Treatment Guidelines
from The Medical Letter®

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Drugs for Bacterial Infections

The text that follows reviews some common bacterial infections and their empiric treatment pending the results of culture and susceptibility testing. The recommendations made here are based on the results of susceptibility studies, clinical trials, and the opinions of Medical Letter reviewers. Tables listing the usual dosages of antibacterial drugs can be found on pages 66-67 and 70-71.

SKIN, SOFT TISSUE AND BONE INFECTIONS

SKIN AND SOFT TISSUE — Uncomplicated skin and soft tissue infections in immunocompetent patients are most commonly caused by *Staphylococcus aureus* or *Streptococcus pyogenes* or other beta-hemolytic streptococci. Complicated infections, such as those that occur in patients with burns, diabetes mellitus, infected pressure ulcers, and traumatic or surgical wound infections, are more commonly polymicrobial and often include anaerobes and gram-negative bacilli, such as *Escherichia coli* and *Pseudomonas aeruginosa.* Group A streptococci, *S. aureus* or *Clostridium* spp., with or without other anaerobes, can cause fulminant soft tissue infections and necrosis, particularly in patients with diabetes mellitus.

MRSA – Methicillin-resistant *S. aureus* (MRSA) has become the predominant cause of suppurative skin infection in many parts of the US.[1] Community-associated MRSA (CA-MRSA), MRSA that occurs in the absence of healthcare exposure, usually causes furunculosis, cellulitis and abscesses, but necrotizing fasciitis and sepsis can occur.[2] **CA-MRSA** strains are usually susceptible to trimethoprim/sulfamethoxazole, clindamycin and tetracyclines; **nosocomial** strains of MRSA often are not.

For simple abscesses and other **less serious CA-MRSA** skin and soft tissue infections, incision and drainage alone may be effective. When it is not, oral trimethoprim/sulfamethoxazole, minocycline, doxycycline, clindamycin or linezolid could be tried.[3] Fluoroquinolones should not be used empirically to treat MRSA infections because resistance is common and is increasing in both nosocomial and community settings.

Patients with **more serious** skin and soft tissue infections suspected to be caused by MRSA should be treated empirically with vancomycin, linezolid or daptomycin. For complicated polymicrobial infections that could include MRSA, one of these drugs could be added to a broad-spectrum parenteral antibiotic, such as piperacillin/tazobactam or a carbapenem. Ceftaroline fosamil, a new IV cephalosporin with activity against MRSA, may be effective as monotherapy if infection with *P. aeruginosa* and anaerobic bacteria is unlikely.[4]

Non-MRSA Infections – For **uncomplicated** skin and soft tissue infections unlikely to be caused by MRSA (no recent hospitalizations or antibiotic use, not known to be colonized, and not in a geographic area with high prevalence), an oral antistaphylococcal penicillin such as dicloxacillin or a first-generation cephalosporin such as cephalexin is a reasonable choice. If the patient requires hospitalization, IV nafcillin, oxacillin or cefazolin can be given. Vancomycin or clindamycin could be used in patients who are allergic to beta-lactams.

For **complicated** infections that could be polymicrobial and are unlikely to involve MRSA, ampicillin/sulbactam, piperacillin/tazobactam, ticarcillin/clavulanate, or a carbapenem would be reasonable empiric monotherapy. If group A streptococcus or *Clostridium*

