibiotic streamlining.		
Defines combination antibiotic therapy and describes its role in the treatment of infections.		
Monitors patients receiving antibiotic therapy for duplicate therapy; avoidance of drug-drug, drug-food, and drug-disease interactions; adverse drug reactions; and other medication-related problems.		
Recommends appropriate antibiotic streamlining regimens for patients receiving inappropriate or broad-spectrum antibiotics.		
Makes recommendations to manage adverse effects, and other medication-related problems and ensure positive therapeutic outcomes in patients receiving antibiotic therapy.		

Competence certified by: _____ **Date:** _____

Antibiotic Streamlining

Name: _____ Date: _____

Use the following case report to select the best answers to questions 1 through 6.

B.W. is a 37-year-old female who presented to the ED with a 2-day history of persistent fevers, chills, and difficulty breathing. She states she has had frequent bouts of coughing, which produce greenish-yellow sputum. She has not received any antibiotics in the past year. Her past medical history includes asthma, which is well-controlled with inhaled corticosteroids and bronchodilators. Up until this episode, her only other hospitalization was for the birth of her only child 2 years ago. Her social history reveals that she is a nonsmoker and only drinks alcohol occasionally. She does not have any allergies.

Her temperature on arrival was 101.7°F, blood pressure was 117/82 mm Hg, heart rate was 104 beats/minute, and her respiratory rate was 22 breaths/minute. Her oxygen saturation is approximately 91%. A chest x-ray is obtained, and the results show bilateral infiltrates. The patient's white blood cell (WBC) count was 19,800 cells/mm³ (normal 4,000–11,000 cells/mm³), and a left shift was noted. All other labs were normal. Blood and sputum cultures were obtained and the results are pending.

She is started on ceftriaxone 1 g IV daily and azithromycin 500 mg IV daily and is admitted to the hospital's general medical floor for further observation.

- ___ 1. Which of the following would be considered a *sign* of infection?
- a. Frequent chills
 - b. Temperature of 101.7°F
 - c. Difficulty breathing
 - d. Cough
- ___ 2. Which stage of infection is the patient in?
- a. Stage I
 - b. Stage II
 - c. Stage III
 - d. Stage IV

The next day the results of the blood and sputum cultures return. The blood culture report states that there was no growth in either sample. The sputum results show the following:

Source: Sputum**Ward:** ER**Preliminary Gram Stain:** Moderate WBCs, few epithelial cells, many gram-positive cocci, few yeast**Final report:** *Streptococcus pneumoniae**(Selected susceptibility results)*

<i>Drug Name</i>	<i>MIC (mcg/mL)</i>	<i>Interpretation</i>
Amoxicillin	≤2	S
Azithromycin	1	I
Cefotaxime	≤1	S
Ceftriaxone	≤1	S
Penicillin	≥2	R

- ___ 3. What do the numbers listed on this report reflect?
- Minimum invasive concentration
 - Maximum inhibitory concentration
 - Marginal inhibitory concentration
 - Minimum inhibitory concentration
- ___ 4. Which of the following statements is TRUE?
- Streptococcus pneumoniae* is the likely organism causing B.W.'s infection.
 - Azithromycin is the best choice of antibiotic to treat B.W.'s infection.
 - Aztreonam has activity against this isolate of *Streptococcus pneumoniae*.
 - Penicillin has activity against this isolate of *Streptococcus pneumoniae*.
- ___ 5. How can you streamline B.W.'s regimen based on this culture and susceptibility report?
- Add clindamycin.
 - Stop all antibiotics.
 - Discontinue azithromycin, but continue ceftriaxone.
 - Discontinue ceftriaxone, and continue azithromycin.
- ___ 6. Why did the lab refrain from conducting susceptibility testing on the yeast species that was reported on the gram stain?
- It reflects colonization and not infection.
 - It was an oversight by the laboratory.
 - Yeast speciation cannot be conducted on sputum cultures.
 - Yeast speciation cannot be conducted when a bacteria is present.

Use the following case report to select the best answers to questions 7 through 12.

S.B. is a 70-year-old female admitted from home who presented with a 3-day history of worsening abdominal pain accompanied by nausea, diarrhea, and high fevers. Her symptoms were sudden in onset and she noted that they began approximately 6 hours after eating at a local restaurant. Her lower abdomen is distended and there is left lower quadrant abdominal tenderness. Her past medical history includes heart failure, gout, diabetes (Type II), chronic atrial fibrillation, and osteoporosis. Bowel sounds are present and her stool is guaiac-negative. Her temperature is 102.3°F, heart rate (HR) is 106 beats/minute, and her blood pressure is 96/63 mm Hg. A CBC with differential shows a WBC count of 23,000 cells/mm³ with 54% segmented neutrophils (normal 36% to 66%) and 17% bands (normal 0% to 8%). The physician starts S.B. on piperacillin/tazobactam and metronidazole after blood and stool cultures are obtained. The patient has no medication allergies. Later that day, the lab calls and states that there are gram-negative rods growing from her blood cultures and her *C. difficile* toxin assay is negative.

- ___ 7. What signs and symptoms are present to suggest that there is an infection present?
- Normal HR, elevated WBC count, normal temperature, Type II diabetes
 - Elevated HR, no left shift, elevated temperature, guaiac-negative stool
 - Elevated WBC count, preliminary blood cultures are positive, diarrhea, and worsening abdominal pain
 - Normal WBC count, a left shift, hypertension, abdominal pain
- ___ 8. Which of the following organisms is most likely to be a cause of S.B.'s gastroenteritis?
- Moraxella catarrhalis*
 - Methicillin resistant *Staphylococcus epidermidis*
 - Acinetobacter baumannii*
 - Escherichia coli*
- ___ 9. Piperacillin/tazobactam and metronidazole both have activity against what type of organisms?
- Gram negative
 - Anaerobic
 - Aerobic
 - Gram positive
- ___ 10. The next day the lab reports that there are gram-negative rods and *Enterococcus spp.* growing from the stool culture. Which of the following is true in regards to the presence of the enterococcus?
- It is likely the infecting organism causing S.B.'s illness.
 - It represents normal flora.
 - It represents a secondary infection.
 - None of the above.
- ___ 11. S.B.'s final blood culture results are reported and the gram-negative rod (identified in question #8) is reported to be susceptible to all antibiotics. What do you recommend?
- Continue current therapy.
 - Replace clindamycin with metronidazole for better anaerobic coverage.

