Geisinger

Make it the best antibiotic:

The Geisinger Antimicrobial Stewardship Program Handbook

Editor-in-chief:
Stanley I. Martin, MD

Edited and authored by:

Alison Brodginski, DO

Manish Doshi, MD

Stanley I. Martin, MD

Raquel Martinez, PhD, D(ABMM)

Deshaun Richards, PharmD, BS, RPh

Sally A. Tice, PharmD, BCPS, RPh, MHA

Brought to you by the
Geisinger Antimicrobial Stewardship Program

Alison Brodginski, DO
Michelle Budzyn, PharmD
Manish Doshi, MD
Lisa Esolen, MD
Anthony Fredo, PharmD
Robert Gotoff, MD
Swathi Gowtham, MD
Kelly Guza, PharmD
Sarah Hale, PharmD
Kathryn Kopelcheck, RPh
Kimberly LaPointe, PharmD
Fred Leri, PharmD
Stanley I. Martin, MD
Raquel Martinez, PhD, D(ABMM)
Dean Parry, PharmD
Rick Rampulla, PharmD
Deshaun Richards, PharmD
Jeremy Scott, PharmD
Sally Tice, PharmD
Donna M. Wolk, MHA, PhD, D(ABMM)

Table of contents

Introduction

Don’t just do something. Stand there!

The first rule of medicine is often broken by our well-meaning attempts to do everything we can for our patients. Nowhere is that more obvious than in our extensive overuse of antibiotics in modern medicine. Placing a patient on an unnecessary and potentially harmful medication is just one mouse-click away. The arms race between mankind and bacteria that was predicted by the discoverer of penicillin himself, Sir Alexander Fleming, during his Nobel Prize acceptance speech in 1945 has blossomed this past 70 years in a way that even he could not have predicted. In the United States alone, antibiotic resistance contributes to over 2 million illnesses and $20 billion in excess healthcare costs. Disruption of the individual patient’s microbiome is increasingly associated with harmful outcomes, and antibiotic resistance has been declared a public threat by the World Health Organization, making combating antibiotic resistance a true national priority.

This handbook is intended to be a reminder of the importance that should be placed on every antibiotic order from those of us who take care of patients. It is also intended to educate and guide us all through the increasingly complicated world of diagnosing and treating infections in our patients. The goal of any antimicrobial stewardship program is not just to remind us that patients often do not need antibiotics for many illnesses, but when they do, to ensure that every patient receives the right antibiotic — at the right time, at the right dose and for the right duration. So don’t just do something. Stand there and read this guide before you act. Make Abigail Geisinger proud, and make your patient’s antibiotic the best.

Stanley I. Martin, MD, FACP, FIDSA
Director of the Division of Infectious Diseases
Director of the Antimicrobial Stewardship Program
Geisinger

Click to return to table of contents

Restricted antimicrobial agents at Geisinger and their indications for use

Amikacin*

- Management of aerobic Gram-negative bacilli resistant to gentamicin and tobramycin but susceptible to amikacin as an alternative agent
- Management of multidrug-resistant Gram-negative bacilli susceptible to tobramycin or amikacin often in combination with a ß-lactam antimicrobial agent (monotherapy may be used for multidrug-resistant organisms causing cystitis) when tobramycin cannot be used
- Treatment of infections due to susceptible or presumably susceptible non-tuberculous mycobacteria in combination with other agents
- Treatment of infections due to *Nocardia* species infections in combination with other agents

Aztreonam

- Empiric or directed therapy of suspected Gram-negative infections in patients with immediate hypersensitivity reactions to penicillins, cephalosporins and/or carbapenems
- Directed treatment of Gram-negative infections where organism is likely to have resistance secondary to metallo-ß-lactamase production (e.g., New Delhi carbapenemase *E. coli*, MDR *Pseudomonas*) and is tested as susceptible to aztreonam only
- Empiric therapy for febrile neutropenia in patients with immediate hypersensitivity reactions to penicillins, cephalosporins and/or carbapenems

Cefepime

- Therapy for pneumonia in a patient with known colonization or infection due to *Pseudomonas aeruginosa* or AmpC-producing Gram-negative rod infections
- Empiric therapy for healthcare-associated pneumonia
- Empiric therapy for complicated urinary tract infections in patients with, or at risk for, infection due to *Pseudomonas aeruginosa*
- Empiric therapy for undifferentiated severe sepsis or septic shock

Click to return to table of contents

- Febrile neutropenia
- Intraabdominal infections (when combined with other agents) in patients with, or at risk for, infection due to *Pseudomonas aeruginosa* or AmpC-producing Gram-negative rod infections
- Postsurgical meningitis or postsurgical brain abscess
- Skin, soft tissue infection or osteomyelitis due to *Pseudomonas aeruginosa*
- Alternative to cefotaxime for pediatric patients less than 3 months old, if cefotaxime is not available due to shortage or backorder

Ceftaroline*

- Bacteremia, endocarditis, soft tissue infection or pneumonia caused by documented methicillin-resistant *Staphylococcus aureus* (MRSA) infection in patients who are intolerant of vancomycin or failed vancomycin therapy defined as one of the following:
  - Clinical decompensation after 3 to 4 days of vancomycin therapy
  - Failure to clear blood cultures after at least 3 days, despite therapeutic vancomycin trough levels of 15 to 20 mg/L
  - MRSA isolates with an MIC to vancomycin of 2 mg/L or higher

Ceftolozane/tazobactam*

- Management of any serious infection due to confirmed multidrug-resistant *Pseudomonas aeruginosa* resistant to cefepime, piperacillin-tazobactam and/or meropenem
- Treatment of serious infections caused by ESBL-producing Enterobacteriaceae

Colistin*

- Management of any serious infection in patients with confirmed Gram-negative rod such as *Acinetobacter* species, enteric Gram-negative rods, *Pseudomonas aeruginosa* and others resistant to carbapenems, cephalosporins and piperacillin/tazobactam
- Should be used in combination with another antimicrobial agent such as high-dose extended infusion carbapenem and/or tigecycline (monotherapy may be used for qualifying organisms causing urinary tract infections)
- Nebulized treatment for cystic fibrosis patients with active or a history of multidrug-resistant *Pseudomonas aeruginosa* infection and colonization

Daptomycin*

- Bacteremia or endocarditis due to susceptible MRSA or methicillin-resistant coagulase-negative staphylococci in patients who have failed or who cannot tolerate vancomycin therapy
- Bacteremia or endocarditis due to vancomycin-resistant *Enterococcus* (VRE)
- Intraabdominal infection with VRE or susceptible MRSA
- Skin, soft tissue infection or osteomyelitis due to VRE or susceptible MRSA in patients who have failed or who cannot tolerate vancomycin therapy
- Urinary tract infections due to VRE that cannot be treated with alternative agents such as amoxicillin/ampicillin, nitrofurantoin, doxycycline or fosfomycin

Ertapenem

- Directed therapy toward patients with infection due to ESBL-related Gram-negative rod infections
- Empiric treatment of patients with a history of ESBL-related Gram-negative rod infections presenting with a new infectious syndrome
- Infection due to susceptible bacteria in patients with penicillin or cephalosporin allergy
- Test dose administration in patients being transitioned to ertapenem for extended outpatient therapy

Levofloxacin

- Empiric therapy for community-acquired pneumonia
- Treatment of enteric Gram-negative pneumonia if the organism is deemed susceptible to levofloxacin
- For treatment of other Gram-negative infections deemed susceptible to levofloxacin in patients with ciprofloxacin intolerance
- Febrile neutropenia prophylaxis

Linezolid*

- Bacteremia or endocarditis due to VRE
- Directed therapy toward bacterial meningitis due to VRE or MRSA
- Intraabdominal infection with VRE or MRSA in patients who have failed or who cannot tolerate vancomycin therapy
- Pneumonia due to MRSA
- Skin, soft tissue infection or osteomyelitis due to VRE or susceptible MRSA in patients who have failed or who cannot tolerate vancomycin therapy
- Urinary tract infections due to VRE that cannot be treated with alternative agents such as amoxicillin/ampicillin, nitrofurantoin, doxycycline or fosfomycin

Meropenem

- Directed therapy toward patients with infection due to *Pseudomonas aeruginosa* who are coinfected with ESBL enteric Gram-negative rods
- Directed therapy toward patients with infection or history of infection due to *Pseudomonas aeruginosa* where resistance to other ß-lactams is identified
- Directed therapy toward patients with infection or history of infection due to *Acinetobacter baumannii*
- Empiric treatment of febrile neutropenia in patients with penicillin and/or cephalosporin allergy
- Empiric treatment of patients with a history of ESBL-related Gram-negative rod infections presenting with a new infectious syndrome
- Empiric treatment of patients with cystic fibrosis
- Empiric treatment of suspected or proven bacterial meningitis in patients with cephalosporin allergy or intolerance

Piperacillin/tazobactam

- Directed therapy toward patients with infection or history of infection due to *Pseudomonas aeruginosa* where resistance to cefepime is identified
- Empiric therapy for complicated urinary tract infections in patients with, or at risk for, infection due to *Pseudomonas aeruginosa*
- Empiric therapy for undifferentiated severe sepsis or septic shock
- Intraabdominal infections in patients with, or at risk for, infection due to *Pseudomonas aeruginosa*
- Skin, soft tissue infection or osteomyelitis due to *Pseudomonas aeruginosa*

Tigecycline*

- Management of infections due to multidrug-resistant Gram-negative bacilli such as carbapenemase-producing *E. coli*, *Klebsiella* and *Acinetobacter*
- Salvage therapy for polymicrobial infections in which multidrug-resistant Gram-negative organisms and VRE need to be covered

Vancomycin

- Treatment of serious infections caused by, or suspected to be caused by, ß-lactam-resistant Gram-positive bacteria
- Treatment of serious infections due to Gram-positive bacteria in patients with serious allergic reactions (anaphylaxis) to ß-lactam antimicrobials
- Surgical prophylaxis per institutional guidelines
- Oral vancomycin for treatment of moderate to severe *Clostridium difficile* infections**
- Prophylaxis for group B *Streptococcus* coverage during labor for patient with serious allergic reactions (anaphylaxis) to ß-lactam antimicrobials

*Prescription requires mandatory formal Infectious Diseases consultation.
**Prescription in combination with metronidazole requires formal Infectious Diseases consultation.