Table 1. Some Oral Antibacterial Drugs

Drug	Some Available Formulations	Usual Adult Dosage[1]	Usual Pediatric Dosage[1]	Cost[2]
Cephalosporins				
Cefaclor – generic	250, 500 mg caps[3]	250-500 mg q8h	20-40 mg/kg/d divided q8-12h	$26.14
extended-release – generic	375, 500 mg ER tabs	500 mg q12h	10-20 mg/kg q12h	37.35
Cefadroxil – generic	500 mg caps; 1 g tabs[3]	500 mg-1 g q12h	15 mg/kg q12h	5.70
Cefdinir – generic	300 mg caps[3]	300 mg q12h or 600 mg once daily	7 mg/kg q12h or 14 mg/kg once daily	32.18
Cefditoren pivoxil – *Spectracef* (Cornerstone)	200, 400 mg tabs	200-400 mg q12h	≥12 yrs: 200-400 mg q12h	132.66
Cefpodoxime proxetil– generic	100, 200 mg tabs[3]	100-400 mg q12h	5 mg/kg q12h	47.73
Cefprozil – generic	250, 500 mg tabs[3]	500 mg q12-24h	7.5-15 mg/kg q12h	55.00
Ceftibuten – *Cedax* (Pernix)	400 mg caps[3]	400 mg once daily	4.5 mg/kg bid or 9 mg/kg once daily	74.78
Cefuroxime axetil – generic	250, 500 mg tabs[3]	125-500 mg q12h	10-15 mg/kg q12h	4.20
Ceftin (GSK)				140.00
Cephalexin – generic	250, 500 mg tabs, caps[3]	250 mg-1 g q6-12h	25-100 mg/kg/d divided q6-8h	2.80
Keflex (Shionogi)	250, 500, 750 mg caps			151.00
Fluoroquinolones				
Ciprofloxacin – generic	100, 250, 500, 750 mg tabs[3]	250-750 mg q12h	10-20 mg/kg q12h[4]	2.22
Cipro (Bayer)	250, 500 mg tabs[3]			44.59
extended-release – generic	500, 1000 mg ER tabs	1000 mg once daily	See footnote 4	44.63
Cipro XR				49.65
Gemifloxacin – *Factive* (Cornerstone)	320 mg tabs	320 mg once daily	See footnote 4	199.30
Levofloxacin – generic	250, 500, 750 mg tabs[3]	250-750 mg once daily	See footnote 4	2.25
Levaquin (Janssen)				94.10
Moxifloxacin – *Avelox* (Bayer)	400 mg tabs	400 mg once daily	See footnote 4	104.35
Norfloxacin – *Noroxin* (Merck)	400 mg tabs	400 mg q12h	See footnote 4	40.33
Ofloxacin – generic	200, 300, 400 mg tabs	200-400 mg q12h	See footnote 4	38.27
Macrolides				
Azithromycin – generic	250, 500, 600 mg tabs[3]	500 mg day 1, then 250 mg once daily	5-10 mg/kg once daily	8.53
Zithromax (Pfizer)				82.98
Zmax	2 g/60 mL ER susp	2 g single dose	60 mg/kg single dose	106.97
Clarithromycin – generic	250, 500 mg tabs[3]	250-500 mg q12h	7.5 mg/kg q12h	40.31
Biaxin (Abbvie)				67.20
extended-release – generic	500 mg ER tabs	1000 mg once daily	—	37.50
Biaxin XL				71.60
Erythromycin base, delayed-release capsules generic	250 mg caps	250-500 mg q6h	7.5-12.5 mg/kg q6h	55.80
Erythromycin base, enteric-coated tablets *Ery-tab* (Arbor)	250, 333, 500 mg tabs	250-500 mg q6h	7.5-12.5 mg/kg q6h	32.00
Erythromycin base, film-coated tablets – generic	250, 500 mg tabs			56.60
Fidaxomicin – *Dificid* (Optimer)	200 mg tabs	200 mg q12h	—	1478.80

1. Dosage may vary based on the site of infection, infecting organism and patient specific characteristics, such as renal and hepatic function. Higher or lower doses than those listed here may be needed. Listed pediatric dosages may not apply for premature infants and newborns. Pediatric dosage generally should not exceed maximum adult dosage.
2. Wholesale acquisition cost (WAC) of 5 days' treatment with the lowest recommended adult dosage and least frequency of administration. $source® Monthly (Selected from FDB MedKnowledge™) June 5, 2013. Reprinted with permission by FDB, Inc. All rights reserved. ©2013. www.fdbhealth.com/policies/ drug-pricing-policy. Actual retail prices may be higher.
3. Also available as a suspension or solution which may not be equivalent on a mg/mg basis to the tablets or capsules.
4. Not recommended for routine use in children or adolescents <18 years old.

spp. is suspected, a combination of clindamycin and a penicillin is recommended. In severely ill patients, vancomycin, linezolid or daptomycin should be added until MRSA is ruled out. Surgical debridement is essential to the management of necrotizing skin and soft tissue infections.