- c. Discontinue metronidazole and streamline piperacillin/tazobactam to a more narrow spectrum antibiotic that has activity specifically against the infecting organism.
- d. Discontinue both antibiotics and initiate daptomycin to provide the needed broad spectrum coverage.

- ___ 12. What is the benefit of streamlining S.B.'s antibiotic regimen?
- a. Increases morbidity and mortality
 - b. Decreases morbidity and mortality
 - c. Increases the likelihood that a secondary infection may develop
 - d. Increases healthcare expenditures

Use the following case report to select the best answers to questions 13 through 17.

R.C. is a 62-year-old homeless man who presents to the ED with a large infected ulcer on his lower right leg. He does not recall how long the ulcer has been present but reports that it has become progressively painful over the last 2 days and he now rates the pain as 9 out of 10. His past medical history includes uncontrolled Type II diabetes, chronic renal insufficiency, and Hepatitis C. He is currently taking no medications. He drinks approximately two beers per day and smokes occasionally. He has no known medication allergies.

His temperature on arrival was 100.9°F, blood pressure was 117/65 mm Hg, heart rate was 99 beats/minute, and his respiratory rate was 16 breaths/minute. Other pertinent labs include a WBC count of 18,800 cells/mm³ and a serum creatinine of 2.8 mg/dL. The patient weighs 75 kg and is approximately 5 ft. 11 in. tall. He is started on ampicillin/sulbactam 3 g IV q 6 hr and gentamicin 80 mg IV q 8 hr. Upon physical examination, it is determined that the wound is invasive enough that R.C. will have to be admitted and undergo surgical debridement the following day. During surgery, a deep tissue specimen is obtained and sent to the lab for culture and susceptibility testing.

- ___ 13. Which of the following statements is true regarding the general spectrum of activity of ampicillin/sulbactam?
- a. It is a broad spectrum antibiotic that has coverage against multiple bacteria, including anaerobes.
 - b. It is a narrow spectrum agent and only has activity against gram-positive organisms.
 - c. It has activity against gram-positive and gram-negative bacteria but not anaerobes.
 - d. It has synergistic activity against *P. aeruginosa* when combined with gentamicin.
- ___ 14. Which of the following is true regarding this patient's antibiotics based on the patient-specific factors presented in this case?
- a. The dose should be reduced because of the patient's age.
 - b. The dose should be reduced because the patient has Hepatitis C.
 - c. The dose should be reduced due to his renal insufficiency.
 - d. Ampicillin/sulbactam should be discontinued due to medication allergies.

Following debridement, the cultures return and show the following:

Source: Wound **Ward:** 6W
Preliminary Gram Stain: Moderate WBCs, few epithelial cells, many gram positive cocci

Final report: *Staphylococcus aureus*
Staphylococcus epidermidis

(Selected susceptibility results)

<u>Drug Name</u>	<u><i>S. aureus</i></u>	<u><i>S. epidermidis</i></u>
Ampicillin/sulbactam	Resistant	Resistant
Azithromycin	Resistant	Resistant
Ceftriaxone	Resistant	Resistant
Levofloxacin	Intermediate	Resistant
Oxacillin	Resistant	Resistant
Rifampin	Susceptible	Susceptible
Trimethoprim/sulfa	Susceptible	Susceptible
Vancomycin	Susceptible	Susceptible

- ___ 15. What would be a reasonable alternative to therapy based on the patient's culture results?
- Discontinue gentamicin.
 - Discontinue both antibiotics and initiate rifampin.
 - Discontinue all antibiotics as this result reflects normal flora.
 - Discontinue both antibiotics and initiate vancomycin.
- ___ 16. B.B. is a 83-year-old male who presents to the ED with a chief complaint of dyspnea. He has a complex past medical history that includes Type II diabetes, atrial fibrillation, congestive heart failure, chronic obstructive pulmonary disease, and a stroke 2 years ago. His vital signs are noted to be stable with the exception of a heart rate of 118 beats/minute. He is admitted and is placed on several medications including cefepime 2 g IV q 12 hr. Two days later, it is determined that his dyspnea was the result of a CHF exacerbation. Blood and sputum cultures that were obtained showed no growth and the attending physician states in the progress notes that an infection has been ruled out. How can B.B.'s regimen be streamlined?
- Discontinue antibiotics.
 - Reduce the dose of cefepime to 1 g q 12 hr.
 - Change the cefepime to ceftriaxone 1 gram daily
 - Antibiotics should be continued until the patient is discharged from the hospital

- ___ 17. R.N. is a 63-year-old female who has positive cultures for an ESBL producing strain of *K. pneumoniae* from multiple sites. What would be the preferred treatment for her infection assuming she has no medication allergies and a creatinine clearance of 72 mL/min?
- a. Cefoxitin
 - b. Meropenem
 - c. Ticarcillin/clavulanate
 - d. Cefepime

Antibiotic Streamlining

Answer Key

1. b
2. a
3. d
4. a
5. c
6. a
7. c
8. d
9. b
10. b
11. c
12. b
13. a
14. c
15. d
16. a
17. b