Clinical pathways

Lower respiratory tract infections

Community-acquired pneumonia

Diagnostic considerations

Indication	Diagnostic test						
	Chest radiograph	Sputum culture*	Blood culture*	*Legionella* urinary antigen	Respiratory viral panel	Procalcitonin	Other
Fever	X	X	X		X	X	
ICU admission	X	X	X	X	X	X	X[a]
Immunocompromised host	X	X	X	X	X		X[b]
Asplenia	X	X	X				
Cavitary lung disease	X	X					X[c]
Pleural effusion	X	X	X	X	X	X	X[d]
COPD	X	X			X	X	
Foreign travel	X	X	X	X	X	X	X[e]

**For outpatients who are otherwise stable, sputum and blood cultures may not be indicated. For patients unable to produce sputum on their own, induced samples should be obtained.*

a For patients admitted to the ICU requiring mechanical ventilation, substitute endotracheal aspiration or bronchoalveolar lavage.

b For immunocompromised hosts, consider obtaining fungal antigens such as galactomannan and ß-D-glucan, as well as fungal and AFB sputum smears and cultures. *Pneumocystis* pneumonia and other atypical pathogens must also be considered. Formal Infectious Diseases consultation is recommended.

c For patients with cavitary lung disease, consider malignancy, pyogenic abscess and fungal and mycobacterial pathogens. For patients with possible risk factors for tuberculosis, placement into airborne isolation is indicated.

d For patients with pleural effusions, thoracentesis and pleural fluid cultures should be considered.

e For patients with significant foreign travel, consideration of unique pathogens such as tuberculosis, *Legionella*, *Coccidioides*, viral pathogens, *Burkholderia*, SARS and MERS may be considered. For first-time-positive AFB smears for inpatients, *M. tuberculosis* PCR will automatically be performed. For outpatient positive AFB smears, PCR must be cleared by Infectious Diseases or Clinical Microbiology.

Click to return to table of contents

Treatment considerations

Condition	Empiric regimens			
Outpatient treatment				
Previously healthy and no recent antibiotic use	Azithromycin alone **or**	Doxycycline alone[a]		
Comorbid condition or use of antibiotics in the previous 3 months	Amoxicillin-clavulanate plus azithromycin **or**	Cefdinir[b] plus azithromycin **or**	Levofloxacin[c]	
Inpatient treatment				
Non-ICU treatment[d]	Amoxicillin-clavulanate plus azithromycin **or**	Cefdinir[b] plus azithromycin **or**	Ceftriaxone plus azithromycin **or**	Levofloxacin[c]
ICU treatment[c]	Ceftriaxone plus azithromycin **or**	Ampicillin-sulbactam plus azithromycin **or**	Levofloxacin[c]	

a Doxycycline should be avoided in pregnant women.

b Amoxicillin-clavulanate is preferred in most cases over cephalosporins. For outpatients, cefpodoxime or cefuroxime are oral cephalosporins that can be considered as alternatives to cefdinir.

c The risks versus benefits of using levofloxacin should be weighed prior to prescribing given its higher side effect profile and increased risk for *Clostridium difficile* infection. Levofloxacin should be avoided in pregnant women.

d For patients with individual risk factors for *Pseudomonas aeruginosa*, MRSA or other multidrug-resistant pathogens, consideration of broader therapy should be given (see *Hospital-acquired pneumonia* section). Formal Infectious Diseases consultation recommended.

Other considerations

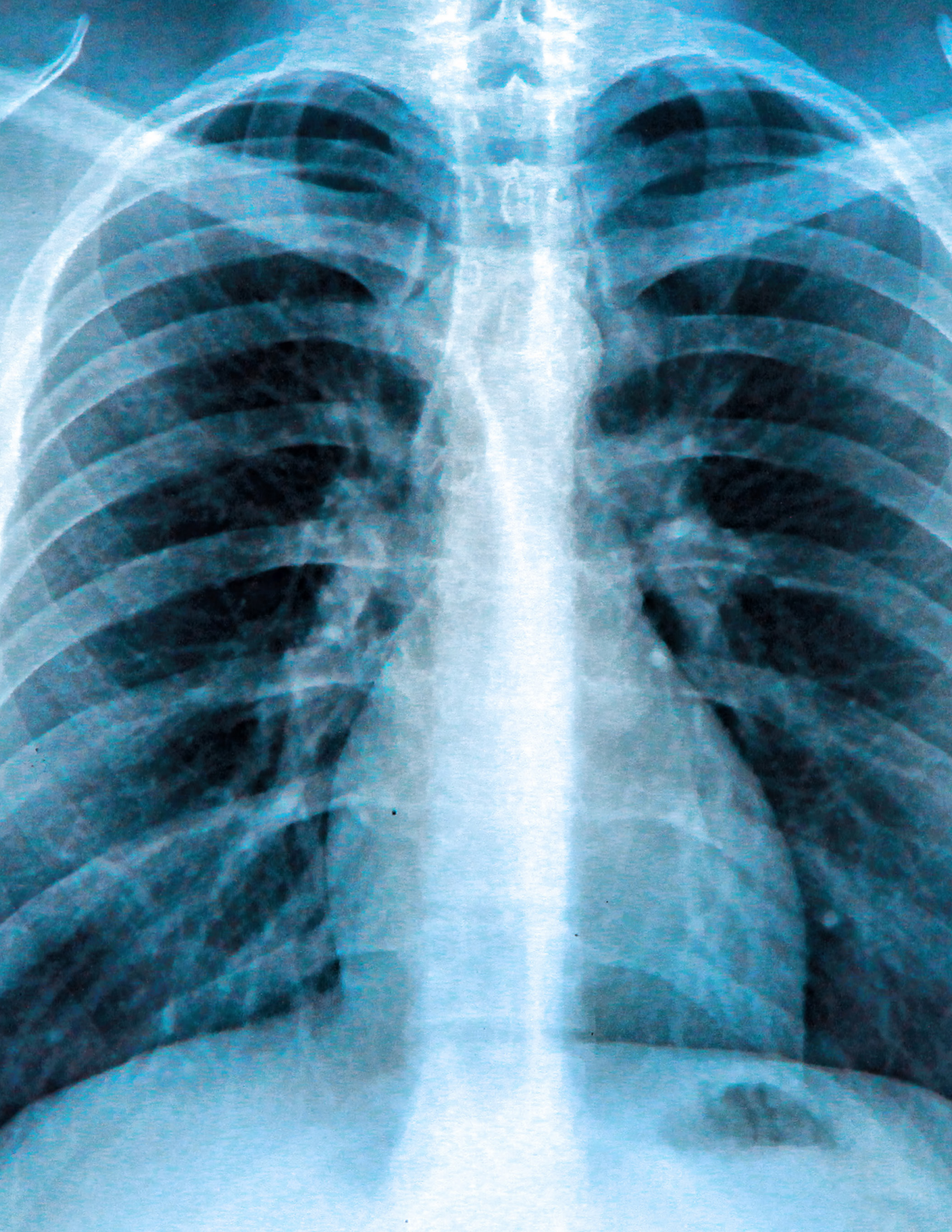
When trying to determine inpatient vs. outpatient treatment, use the CURB-65 score to determine the best treatment plan:

Clinical factor	Point
Confusion	1
Urea (serum) level >19 mg/dL	1
Respiratory rate ≥30/minute	1
Blood pressure: systolic <90 mmHg or diastolic ≥60 mmHg	1
65 years or older	1
Total points:	

By adding the points together for your patient, you can determine prognosis and potential care plan:

CURB-65 score	Deaths/total (%)	Recommendation
0	7/1,223 (0.6)	Low risk; consider outpatient therapy
1	31/1,142 (2.7)	Low risk; consider outpatient therapy
2	69/1,019 (6.8)	Consider inpatient therapy and monitoring
3	79/563 (14)	Severe pneumonia; inpatient therapy and monitoring
4 or 5	44/158 (27.8)	Severe pneumonia; inpatient therapy and monitoring with possible ICU admission

- If cultures or other microbiological assays yield a specific diagnosis, then therapy should be tailored to the individual pathogen.
- IV to PO switch should always be taken into consideration for inpatient care. Patients should be switched from IV to PO therapy when clinically improving, hemodynamically stable, able to ingest oral medications and have a functioning GI tract.
- Duration of treatment for community-acquired pneumonia is generally no longer than 5 to 7 days. Longer duration should only be considered in patients with extrapulmonary disease or slower response to therapy.
- Always consider updating your patient's vaccination status for pneumococcus.



Hospital-acquired pneumonia

Hospital-acquired pneumonia is typically defined as a pneumonia not incubating at the time of hospital admission and occurring 48 hours or more after admission. Ventilator-associated pneumonia (VAP) is a specific form of healthcare-associated pneumonia and is defined as a pneumonia occurring >48 hours after endotracheal intubation.