BONE AND JOINT — *S. aureus* and coagulase-negative staphylococci are the most common cause of **acute osteomyelitis**. Streptococci and enterococci are less common pathogens. *Salmonella* spp. can cause osteomyelitis, particularly in patients with sickle cell disease, as can other gram-negative bacteria (*E. coli, P. aeruginosa*), particularly in patients who have open fractures, have had orthopedic procedures or have vertebral infections. Infections of the feet are common in diabetic patients, can involve both bone and soft tissue, and are often polymicrobial, including both aerobic

Table 1. Some Oral Antibacterial Drugs (continued)

Drug	Some Available Formulations	Usual Adult Dosage[1]	Usual Pediatric Dosage[1]	Cost[2]
Penicillins				
Penicillin VK – generic	250, 500 mg tabs[3]	250-500 mg q6-8h	25-50 mg/kg/d divided q6-8h	$4.05
Amoxicillin – generic	250, 500 mg caps; 500, 875 mg tabs; 125, 250 mg chewable tabs[3]	250-500 mg q8h or 500-875 mg q12h	20-90 mg/kg/d divided q8-12h	1.50
extended-release – *Moxatag* (Shionogi)	775 mg tabs	775 mg once daily	≥12 yrs: 775 mg once daily	72.90
Amoxicillin/clavulanate – generic	250/125, 500/125, 875/125 mg tabs; 200/28.5, 400/57 mg chewable tabs[3]	875 mg q12h or 250-500 mg q8h[5]	25-90 mg/kg/d divided q12h[5]	59.00[6]
Augmentin (Dr Reddy's Lab)				97.00
extended-release – generic	1000/62.5 mg ER tabs	2000 mg q12h[5]	Not for children <40 kg	64.20
Augmentin XR				134.00
Ampicillin – generic	250, 500 mg caps[3]	250-500 mg q6h	12.5-50 mg/kg q6h	2.20
Dicloxacillin – generic	250, 500 mg caps	125-500 mg q6h	12.5-50 mg/kg/d divided q6h	6.00
Tetracyclines				
Doxycycline – generic (capsules)	50, 100 mg caps[3]	100 mg q12h	2-4 mg/kg/d divided q12h[7]	
Vibramycin (Pfizer)			2-4 mg/kg/d divided q12h[7]	34.00
generic (tablets)	50, 75, 100, 150 mg tabs			54.70
Minocycline – generic	50, 75, 100 mg caps; 50, 75, 100 mg tabs	200 mg once, then 100 mg q12h	4 mg/kg once, then 2 mg/kg q12h[7]	44.20
Minocin (Onset Dermatologics)	50, 100 mg caps			5.85
extended-release – generic	45, 65, 90, 135, 115 mg ER tabs	1 mg/kg once daily	≥12 yrs: 1 mg/kg once daily	81.00
Solodyn (Medicis)	55, 65, 80, 105, 115 mg ER tabs			36.90[8]
				144.75[8]
Tetracycline HCl – generic	250, 500 mg caps, tabs	250-500 mg q6h	25-50 mg/kg/d divided q6h[7]	1.00
Other				
Clindamycin – generic	75, 150, 300 mg caps[3]	150-450 mg q6-8h	10 mg/kg q8h	24.82
Fosfomycin – *Monurol* (Forest)	3 g powder/packet	3 grams once	—	50.09
Telithromycin – *Ketek* (Sanofi)	300, 400 mg tabs	800 mg q24h	—	143.90
Linezolid – *Zyvox* (Pfizer)	600 mg tabs[3]	600 mg q12h	10 mg/kg q8h[9]	1115.10
Metronidazole – generic	250, 500 mg tabs; 375 mg caps	500 mg q6-8h	30 mg/kg/d divided q6h	7.35
Flagyl (Pfizer)				88.70
extended-release – *Flagyl ER*	750 mg ER tabs	750 mg once daily		65.80
Nitrofurantoin – macrocrystals – generic	25, 50, 100 mg caps[3]	50-100 mg q6h	5-7 mg/kg/d divided q6h	33.50
Macrodantin (PD-Rx)				42.00
monohydrate-macrocrystals– generic	100 mg caps	100 mg q12h	>12 yrs: 100 mg q12h	25.60
Macrobid (PD-Rx)				35.60
Trimethoprim/sulfamethoxazole generic	400/80 mg tabs	1 tablet q6h	8-12 mg/kg/d (TMP) divided q12h	12.00[6]
Bactrim (AR Scientific)				28.80
double strength (DS) – generic	800/160 mg tabs	1 DS tablet q12h		1.26
Bactrim DS				25.90
Vancomycin[10] – generic	125, 250 mg caps	125 mg q6h	10 mg/kg q6h	501.40
Vancocin (ViroPharma)				545.00[6]

5. Dosage based on amoxicillin content. For doses of 500 or 875 mg, 500-mg or 875-mg tablets should be used, because multiple smaller tablets would contain too much clavulanate. 125 mg/5 mL oral suspension contains 31.25 mg clavulanate; 250 mg/5 mL oral suspension contains 62.5 mg clavulanate.
6. Cost according to a local pharmacy.
7. Not recommended for children <8 years old.
8. Cost based on treatment of a 70-kg patient.
9. For children 5-11 years old. Usual dose for children ≥12 years old is 600 mg q12h.
10. Some pharmacies use the intravenous formulation for oral administration, which costs less.

and anaerobic bacteria.[5] **Chronic osteomyelitis**, common in complicated diabetic foot infection, usually requires surgical debridement of involved bone followed by 4-6 weeks of antibacterial therapy.