Indication	Diagnostic test						
	Chest radiograph	Sputum culture*	Blood culture	*Legionella* urinary antigen	Respiratory viral panel	Procalcitonin	Other
Fever	X	X	X		X	X	
ICU admission	X	X	X	X	X	X	X[a]
Immunocompromised host	X	X	X	X	X		X[b]
Asplenia	X	X	X				
Cavitary lung disease	X	X					X[c]
Pleural effusion	X	X	X	X	X	X	X[d]
COPD	X	X			X	X	

**For patients unable to produce sputum on their own, obtain induced samples.*

a For patients admitted to the ICU requiring mechanical ventilation, substitute endotracheal aspiration or bronchoalveolar lavage.

b For immunocompromised hosts, consider obtaining fungal antigens such as galactomannan, beta-D-glucan, fungal and AFB sputum smears and cultures. *Pneumocystis* pneumonia and other atypical pathogens must also be considered. Formal Infectious Diseases consultation is recommended.

c For patients with cavitary lung disease, consider malignancy, pyogenic abscess and fungal and mycobacterial pathogens. For patients with possible risk factors for tuberculosis, placement into airborne isolation is indicated.

d For patients with pleural effusions, thoracentesis and pleural fluid cultures should be considered.

Treatment considerations

Condition	Empiric regimens		
Patients without obvious risk factors for MRSA	Cefepime **or**	Piperacillin-tazobactam **or**	Levofloxacin[a]
Risk factors for MRSA	Cefepime plus vancomycin **or**	Piperacillin-tazobactam plus vancomycin **or**	Levofloxacin[a] plus vancomycin
Patients presenting in septic shock, requiring pressor support	Cefepime plus tobramycin plus vancomycin **or**	Piperacillin-tazobactam plus tobramycin plus vancomycin	

a The risks vs. benefits of using levofloxacin should be weighed prior to prescribing, given its higher side effect profile and increased risk for *Clostridium difficile* infection. Avoid use of levofloxacin in pregnant women.

- For patients with immediate hypersensitivity reactions to penicillins, cephalosporins, and/or carbapenems, consider use of aztreonam instead of cefepime or piperacillin-tazobactam. Meropenem can be used as an alternative in patients with allergies to penicillins or cephalosporins.
- For patients in septic shock with a known history of Gram-negative rod infection, consider also the addition of tobramycin. For patients at risk for *Acinetobacter*, consider the additional use of colistin.
- Risk factors for drug-resistant hospital-acquired and ventilator-associated pneumonia (*Pseudomonas*, MRSA, and other multidrug-resistant Gram-negative rods) include the following:
  – IV antibiotics in the last 90 days
  – ARDS
  – Prolonged stay in the ICU >5 days
  – Hemodialysis
- For severe cases of hospital-acquired pneumonia, formal Infectious Diseases consultation is recommended.

Other considerations

- Antibiotics should be tailored to specific pathogen based on antimicrobial susceptibility testing.
- If no culture data are available, antibiotics should be de-escalated or stopped after clinical improvement or alternative non-bacterial diagnosis is made.
- Duration of therapy for hospital-acquired pneumonia and ventilator-associated pneumonia is typically seven days.

Urinary tract infections

Diagnostic considerations

As a general rule, you need three things to diagnose a urinary tract infection:

- Evidence of pyuria
- Evidence of significant bacteriuria
- Symptoms consistent with a urinary tract infection

Patients with asymptomatic bacteriuria should not be treated with antimicrobial therapy. Asymptomatic bacteriuria is a positive urine culture with either no symptoms consistent with infection and/or a urinalysis without significant pyuria. The only indications to treat asymptomatic bacteriuria are in pregnancy and in patients about to undergo an invasive urologic procedure. Patients with asymptomatic bacteriuria who are about to undergo non-urologic surgical procedures (e.g., orthopaedic, cardiothoracic) do not benefit from treatment.

To distinguish between cystitis and pyelonephritis, consider clinical factors such as presence of fever, leukocytosis or other markers of systemic infection. Patients with cystitis will not exhibit these findings.

Treatment considerations

Uncomplicated acute bacterial cystitis

Drug	Dose	Duration (days)	Notes
Trimethoprim/ sulfamethoxazole	160/800 mg bid	3	Do not use if TMP/SMX used for UTI in past 3 months.
Cephalexin	250 mg q6h **or** 500 mg q12h	7–14	
Nitrofurantoin (Macrobid®)	100 mg bid	5	Avoid if possibility of pyelonephritis **or** CrCl <50 mL/min.
Nitrofurantoin (Macrodantin®)	100 mg qid	5	Avoid if possibility of pyelonephritis **or** CrCl <50 mL/min.
Ciprofloxacin	250 mg bid	3	Fluoroquinolnes should be reserved for when other antimicrobials cannot be used due to resistance.

Uncomplicated acute pyelonephritis

Drug	Dose	Duration (days)	Notes
Ciprofloxacin	500 mg PO bid	7	Fluoroquinolones should be reserved for when other antimicrobials cannot be used due to resistance.
Trimethoprim/ sulfamethoxazole	160/800 mg bid	14	Do not use if TMP/SMX used for UTI in past 3 months. Where TMP/SMX susceptibility is unknown, initial IV dose of ceftriaxone 1 g **or** consolidated 24-hour dose of aminoglycoside is recommended.
Amoxicillin	500–875 mg bid	14	Gram-positive organisms Where ß-lactam susceptibility is unknown, initial IV dose of ceftriaxone 1 g **or** consolidated 24-hour dose of aminoglycoside is recommended.

Click to return to table of contents

Complicated cystitis

Drug	Dose	Duration (days)	Notes
Ciprofloxacin	500 mg PO bid	5–10	Fluoroquinolones should be reserved for when other antimicrobials cannot be used due to resistance. Parenteral therapy reserved for patients unable to tolerate oral, or infection suspected to be due to resistant organisms.
Ceftriaxone	1 g qd	5–10	Ceftriaxone dosing is 2g daily for patients ≥120kg
Gentamicin	7 mg/kg IV qd	5–10	

Complicated pyelonephritis

IV therapy should be stepped down to oral when clinically appropriate.

Drug	Dose	Duration (days)	Notes
Ciprofloxacin	400 mg IV q12h	5–14	Fluoroquinolones should be reserved for when other antimicrobials cannot be used due to resistance.
Ceftriaxone	1 g IV qd	5–14	Ceftriaxone dosing is 2 g daily for patients ≥120 kg.
Cefepime	1 g IV q6h	5–14	Reserved for severe pyelonephritis and patients with, or at risk for, *Pseudomonas aeruginosa*.
Piperacillin/ tazobactam	3.375 g IV q8h extended infusion	5–14	Reserved for severe pyelonephritis and patients with, or at risk for, *Pseudomonas aeruginosa*.

Catheter-related urinary tract infection

Necessity of catheter should be reevaluated. If catheter is indicated and has been in place longer than 14 days, change catheter and obtain urine culture from new catheter.

Do not obtain urine culture from old catheters.

Drug	Dose	Duration (days)	Notes
Ciprofloxacin	500 mg PO bid	5	Fluoroquinolones should be reserved for when other antimicrobials cannot be used due to resistance.
Trimethoprim/ sulfamethoxazole	160/800 mg PO bid	7	Do not use in communities with >20% resistance **or** if TMP/SMX used for UTI in past 3 months
Ceftriaxone	1 g IV qd	7	
Cefepime	1 g IV q6h	7	Reserved for severe pyelonephritis and patients with, **or** at risk for, *Pseudomonas aeruginosa*.
Piperacillin/ tazobactam	3.375 g IV q8h extended infusion	7	Reserved for severe pyelonephritis and patients with, **or** at risk for, *Pseudomonas aeruginosa*.

Other considerations

In patients with symptoms of a urinary tract infection (e.g., dysuria, urgency), always consider risk of sexually transmitted infections as a potential etiology, as well as candiduria (which generally does not require therapy).

Cellulitis and skin and soft tissue infections

Diagnostic considerations

Always consider the possibility of noninfectious causes of skin erythema that can easily be confused with cellulitis. These include vasculitis, deep venous thrombosis, contact dermatitis, lymphedema and venous stasis dermatitis. For patients presenting with evidence of cellulitis and septic shock, syndromes such as necrotizing fasciitis, toxic shock syndrome or gas gangrene should be considered. Consult the Infectious Diseases service to help with management of these latter cases, as well as for diabetic foot infections and management of osteomyelitis.

Treatment considerations

Nonpurulent cellulitis

No purulent drainage or exudate; no associated abscess

Treatment duration should be limited to 5 days for patients with uncomplicated cellulitis. Duration may be extended up to 14 days if slow response to therapy or severe infection.

	Oral treatment options	Parenteral treatment options[c]
ß-hemolytic streptococci Methicillin-susceptible *S. aureus*	Penicillin VK 500 mg PO q6h Dicloxacillin 500 mg PO q6h Cephalexin 500 mg PO q6h Clindamycin 300 mg PO q6h[a]	Cefazolin 1 g IV q8h Nafcillin 2 g IV q4h Clindamycin 600–900 mg IV q8h[a]
Patients with additional risk factors for methicillin-resistant *S. aureus*[b]	Clindamycin 300 mg PO q6h[a] Amoxicillin 500 mg PO q8h **and** TMP/SMX DS 1 tab PO q12h Amoxicillin 500 mg PO q8h **and** doxycycline 100 mg PO q12h	Vancomycin 15–20 mg/kg/dose q8–12h, maximum 2 g/dose Clindamycin 900 mg IV q8h[a] **ID consult required** Daptomycin 4 mg/kg IV q24h Ceftaroline 600 mg q12h Linezolid 600 mg IV q12h

a Clindamycin should be reserved for patients at risk of severe hypersensitivity reaction to penicillin or cephalosporins.

b Empiric coverage for MRSA should be added for patients who do not respond to initial therapy or who have signs of systemic illness, recurrent infection with underlying predisposing conditions, prior documented MRSA colonization or infection, or cellulitis associated with penetrating trauma, as well as in communities where the prevalence of MRSA >30%.

c Parenteral antibiotic use reserved for patients who are immunocompromised or patients with signs of systemic toxicity, rapid progression of erythema, cellulitis originating on skin directly overlying prosthesis site, and/or persistence of symptoms after 48 to 72 hours of appropriate oral therapy.

Footnotes continue on next page

Purulent cellulitis

Presence of purulent drainage or exudate; no drainable abscess
Treatment duration should be limited to 5 days for patients with uncomplicated cellulitis. Duration may be extended up to 14 days if slow response to therapy or severe infection.

	Oral treatment options	Parenteral treatment options[c]
Methicillin-resistant *S. aureus*[b] Methicillin-susceptible *S. aureus* ß-hemolytic streptococci	Clindamycin 300 mg PO q6h[a] Doxycycline 100 mg PO q12h **ID consult required** Linezolid 600 mg PO q12h	Vancomycin 15 mg/kg/dose q8–12h, maximum 2 g/dose Clindamycin 900 mg IV q8h[a] **ID consult required** Daptomycin 4 mg/kg IV q24h Ceftaroline 600 mg q12h Linezolid 600 mg IV q12h
Culture-documented *S. aureus* infection	TMP/SMX DS 1 tab PO q12h	
Inadequate response to initial therapy within 72 hours		Ampicillin-sulbactam 3 g IV q6h
Inadequate response to initial therapy within 72 hours **and** patient has additional risk factors for *Pseudomonas*[d]		Cefepime 2 g IV q12h Piperacillin-tazobactam 3.375 g IV q8h extended infusion Meropenem 1 g IV q8h[e]

Recurrent cellulitis

Treatment should be continued as long as predisposing factors are present.

	Oral treatment options	Parenteral treatment options[c]
ß-hemolytic streptococci	Penicillin VK 250 mg PO q12h	**Weight ≤27 kg** Penicillin G benzathine injection 600,000 units IM injection monthly or twice a month **Weight >27 kg** Penicillin G benzathine 1.2 million units IM injection monthly **or** twice a month
Staphylococcal infection	Clindamycin 150 mg PO q24h[a] TMP/SMX DS 1 tab PO q12h	

Footnotes continued from previous page

d Empiric coverage for *Pseudomonas* should be initiated in patients who do not respond to initial therapy, have a healthcare-associated infection, immunocompromise, or prior documented *Pseudomonas* colonization or infection.

e Meropenem should be reserved for patients with *Pseudomonas* infection and are coinfected with ESBL enteric Gram-negative rods, or where resistance to other ß-lactams is identified.

Clostridium difficile-associated diarrhea

Diagnostic considerations

Asymptomatic carriage is possible. Patients who test positive by PCR testing and have no signs or symptoms of *C. difficile* colitis generally require no treatment.

All patients with symptomatic C diff infection must be placed into contact isolation with strict adherence to hand hygiene. Hand sanitizers are not effective against C diff, and thorough handwashing with soap and water is indicated.

Repeat testing of stool samples for C diff is not indicated either to test for clearance of the infection or to see if infection is still present after or during treatment. Stool C diff PCR can remain positive for several weeks after successful treatment. There is no test of cure for treated C diff infections.

Treatment considerations

If other antibiotics cannot be stopped prior to completion of C diff therapy, continue C diff therapy until end of antibiotic course, plus at least one additional week afterward.

Use of proton pump inhibitors may promote infection and their cessation should be considered in patients with C diff infection.

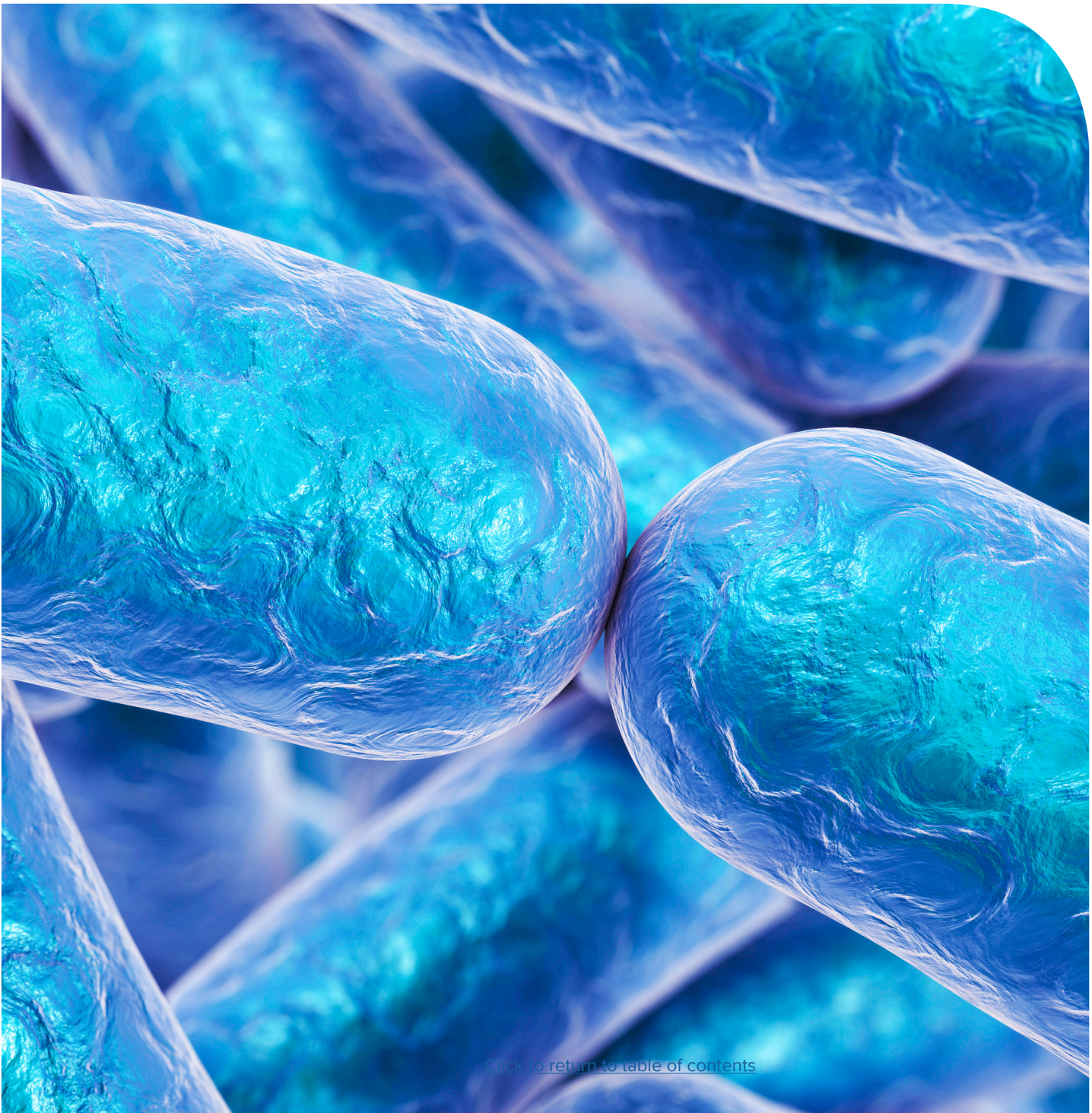
Severe C diff infection is typically defined by significant leukocytosis (>15 WBC) and acute kidney injury (serum creatinine >1.5 times the baseline level). Other factors such as age >60 years, hypoalbuminemia, high fever and underlying immunosuppression are sometimes also used to factor in judging degree of severity.

Initial episode		
Mild	Metronidazole 500 mg PO tid x 10–14 days	
Moderate	Metronidazole 500 mg PO tid x 10–14 days **or**	Vancomycin 125 mg PO qid x 10–14 days
Severe, uncomplicated	Vancomycin 125 mg PO qid x 10–14 days	
Severe, complicated (Ileus and/or hypotension/shock)	Vancomycin 500 mg PO qid plus metronidazole 500 mg IV q8h	Immediate surgical evaluation
Relapsed disease		
First recurrence, mild	Oral vancomycin 125 mg PO qid x 10–14 days	
Second recurrence	Vancomycin taper: 125 mg PO qid x 10–14 days, followed by 125 mg PO bid x 7 days, followed by 125 mg PO qd x 7 days, followed by 125 mg PO qod x 2–8 weeks depending on response and ongoing risk of recurrence	
Multiple relapses	Formal ID consultation, consideration of fecal transplant, use of bezlotoxumab	

Other considerations

Fidaxomicin can be used as an alternative therapy for recurrent episode of C diff as recurrence rate was lower than PO vancomycin for non-NAP-1 strains of *C. difficile*.

For severe complicated disease, consider ID consult. IV metronidazole can be stopped and patient can be decreased to PO vancomycin 125 mg q6h once clinically improved. Role of probiotics for the treatment or prevention of C diff remains unclear.