For empiric treatment of acute osteomyelitis, most expert clinicians would use vancomycin until culture and susceptibility results are available. Ceftriaxone, ceftazidime, cefepime or ciprofloxacin could be added for empiric treatment of gram-negative bacteria. Well-absorbed oral antibacterials, such as trimethoprim/sulfamethoxazole, metronidazole, linezolid, clindamycin or moxifloxacin, can be used depending on the susceptibility of the pathogen isolated from bone cultures.[6,7] Prolonged use of linezolid (>2 weeks) may cause bone marrow suppression and neuropathy.

Septic arthritis may be due to *S. aureus*, *S. pyogenes*, *Streptococcus pneumoniae*, gram-negative bacteria or *Neisseria gonorrhoeae*.[8] Ceftriaxone is a reasonable first choice for empiric treatment. Vancomycin, daptomycin or linezolid should be used for MRSA or methicillin-resistant coagulase-negative staphylococci.

Coagulase-negative staphylococci and *S. aureus* are the most common causes of **prosthetic joint infection**.[9] Empiric treatment is discouraged. Rifampin is often added to antistaphylococcal therapy because of its effectiveness against staphylococcal isolates that are adherent to the prosthesis.[10] Deep prosthetic joint infections can be difficult to eradicate without removal of the prosthesis.

UPPER RESPIRATORY TRACT INFECTIONS

Acute sinusitis in adults is often viral and can be managed with a nasal decongestant and possibly a nasal corticosteroid. When acute sinusitis is likely to be bacterial (symptoms for ≥10 days without improvement, severe symptoms or fever at onset and lasting ≥3 days, or worsening symptoms following a viral illness), it is usually caused by *S. pneumoniae*, *Haemophilus influenzae* or *Moraxella catarrhalis* and can generally be treated with an oral antibacterial such as amoxicillin/clavulanate. Monotherapy with a macrolide (erythromycin, clarithromycin or azithromycin), a cephalosporin, or trimethoprim/sulfamethoxazole is generally not recommended because of increasing resistance among pneumococci. Doxycycline or a fluoroquinolone with good antipneumococcal activity such as levofloxacin or moxifloxacin may be considered for adults who are allergic to penicillin.[11] Addition of an intranasal corticosteroid may improve symptoms and decrease the need for pain medications.[12]

Acute exacerbation of chronic bronchitis (AECB) is often viral. When it is bacterial, it may be caused by *H. influenzae*, *S. pneumoniae* or *M. catarrhalis* and can be treated with the same antimicrobials used to treat acute bacterial sinusitis. In patients with severe COPD, *P. aeruginosa* can be a cause of AECB and use of an antipseudomonal agent, such as ciprofloxacin, levofloxacin, ceftazidime or piperacillin/tazobactam, should be considered.

The most common bacterial cause of **acute pharyngitis** in adults and children is group A streptococci. Penicillin or amoxicillin is usually given for 10 days.[13] A first-generation cephalosporin can be used in patients with a history of non-anaphylactic penicillin allergy. Clindamycin, clarithromycin or azithromycin can be used in patients with a history of more severe penicillin allergy. Pharyngeal isolates of group A streptococci may be resistant to macrolides[14]; susceptibility testing should be performed.

PNEUMONIA

The organism responsible for **community-acquired bacterial pneumonia (CAP)** is often not confirmed, but *S. pneumoniae* and *Mycoplasma pneumoniae* are frequent pathogens. Among hospitalized patients with CAP, *S. pneumoniae* is still probably the most common cause. Other bacterial pathogens include *H. influenzae*, *S. aureus* and, occasionally, other gram-negative bacilli and anaerobic mouth organisms.

In **ambulatory** patients, an oral macrolide (erythromycin, azithromycin or clarithromycin) or doxycycline is generally recommended for otherwise healthy adults. Pneumococci may, however, be resistant to macrolides and to doxycycline, especially if they are resistant to penicillin.[15] A fluoroquinolone with good antipneumococcal activity such as levofloxacin or moxifloxacin is generally used for adults with comorbidities or antibiotic exposure during the past 90 days.[16] Macrolides and respiratory fluoroquinolones can prolong the QT interval and rarely cause life-threatening ventricular arrhythmias; these drugs should be used with caution in patients with cardiovascular disease or risk factors for QT prolongation and arrhythmia.[17] Doxycycline plus amoxicillin may be an alternative in such patients.

In CAP requiring hospitalization (not ICU), an IV beta-lactam (such as ceftriaxone, cefotaxime or ceftaroline) plus a macrolide (azithromycin or clarithromycin), or monotherapy with a fluoroquinolone with good activity against *S. pneumoniae* (levofloxacin or moxifloxacin) is recommended pending culture results.[16] Although clinical data are limited, some expert clinicians would substitute doxycycline for the macrolide in patients with underlying cardiac disease or risk factors for QT interval prolongation. In severe cases, MRSA should be considered as a possible pathogen and vancomycin or linezolid should be added.[3] If aspiration pneumonia is suspected, metronidazole or clindamycin could be added; moxifloxacin or ampicillin/sulbactam, which also have anaerobic activity, are reasonable alternatives.

In treating pneumococcal pneumonia due to strains with an intermediate degree of penicillin resistance (minimal inhibitory concentration [MIC] 4 mcg/mL), ceftriaxone, cefotaxime, or high doses of either IV penicillin or oral amoxicillin can be used. For resistant strains (MIC ≥8 mcg/mL), a fluoroquinolone (levofloxacin or moxifloxacin), vancomycin, or linezolid should be used in severely ill patients (such as those requiring admission to an ICU) and those not responding to a beta-lactam.

Hospital-acquired, healthcare-associated and ventilator-associated pneumonia are often caused by gram-negative bacilli, especially *Klebsiella* spp., *E. coli*, *Enterobacter* spp., *Serratia* spp., *P. aeruginosa*,

and *Acinetobacter* spp.; they can also be caused by *S. aureus*, usually MRSA. Many of these bacteria may be multi-drug resistant, particularly when disease onset is after a long hospital admission with prior antibacterial therapy, and further resistance can emerge during treatment. Pneumonia with *S. aureus*, particularly methicillin-resistant strains, is also more common in patients with diabetes mellitus, head trauma, or who are admitted to an ICU. Hospital-acquired pneumonia due to *Legionella* species can also occur, usually in immunocompromised patients.[18]

In the absence of risk factors for multi-drug resistant organisms, initial empiric therapy can be limited to one antibiotic, such as ceftriaxone, a fluoroquinolone (levofloxacin or moxifloxacin) or ertapenem. In other patients, however, particularly those who are severely ill or in the ICU, broader-spectrum coverage with an antipseudomonal beta-lactam such as piperacillin/tazobactam, cefepime, imipenem, doripenem or meropenem would be a reasonable choice. Addition of vancomycin or linezolid should be considered in institutions where MRSA is common.

GENITOURINARY TRACT INFECTIONS

URINARY TRACT INFECTION (UTI) — *E. coli* causes most episodes of uncomplicated cystitis and pyelonephritis. Most of the remaining cases are caused by *Staphylococcus saprophyticus*, *Klebsiella pneumoniae*, *Proteus* spp., other gram-negative rods or enterococci. Asymptomatic bacteriuria and pyuria in women is usually not an indication for antibiotic treatment.[19]

Fluoroquinolones (especially ciprofloxacin) have become the most common class of antibiotics prescribed for UTI, but they should not be used as first-line agents for empiric treatment of acute uncomplicated cystitis.[20] Other drugs are generally preferred due to concerns about cost-effectiveness and emerging resistance. The drug of choice for empiric treatment of **acute uncomplicated cystitis** for non-pregnant women is trimethoprim/sulfamethoxazole for 3 days, as long as the local rate of resistance to trimethoprim/sulfamethoxazole among urinary pathogens is <20%. An equally effective alternative with a low rate of resistance among *E. coli* is nitrofurantoin for 5 days.[21] A single dose of fosfomycin, which has a broad spectrum of activity against the usual uropathogens, is another alternative.[22] Beta-lactams such as amoxicillin/clavulanate, cefdinir, cefpodoxime or ceftibuten could also be considered, but are less likely to be effective.[23] Based on the results of susceptibility testing, nitrofurantoin, amoxicillin or a cephalosporin could be used to treat UTIs in pregnant women, but nitrofurantoin should not be given in the third trimester or during labor and delivery because it can cause hemolytic anemia in the newborn.[24]