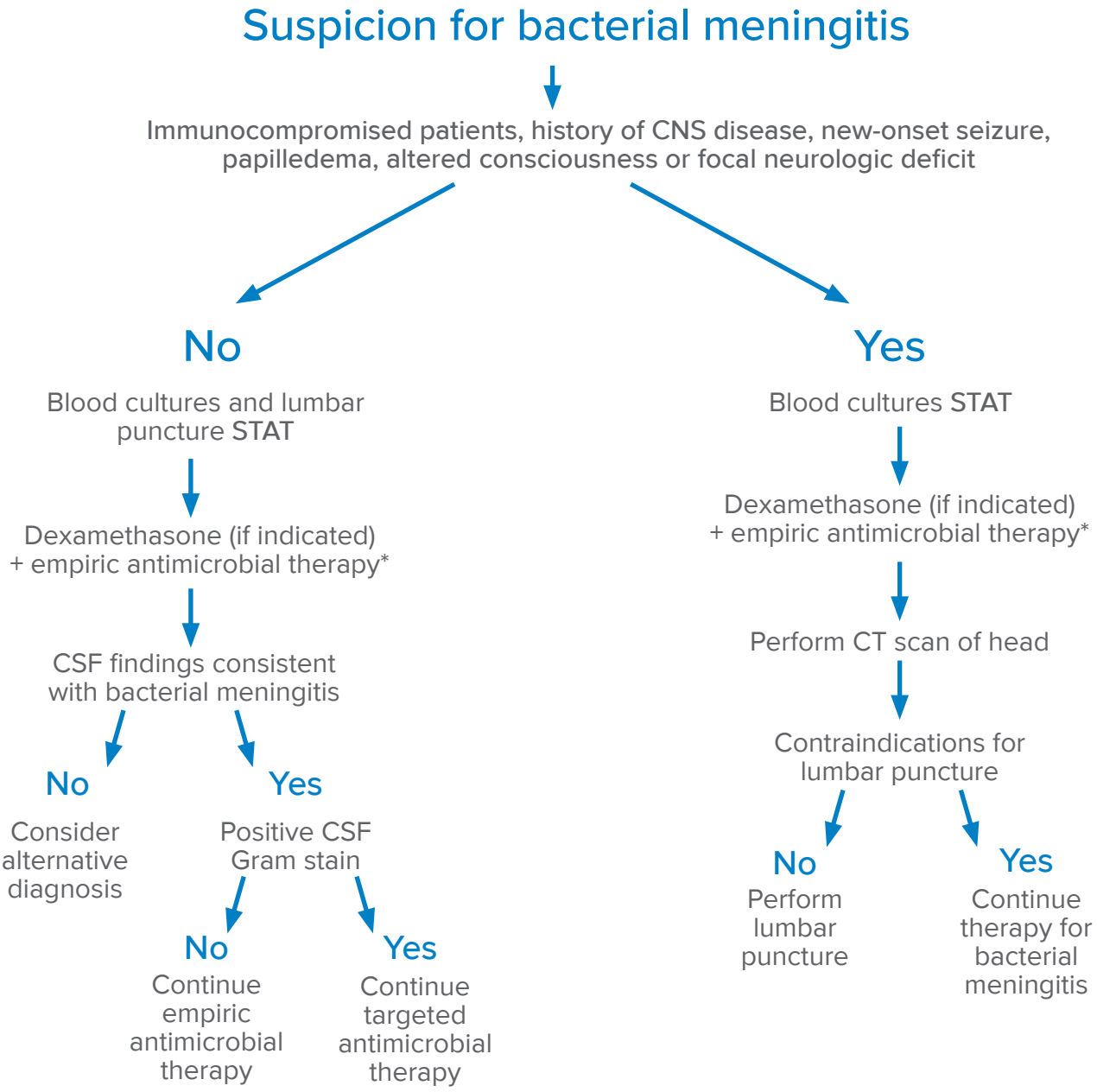


Click to return to table of contents

Meningitis and infections of the central nervous system

Community-acquired CNS infection

Diagnostic considerations



*When used, dexamethasone should only be given 15 to 20 minutes prior to or at time of antibiotic administration at a dose of 0.15 mg/kg IV q6h x 4 days. If patients have already received IV antibiotics, dexamethasone is not indicated. If patients have suspected or proven pneumococcal meningitis, dexamethasone may be continued for the full 4 days.

Typical cerebrospinal fluid findings in CNS infections

	Glucose (mg/dL) <10	Glucose (mg/dL) 10–40	Protein (mg/dL) 100–500	Protein (mg/dL) 50–300	Total WBC (cells/µl) >1,000	Total WBC (cells/µl) 100–1,000	Total WBC (cells/µl) 5–100
More common	Bacterial meningitis	Bacterial meningitis	Bacterial meningitis	Viral meningitis CNS Lyme Neurosyphilis TB meningitis	Bacterial meningitis	Bacterial or viral meningitis TB meningitis	Early bacterial meningitis Viral meningitis TB meningitis
Less common	TB or fungal meningitis	Neurosyphilis **or** viral infections			Mumps	Encephalitis	Encephalitis

Treatment considerations

Recommendations for antimicrobial therapy in adults

Organism	Recommended therapy and dose	Alternative therapies
Empiric therapy when organism not known	Ceftriaxone 2 g IV q12h plus vancomycin 30–45 mg/kg plus ampicillin in some cases[a]	Meropenem plus vancomycin (Seek ID consultation)
Streptococcus pneumoniae		
• PCN MIC <0.1 mcg/mL	PCN G (24 million units/day) **or** ampicillin (12 g/day)	Seek ID consultation
• PCN MIC 0.1–1.0 mcg/mL	Ceftriaxone (2 g q12h)	
• PCN MIC ≥2 mcg/mL	Vancomycin 30–45 mg/kg **and** ceftriaxone (2 g q12h)	
Neisseria meningitidis	Ceftriaxone 2 g q12h	Seek ID consultation
Listeria monocytogenes[a]	Ampicillin (12 g/day) or penicillin G (24 million units/day)	Trimethoprim/sulfamethoxazole (Seek ID consultation)
Haemophilus influenzae	Ceftriaxone (2 g q12h)	Chloramphenicol, cefepime, meropenem, fluoroquinolone (Seek ID consultation)

a Indications for empiric treatment of *Listeria* include immunocompromised state, age >50 years and pregnancy.

Duration of antimicrobial therapy for bacterial meningitis based on pathogen

Organism	Duration of therapy in days
Streptococcus pneumoniae	10–14
Neisseria meningitidis	7
Listeria monocytogenes	≥21
Haemophilus influenzae	7

Healthcare-associated meningitis and ventriculitis

Diagnostic considerations

- New headache, fever, evidence of meningeal irritation, seizures and/or worsening mental status are suggestive in the setting of recent trauma or neurosurgery.
- Fever, in the absence of another clear source of infection, can be suggestive of CNS infection in the setting of recent head trauma or neurosurgery.
- New headache, nausea, lethargy and/or change in mental status are suggestive of CSF shunt infection.
- Erythema and tenderness over the subcutaneous shunt tubing are suggestive of CSF shunt infection.
- Symptoms and signs of peritonitis or abdominal tenderness in patients with ventriculoperitoneal shunts, in the absence of another clear etiology, are indicative of CSF shunt infection.
- Single or multiple positive CSF cultures in patients with CSF pleocytosis and/or hypoglycorrhachia, or an increasing cell count, and clinical symptoms suspicious for ventriculitis or meningitis, is indicative of CSF drain infection.
- CSF cultures are the most important test to establish the diagnosis of healthcare-associated ventriculitis and meningitis.
- If initial CSF cultures are negative in patients with CSF shunts or drains with suspected infection, it is recommended that cultures be held for at least 10 days in an attempt to identify organisms such as *Propionibacterium acnes* or fungal pathogens such as *Candida* spp.
- CSF and blood cultures in selected patients should be obtained before the administration of antimicrobial therapy; a negative CSF culture in the setting of previous antimicrobial therapy does not exclude healthcare-associated ventriculitis and meningitis.
- CSF pleocytosis with a positive culture and symptoms of infection are indicative of a diagnosis of healthcare-associated ventriculitis or meningitis.
- Neuroimaging is recommended in patients with suspected healthcare-associated ventriculitis and meningitis.
- MRI with gadolinium enhancement and diffusion-weighted imaging is recommended for detecting abnormalities in patients with healthcare-associated ventriculitis and meningitis.

Treatment considerations

Predisposing factor	Common pathogens	Antimicrobial therapy
Head trauma		
Basilar skull fracture	*S. pneumoniae, H. influenzae*, group A ß-hemolytic streptococci	Vancomycin plus ceftriaxone
Penetrating trauma	*Staphylococcus aureus*, coagulase-negative staphylococci (especially *Staphylococcus epidermidis*), aerobic Gram-negative bacilli (including *Pseudomonas aeruginosa*)	Vancomycin plus cefepime **or** vancomycin plus meropenem. In settings of CSF leak, consider also use of metronidazole.
Postneurosurgery	Aerobic Gram-negative bacilli (including *P. aeruginosa*), *S. aureus*, coagulase-negative staphylococci (especially *S. epidermidis*), *Candida* spp.	Vancomycin plus cefepime **or** vancomycin plus meropenem
Immunocompromised state	*S. pneumoniae, N. meningitidis, L. monocytogenes*, aerobic Gram-negative bacilli (including *P. aeruginosa*)	Vancomycin plus ampicillin plus cefepime **or** vancomycin plus ampicillin plus meropenem or vancomycin plus TMP-SMX (PCN allergic) plus cefepime **or** meropenem

Antibiotics and doses administered intraventricularly (consult Infectious Diseases)

Antimicrobial agent	Dose
Vancomycin	5–20 mg/day
Gentamicin	4–8 mg/day in adults
Tobramycin	5–20 mg/day
Amikacin	5–50 mg/day
Polymyxin B	5 mg/day in adults
Colistin	3.75 mg/day or divided into two daily doses given every 12 hours
Amphotericin B	0.1–1 mg daily

There are no specific data that define the exact dose of an antimicrobial agent that should be administered by the intraventricular route.