In areas where the prevalence of resistance to fluoroquinolones among uropathogens is <10%, a 7-day course of ciprofloxacin or 5 days of levofloxacin is a reasonable first choice for empiric outpatient treatment of non-pregnant women with **acute uncomplicated pyelonephritis**. Trimethoprim/sulfamethoxazole for 7-14 days is an alternative for treatment of susceptible uropathogens. Another alternative is a single IV dose of the third-generation cephalosporin ceftriaxone, followed by 7-14 days of an oral antimicrobial to which the pathogen is susceptible. Oral beta-lactams are generally considered less effective for treatment of pyelonephritis than fluoroquinolones or trimethoprim/sulfamethoxazole.[23]

Complicated UTIs occur in patients with indwelling urinary catheters or anatomic or functional abnormalities of the urinary tract and are more likely to be caused by antibiotic-resistant gram-negative bacilli, *S. aureus* or enterococci (including vancomycin-resistant strains). An oral fluoroquinolone, such as ciprofloxacin or levofloxacin, can be used to treat such infections in outpatients. Other oral antibiotics that can be used if the infecting organism is found to be susceptible include trimethoprim/sulfamethoxazole, amoxicillin/clavulanate or an oral third-generation cephalosporin such as cefdinir or ceftibuten. In hospitalized patients with complicated UTI, empiric parenteral treatment with cefepime, a third-generation cephalosporin such as ceftriaxone, a fluoroquinolone, ticarcillin/clavulanate, piperacillin/tazobactam, or a carbapenem is generally recommended.

PROSTATITIS — Acute bacterial prostatitis may be caused by enteric gram-negative bacteria, especially *E. coli*, *Proteus* spp. and *Klebsiella* spp., or by *P. aeruginosa* or *Enterococcus* spp.. Occasionally, a sexually transmitted organism such as *N. gonorrhoeae*, *Chlamydia trachomatis* or *Ureaplasma urealyticum* is responsible. Chronic prostatitis may be caused by the same bacteria as acute prostatitis, or by *S. aureus* or coagulase-negative staphylococci.

An oral fluoroquinolone with activity against *P. aeruginosa* (ciprofloxacin or levofloxacin) is a reasonable choice for initial treatment of acute bacterial prostatitis in a patient who does not require hospitalization. Trimethoprim/sulfamethoxazole could be used as an alternative. For more severe prostatitis, an IV fluoroquinolone or third-generation cephalosporin could be used. Prostatic abscesses may require drainage in addition to antimicrobial treatment. Chronic bacterial prostatitis is generally treated with a long course (4-12 weeks) of an oral fluoroquinolone or trimethoprim/sulfamethoxazole.[25]

Table 2. Some Parenteral Antibacterial Drugs

Drug	Some Available Formulations	Usual Adult Dosage[1]	Usual Pediatric Dosage[1]	Cost[2]
Aminoglycosides				
Amikacin – generic	50, 250 mg/mL vials	7.5 mg/kg q12h or 15-20 mg/kg once dialy	7.5 mg/kg q12h	$46.15
Gentamicin – generic	10, 40 mg/mL vials	5-7 mg/kg once daily or 1-2.5 mg/kg q8h	1-2.5 mg/kg q8h	26.25
Tobramycin – generic	10, 40 mg/mL vials; 1.2 g vial	5-7 mg/kg once daily or 1-2.5 mg/kg q8h	1-2.5 mg/kg q8h	49.50
Carbapenems				
Doripenem – *Doribax* (Janssen)	250, 500 mg vials	500 mg q8h	—	574.95
Ertapenem – *Invanz* (Merck)	1 g vial	1 g once daily	15 mg/kg q12h	353.70
Imipenem/cilastatin – generic	250, 500 mg vials	500 mg-1 g q6-8h	15-25 mg/kg q6h	255.15
Primaxin (Merck)				489.75
Meropenem – generic	500, 1 g vial	500 mg-2 g q8h	20-40 mg/kg q8h	90.00
Merrem (AstraZeneca)				503.40
Cephalosporins				
Cefazolin – generic	500 mg, 1, 10 g vials	500 mg-2 g q6-8h	25-100 mg/kg/d divided q6-8h	27.00
Cefepime – generic	500 mg, 1, 2 g vials	1-2 g q8-12h	50 mg/kg q8-12h	82.64
Maxipime (Hospira)				65.00
Cefotaxime – generic	500 mg, 1, 2, 10 g vials	1-2 g q4-12h	50-200 mg/kg/d	51.86
Claforan (Sanofi)			divided q4-6h	24.60
Cefotetan – generic	1, 2, 10 g vials	500 mg-3 g q12h	20-50 mg/kg q12h	56.90
Cefoxitin – generic	1, 2, 10 g vials	1-2 g q6-8h	80-160 mg/kg/d divided q6h	97.50
Ceftaroline – *Teflaro* (Forest)	400, 600 mg vials	600 mg q12h	—	499.80
Ceftazidime – generic	500 mg, 1, 2, 6 g vials	500 mg-2 g q8-12h	30-100 mg/kg q8h	55.00
Fortaz (Covis)				59.30
Ceftriaxone – generic	250, 500 mg, 1, 2, 10 g vials	1-2 g q12-24h	50-100 mg/kg/d	17.50
Rocephin (Roche)	500 mg, 1 g vials		divided q12-24h	308.25
Cefuroxime – generic	750 mg, 1.5, 7.5 g vials	750 mg-1.5 g q8-12h	50-150 mg/kg/d	26.00
Zinacef (Covis)			divided q8h	58.40
Fluoroquinolones				
Ciprofloxacin – generic	400 mg/40 mL, 200 mg/20 mL	400 mg q8-12h	10-15 mg/kg q8-12h[3]	29.50
Cipro (Bayer)	vials			31.50
Levofloxacin – generic	500 mg/20 mL, 750 mg/30 mL	250-750 mg once daily	See footnote 3	105.99
Levaquin (Janssen)	vials			182.60
Moxifloxacin – *Avelox* (Bayer)	400 mg/250 mL bag	400 mg once daily	See footnote 3	175.00
Macrolides				
Azithromycin – generic	500 mg vial	500 mg once daily	5-10 mg/kg once daily	36.45
Zithromax (Pfizer)				30.00
Erythromycin – generic	500 mg, 1 g vials	500 mg-1 g IV q6h	15-50 mg/kg/d divided q6h	472.60

1. Dosage may vary based on the site of infection, infecting organism and patient specific characteristics, such as renal and hepatic function. Higher or lower doses than those listed here may be needed. Listed pediatric dosages may not apply for premature infants and newborns. Pediatric dosage generally should not exceed maximum adult dosage.
2. Wholesale acquisition cost (WAC) of 5 days' treatment for a 70-kg patient with the lowest recommended adult dosage. $ource® Monthly (Selected from FDB MedKnowledge™) June 5, 2013. Reprinted with permission by FDB, Inc. All rights reserved. ©2013. www.fdbhealth.com/policies/drug-pricing-policy. Actual retail prices may be higher.
3. Not recommended for routine use in children or adolescents <18 years old.

INTRA-ABDOMINAL INFECTIONS

Most intra-abdominal infections, such as **cholangitis** and **diverticulitis,** are caused by enteric gram-negative organisms, most commonly *E. coli*, but also *Klebsiella* or *Proteus* spp.. Enterococci and anaerobes, particularly *Bacteroides fragilis*, are also common. Changes in bowel flora, such as those that occur in hospitalized patients treated with antibiotics, lead to an increased risk of infections due to *P. aeruginosa* and *Candida* spp.. Many intra-abdominal infections, particularly abscesses, are polymicrobial.

Empiric therapy should cover both enteric aerobic gram-negative and anaerobic organisms and gram-positive streptococci. For community-acquired infection of mild to moderate severity, monotherapy with ticarcillin/clavulanate, ertapenem or moxifloxacin would be a reasonable choice. Ampicillin/sulbactam, cefotetan and clindamycin should no longer be used.[26] In severely ill patients and those with prolonged hospitalization, treatment should include coverage for *P. aeruginosa.* Reasonable choices would include an antipseudomonal penicillin (piperacillin/tazobactam) or carbapenem (imipenem, meropenem or doripenem). Ceftazidime, cefepime, aztreonam or ciprofloxacin, each plus metronidazole for *B. fragilis* coverage, could also be given. Tigecycline, an IV tetracycline with a very broad spectrum of activity, is FDA-approved for treatment of complicated intra-abdominal infections,

Table 2. Some Parenteral Antibacterial Drugs (continued)