Colonization vs. infection pearls: When to treat

Blood cultures

Clues for deciding contamination vs infection:

Identity of organism

Bacteria considered more likely to be contaminants are:

- Coagulase-negative *Staphylococcus* (*Staphylococcus* species, non-*aureus*), with the exception of *Staphylococcus lugdunensis*
- *Corynebacterium* spp., with the exception of *C. jeikeium*
- *Bacillus* spp., with the exception of *B. anthracis*
- *Propionibacterium acnes*
- *Micrococcus* species
- Viridans group *Streptococcus* (alpha-hemolytic streptococci)

All of these organisms can reflect true bacteremia, however, in the presence of a central venous catheter or other clinical circumstances.

Systemwide, the incidence of contaminated blood cultures based on chart review of these microbes is generally less than 1 percent of all blood cultures.

Number of positive blood culture sets

- If only one of at least two blood culture sets grows an organism known to be a contaminant, this suggests contamination.
- Positive blood culture sets for different organisms (and/or different strains) suggests contamination.
- The Microbiology Laboratory adds a comment to indicate possible contamination and need for clinical correlation.

Source of blood cultures

- Blood cultures drawn from peripheral/tunneled catheters or ports are generally not recommended and can either be true bacteremia, culture contaminants or catheter colonization. Results must be interpreted carefully.
- Positive catheter-segment cultures in absence of positive blood cultures suggest catheter colonization.

Time to growth

Blood cultures that turn positive >3–5 days after incubation with organisms likely to be skin flora are suggestive of contamination.

Clinical indicators

Temperature of <36° C or >40° C, WBC count of <4,000/µl or >20,000/µl, and hypotension are more suggestive of true infection as opposed to contamination.

Respiratory cultures

- Gram stains of sputum cultures with >10 epithelial cells/hpf are not considered acceptable specimens for processing and interpretation.
- Various organisms can colonize the respiratory tract in the setting of chronic illness or recent hospitalization. The type of organism and source of culture (tracheostomy, ET tube) factor into determining infection vs. colonization.
- Some organisms are seldom pulmonary pathogens, such as *Candida* spp., coagulase-negative staphylococci, enterococci, *Bacillus* spp. (except *B. anthracis*), *Corynebacterium* spp., and streptococci other than *S. pneumoniae, S. pyogenes, S. agalactiae,* and *S. anginosus*.

Click to return to table of contents

Urine cultures

- Asymptomatic bacteriuria is common in women and the incidence increases with age. Although symptomatic bacteriuria is rare in healthy young men, prevalence also increases with age, especially after 60 years of age.
- Routine screening and treatment of bacteriuria in asymptomatic patients is not recommended unless patient is pregnant or undergoing urologic procedures associated with mucosal bleeding.
- The presence or absence of odorous or cloudy urine alone should not be used to differentiate UTIs from asymptomatic bacteriuria or as an indication for urine culture or antimicrobial therapy
- Treatment of bacteriuria in asymptomatic patients with short- or long-term urinary catheterization is not recommended.
  - Patients with urinary catheters can become colonized with bacteria. Colonization increases as duration of catheter increases. Removal of unnecessary urinary catheters is always indicated.
  - In the catheterized patient, pyuria is not diagnostic of CA-bacteriuria or CA-UTI, and should not be used to differentiate the two.
  - Unnecessary treatment of asymptomatic bacteriuria in a catheterized patient leads to increased resistance of colonizing organisms, making treatment of actual infections a challenge should the patient develop a true CA-UTI at some point in the future
  - Indwelling catheters should be removed as soon as they are no longer required to reduce the risk of CA-bacteriuria (IDSA catheter-associated UTI).
  - The urine culture should be obtained from the freshly placed catheter prior to the initiation of antimicrobial therapy to help guide treatment. If use of the catheter can be discontinued, obtain a culture of a voided midstream urine specimen prior to initiating antimicrobial therapy to help guide treatment.
- Urine cultures from patients with ileal conduits/stomas are not sterile and should be interpreted with caution.
- Presence of skin flora such as *Staphylococcus aureus* in urine along with presence of bacteremia should raise concern for secondary seeding of urine from endocarditis as opposed to having primary UTI.

Tissue cultures

- Tissue swabs from ulcers or skin lesions do not necessarily reflect infection and may just be cutaneous colonizers. Evidence of actual infection is denoted by surrounding cellulitis, purulent drainage and/or tissue necrosis. Cultures taken from tissue samples or biopsies in these cases may be more predictive.
- Pus is not the best specimen to use for cultures from open wounds associated with infections. Try removing the pus, flushing with saline, and rubbing the swab vigorously along the leading edge of the wound for best recovery of pathogens.

Approach to antimicrobial allergies

- Antibiotic allergies are often overdiagnosed.
- Penicillin-type drugs (ß-lactam drugs) can be very effective and are the drugs of choice for many infections.
- Adverse reactions to penicillin are reported in 0.7 to 10 percent of patients who take penicillin (including GI symptoms and CNS complaints).
- Only 0.004 to 0.015 percent of all penicillin courses will result in anaphylaxis. This is most common in patients 20 to 49 years of age.
- A patient who develops anaphylaxis and/or hypotension, laryngeal edema, wheezing, angioedema (facial or mouth swelling) or urticaria (hives) immediately or within 72 hours of treatment with penicillin should not be administered ß-lactam drugs (penicillins, cephalosporins, carbapenems) without skin testing or desensitization. These types of reactions are IgE-mediated and are called *Type I hypersensitivity*.
- A maculopapular rash that develops >72 hours into treatment with penicillin or other ß-lactams is not likely to be a Type I IgE-mediated hypersensitivity reaction. Instead, these reactions are classified as *idiopathic*. They do not predictably recur on reexposure to penicillin and may subside with continued treatment. Idiopathic rashes occur in 1 to 4 percent of all patients receiving penicillin and with an increased frequency with ampicillin/amoxicillin (5.2 to 9.5 percent).
- Idiopathic rashes are more common in patients who have certain concomitant viral illnesses (Epstein-Barr virus, CMV, Echovirus, Coxsackie virus).
- Patients with idiopathic rashes to penicillin can be treated with other ß-lactam drugs (penicillin analogues, cephalosporins, carbapenems, monobactams) with no greater risk of anaphylaxis than the general population.
- Patients who have a penicillin allergy may have to be prescribed a second-choice drug, a more expensive drug, a less-well tolerated drug or even have therapy delayed because skin-testing or desensitization is needed.
- If there is not a "true" penicillin allergy (a Type I hypersensitivity), then ß-lactam drugs can be used.

Antimicrobial IV to PO conversion

Patient must meet at least one of the inclusion criteria and none of the exclusion criteria.

Inclusion criteria

One of these conditions must be met:

- Patient is receiving oral/enteral medications and/or oral/enteral diet already.
- If taking fluids, adults should be tolerating at least 1,000 mL per day orally. Pediatric patients exhibit tolerance of fluid intake.
- If receiving enteral nutrition, patient is tolerating feeds.
- Receives other medication by the oral route.
- No specific contraindication to the use of the ordered oral dosage form.

Exclusion criteria

Cannot switch if any of these are present:

- Admitted <24 hours ago
- Unable to swallow or on NPO status
- Grade III or IV mucositis
- Severe nausea or vomiting
- Severe diarrhea
- Patient in a shock state (e.g., receiving high doses of vasopressors) that would decrease enteric absorption
- Any GI obstruction or patient receiving continuous gastric suctioning
- Malabsorptive syndromes or short bowel syndrome
- Active GI bleed
- Antibiotics being used for the following indications:
  - Meningitis or other CNS infection
  - Endocarditis
  - Gram-positive bacteremia
- Status epilepticus

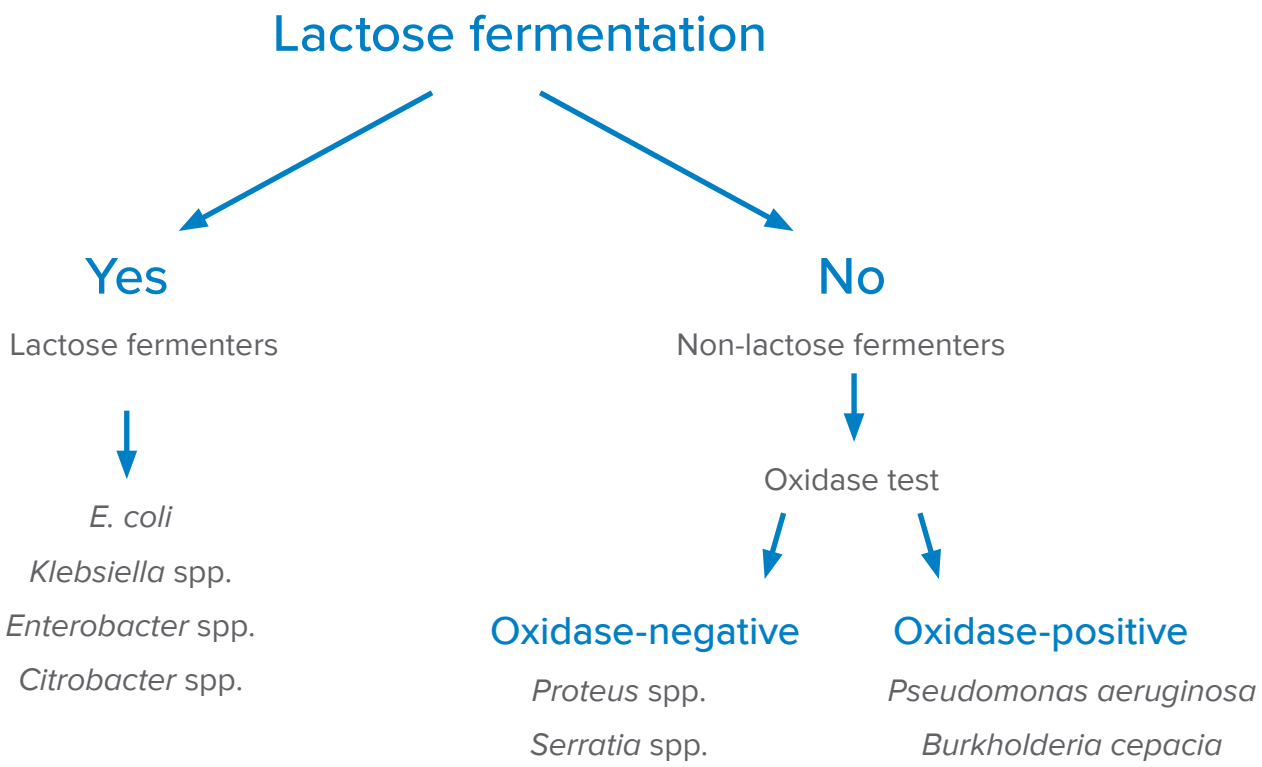
Click to return to table of contents

Antimicrobial IV to PO conversion table

Drug	IV equivalent	PO equivalent	IV to PO ratio
Azithromycin	250 mg IV qd 500 mg IV qd	250 mg PO qd 500 mg PO qd	1:1
Ciprofloxacin	200 mg IV q12h 400 mg IV q12h 400 mg IV q8h	250 mg PO q12h 500 mg PO q12h 750 mg PO q12h	0.8:1
Doxycycline	100 mg IV qd	100 mg PO qd	1:1
Fluconazole	200 mg IV qd 400 mg IV qd 600 mg IV qd 800 mg IV qd	200 mg PO qd 400 mg PO qd 600 mg PO qd 800 mg PO qd	1:1
Levofloxacin	250 mg IV qd 500 mg IV qd 750 mg IV qd	250 mg PO qd 500 mg PO qd 750 mg PO qd	1:1
Linezolid	600 mg IV q12h	600 mg PO bid	1:1
Metronidazole	250 mg IV q6–8h 500 mg IV q8h	250 mg PO q6–8h 500 mg PO tid	1:1
Rifampin	300 mg IV qd 600 mg IV qd	300 mg PO qd 600 mg PO qd	1:1
Voriconazole	200 mg IV bid	200 mg PO bid	1:1

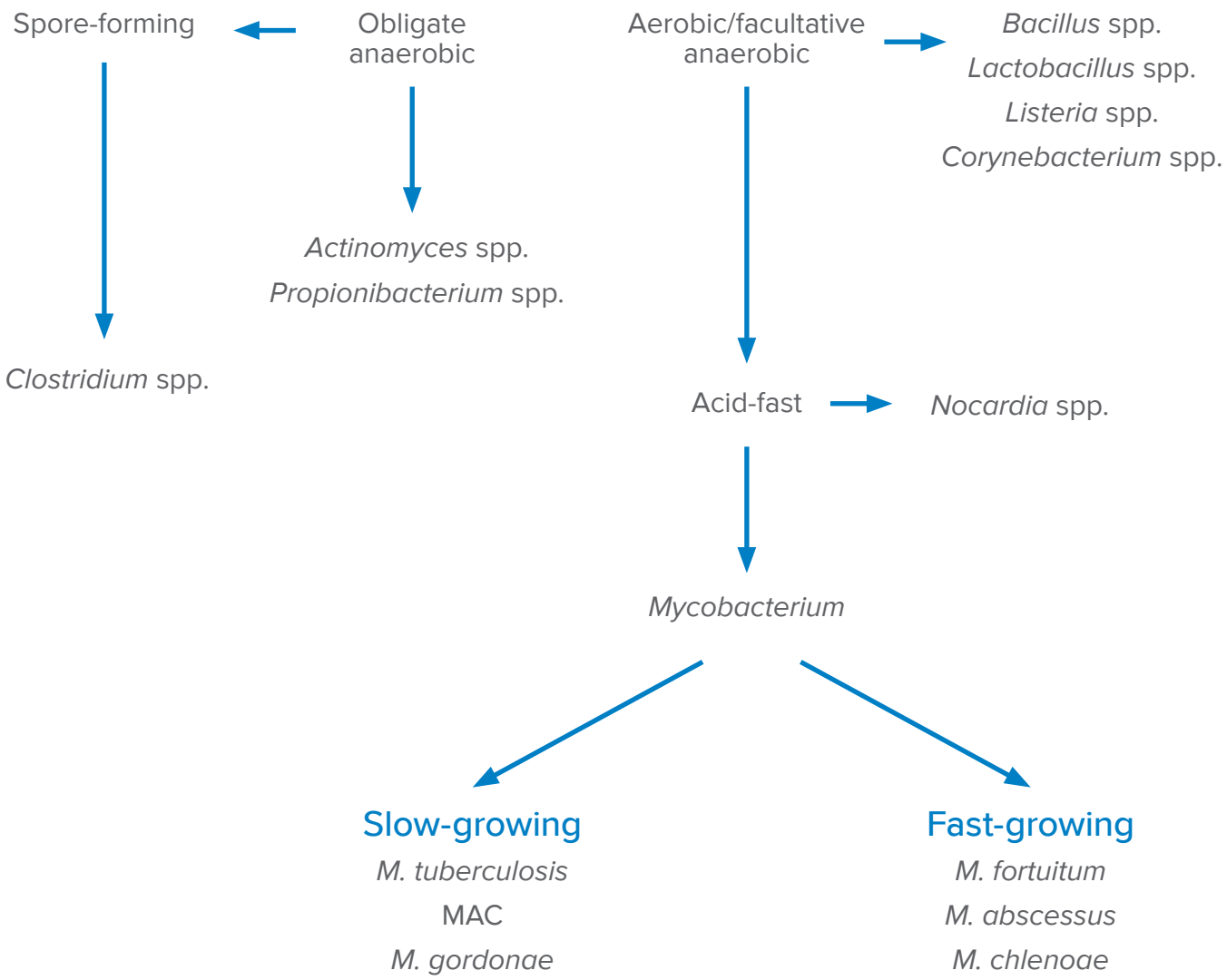
Microbiology flow charts

Gram-negative rods

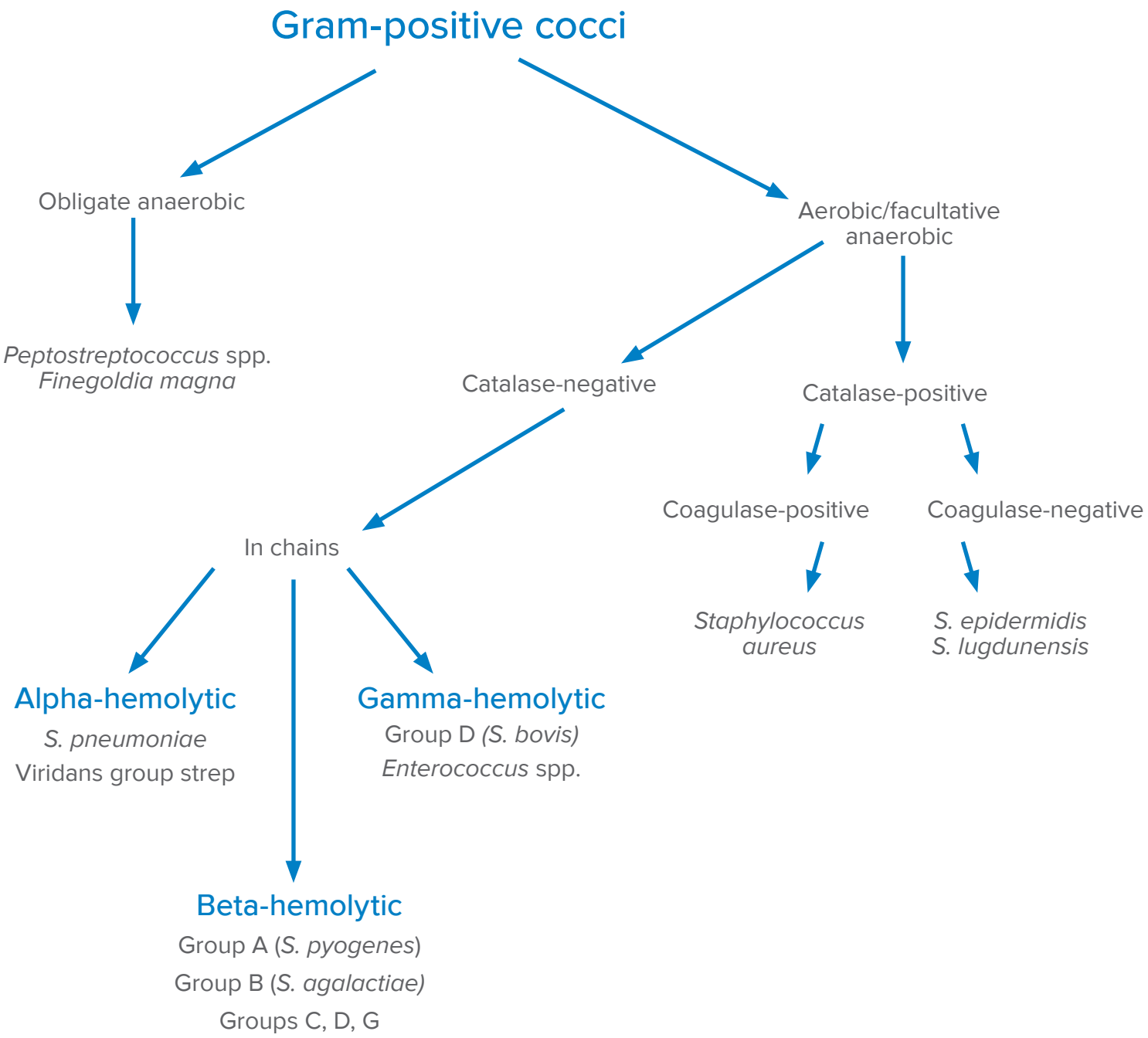


Click to return to table of contents

Gram-positive rods



Click to return to table of contents



Click to return to table of contents

Antibiograms for Geisinger (all platforms)

Jan. 1, 2016 – Dec. 31, 2016				
Gram-positive organism – % susceptible				
	MRSA	MSSA	*Staphylococcus*, coagulase-negative	*Streptococcus pneumoniae*
Clindamycin	66	76	62	84
Erythromycin	13	60	41	55
Gentamicin	98	99	89	
Oxacillin	0	100	49	
Tetracycline	92	95	84	
Trimethoprim/sulfamethoxazole	93	98	61	83
Vancomycin	100	100	100	
Amoxicillin				91
Ceftriaxone meningitis				100
Ceftriaxone non-meningitis				100
Ceftriaxone				100
Levofloxacin				98
Penicillin meningitis				74
Penicillin non-meningitis				99

Jan. 1, 2016 – Dec. 31, 2016			
Gram-positive organism – % susceptible			
	Enterococcus faecalis	*Enterococcus faecium*	*Enterococcus* spp.
Number of isolates	199	237	4,553
Ampicillin	100	4	93
Gentamicin synergy	56	93	78
Nitrofurantoin	100	26	94
Streptomycin synergy	73	86	83
Tetracycline		3	23
Vancomycin	67	7	96

Jan. 1, 2016 – Dec. 31, 2016 Gram-negative organism – % susceptible												
	Acinetobacter baumannii complex	*Citrobacter freundii*	*Enterobacter aerogenes*	*Enterobacter cloacae* complex	*Escherichia coli*	*Klebsiella oxytoca*	*Klebsiella pneumoniae*	*Morganella morganii*	*Proteus mirabilis*	*Pseudomonas aeruginosa* – CF	*Pseudomonas aeruginosa* – non-CF	*Serratia marcescens*
Number of isolates	140	286	340	611	15,835	471	3,423	345	2,027	171	1,942	438
Ampicillin	0	0	0	0	54	0	0	1	79	0	0	0
Ampicillin/sulbactam	93	0	0	0	60	59	78	3	87	0	0	0
Cefepime	57	100	100	99	97	99	93	100	100	31	91	100
Cefoxitin		0	0	0	89	96	90	33	93			29
Ceftazidime										33	91	
Ceftriaxone	8	79	84	80	91	94	90	82	99	0	0	95
Ciprofloxacin	72	91	96	96	76	97	89	55	49	25	77	96
Gentamicin	71	94	99	97	92	99	92	77	86		88	99
Levofloxacin	74	92	96	96	76	97	90	56	53		73	96
Meropenem	79	100	100	100	100	100	96	100	100	73	93	99
Nitrofurantoin		93	15	45	97	85	44	0	0			0
Piperacillin/tazobactam		87	86	82	97	92	89	98	100		100	73
Tobramycin	97	95	99	97	92	99	90	90	89	84	97	83
Trimethoprim/sulfamethoxazole	68	80	98	91	78	97	86	57	70	0	0	99

Click to return to table of contents

References

1. Combating Antibiotic-Resistant Bacteria. Washington DC: The White House Office of the Press Secretary, Sept. 18, 2014. whitehouse.gov/the-press-office/2014/09/18/executive-order-combating-antibiotic-resistant-bacteria. Accessed Aug. 29, 2015.
2. Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2013. cdc.gov/drugresistance/threat-report-2013/. Accessed Nov. 16, 2016.
3. Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Clin Infect Dis 2016; 62(10): e51-77.
4. Tamma P, Cosgrove SE. Antimicrobial Stewardship. Infect Dis Clin North Am. 2011; 25(1): 245-60. PMID: 21316003.
5. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007; 44 Suppl 2:S27.
6. Gross AE, Van Schooneveld TC, Olsen KM, et al. Epidemiology and predictors of multidrug-resistant community-acquired and health care-associated pneumonia. Antimicrob Agents Chemother 2014; 58:5262.
7. Lim WS, van der Eerden MM, Laing R, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax 2003; 58:377–82.
8. Kalil AC, Metersky ML, Klompas M, et al. Management of Adults with Hospital-Acquired and Ventilator-Associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis 2016; 63: e61.
9. Gupta K, Hooton TM, Naber KG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis 2011; 52: e103.
10. Wieczorkiewicz SM, Sincak CS. The pharmacist's guide to antimicrobial therapy and stewardship. Am Soc of Health-Syst Pharm. 2016; 76.
11. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases society of America. Clin Infect Dis 2014; 59: 147.
12. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis 2012; 54: e132.
13. Cohen SH, Gerding DN, Johnson S, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the Infectious Diseases society of America (IDSA). Infect Control Hosp Epidemiol 2010; 31:431.
14. Zar FA, Bakkanagari SR, Moorthi KM, et al. A comparison of vancomycin and metronidazole for the treatment of *Clostridium difficile*-associated diarrhea, stratified by disease severity. Clin Infect Dis 2007; 45: 302.

15. Louie TJ, Miller MA, Mullane KM, et al. Fidaxomicin versus vancomycin for *Clostridium difficile* infection. N Engl J Med. 2011;364(5):422.
16. Tunkel AR et al. Practice Guidelines for Bacterial Meningitis. Clin Infect Dis; 2004;39:1267-1284.
17. Tunkel AR et al. 2017 Infectious Diseases Society of America's Clinical Practice Guidelines for Healthcare-Associated Ventriculitis and Meningitis. Clin Infect Dis; 2017;64:e34.
18. Brouwer MC, Thwaites GE, Tunkel AR, van de Beek D. Dilemmas in the diagnosis of acute community-acquired bacterial meningitis. Lancet 2012; 380: 1684.
19. Hall KK, Lyman JA. Updated Review of Blood Culture Contamination. Clinical Microbiology Reviews. Oct. 2006, pp. 788–802.
20. Clinical and Laboratory Standards Institute. M47-A. Principles and Procedures for Blood Cultures; Approved Guideline. May 2007.
21. Weinstein, MP. 2003. Blood culture contamination: persisting problems and partial progress. J Clin Microbiol. 41:2275–2278.
22. Weinstein, MP. 1996. Current blood culture methods and systems: clinical concepts, technology, and interpretation of results. Clin Infect Dis. 23:40–46
23. Sharma M, Riederer K, Johnson LB, Khatib R. 2001. Molecular analysis of coagulase-negative *Staphylococcus* isolates from blood cultures: prevalence of genotypic variation and polyclonal bacteremia. Clin Infect Dis. 33:1317–1323.
24. Wong LK, Barry AL, Horgan SM. Comparison of six different criteria for judging the acceptability of sputum specimens. J Clin Microbiol. 1982;16(4):627.
25. Nicolle LE, Mayhew WJ, Bryan L. Prospective, randomized comparison of therapy and no therapy for asymptomatic bacteriuria in institutionalized elderly women. Am J Med 1987; 83:27–33.
26. Warren JW, Anthony WC, Hoopes JM, Muncie HL Jr. Cephalexin for susceptible bacteriuria in afebrile, long-term catheterized patients. JAMA 1982; 248:454–8.
27. Alling B, Brandberg A, Secberg S, Svanborg A. Effect of consecutive antibacterial therapy on bacteriuria in hospitalized geriatric patients. Scand J Infect Dis 1975; 7:201–7.
28. Lo E, Nicolle LE, Coffin SE, Gould C, Maragakis LL, Meddings J, Pegues DA, Pettis AM, Saint S, Yokoe DS. Strategies to prevent catheter-associated urinary tract infections in acute care hospitals: 2014 update.
29. Arpi M, Renneberg J. The clinical significance of *Staphylococcus aureus* bacteriuria. J Urol 1984;132:697–700.
30. Lee BK, Crossley K, Gerding DN. Th e association between *Staphylococcus aureus* bacteremia and bacteriuria. Am J Med 1978;65:303–6.
31. Demuth PJ, Gerding DN, Crossley K. *Staphylococcus aureus* bacteriuria. Arch Intern Med 1979;139:78–80.
32. Sheth S, DiNubile MJ. Clinical significance of *Staphylococcus aureus* bacteriuria without concurrent bacteremia. Clin Infect Dis 1997;24:1268–9.
33. Salkind AR, Cuddy PG, Foxworth JW. JAMA. May 16, 2001. 285(19):2498–2505.