Drug	Some Available Formulations	Usual Adult Dosage[1]	Usual Pediatric Dosage[1]	Cost[2]
Penicillins				
Ampicillin – generic	125, 250, 500 mg; 1, 2, 10 g vials	500 mg-2 g q6h	25-50 mg/kg q6h	$57.20
Ampicillin/sulbactam – generic	1 g/500 mg, 2 g/1 g,	1.5-3 g q6h	25-50 mg/kg ampicillin q6h	70.00
Unasyn (Pfizer)	10 g/5 g vials			152.00
Oxacillin – generic	1, 2, 10 g vial	1-2 g q4-6h	25-50 mg/kg q6h	228.20
Penicillin G potassium – generic	1, 5, 20 million unit vials	2-4 million units q4h	100,000-250,000 units/kg/d divided q4-6h	525.00
Piperacillin/tazobactam – generic	2 g /250 mg, 3 g/375 mg,	3.375 g q6h	240-300 mg/kg/d piperacillin	195.43
Zosyn (Pfizer)	4 g/500 mg vials	or 4.5 g q6-8h	divided q8h	381.60
Ticarcillin/clavulanic acid – *Timentin* (GSK)	3 g/100 mg, 30 g/1 g vials	3.1 g q4-6h	200-300 mg/kg/d ticarcillin divided q4-6h	271.80
Tetracyclines				
Doxycycline – generic	100 mg vial	100-200 mg q12h	2-5 mg/kg/d divided q12h[4]	68.17
Tigecycline – *Tygacil* (Pfizer)	50 mg vial	100 mg x1, then 50 mg q12h	See footnote 4	612.50
Other				
Aztreonam – generic	1, 2 g vials	1-2 g q6-8h	30 mg/kg q6-8h	494.25
Azactam (BMS)				435.00
Chloramphenicol – generic	1 g vial	12.5-25 mg/kg q6h	12.5-25 mg/kg q6h	598.80
Clindamycin – generic	150 mg/mL vial	300-900 mg q8h	5-10 mg/kg q8h	55.35
Colistin (colistimethate sodium) generic	150 mg vial	2.5 mg/kg q12h[5]	2.5-5 mg/kg/d in 2-3 divided doses[5]	280.00
Coly-Mycin M (JHP Pharms)				
Daptomycin – *Cubicin* (Cubist)	500 mg/vial	4-8 mg/kg q24h		1510.00
Linezolid – *Zyvox* (Pfizer)	200 mg/100 mL, 400 mg/200 mL, 600 mg/300 mL bags	600 mg q12h	10 mg/kg q8h[6]	1203.30
Metronidazole – generic	500 mg/100 mL	500 mg q6-8h	7.5 mg/kg q6-8h	22.39
Flagyl (Pfizer)				N.A.
Polymyxin B – generic	500,000 units/vial	2.5 mg/kg/d divided q12h[7]	≥2 yrs: 2.5 mg/kg/d divided q12h <2 yrs: 2.5-4 mg/kg/d divided q12h	123.75
Vancomycin – generic	500 mg, 1, 5, 10 g vials	15-20 mg/kg IV q8-12h[8]	10-15 mg/kg IV q6h[8]	49.45
Quinupristin/dalfopristin – *Synercid* (King)	150/350 mg vial	7.5 mg/kg q8-12h	7.5 mg/kg q8-12h	3093.15

N.A. = Cost not available
4. Not recommended for children <8 years old.
5. A loading dose of 5 mg/kg is recommended; caution with loading doses >300 mg. Maximum recommended daily maintenance dose is 475 mg. (L Dalfino et al. Clin Infect Dis 2012; 54:1720).
6. For children 5-11 years old; ≥12 yrs: 600 mg q12h. Preterm neonates <1 week old should receive 10 mg/kg q12h initially.
7. 1 mg = 10,000 units. A loading dose of 2.5-3 mg/kg is recommended.
8. Dose based on actual body weight. In seriously ill patients, a loading dose of 25-30 mg/kg can be considered to rapidly achieve target concentrations. Vancomycin should be infused over a period of at least 60 minutes.

but its use for this and other serious infections has been associated with an increase in mortality.[27-29]

Clostridium difficile is the most common identifiable cause of antibiotic-associated diarrhea.[30] The incidence and severity of ***C. difficile* infection (CDI)** have increased in recent years with the emergence of an epidemic hypervirulent strain (NAP1/B1/027), possibly related to widespread use of fluoroquinolones. Oral metronidazole can be used to treat mild to moderate CDI. Patients with severe disease and those with a delayed response to metronidazole should be treated with oral vancomycin.[31,32] First recurrences of CDI are generally treated like the initial episode (metronidazole for mild to moderate and oral vancomycin for severe disease). Subsequent recurrences may be treated with 10-14 days of oral vancomycin followed by a prolonged tapered or pulsed regimen of oral vancomycin to allow for *C. difficile* spore germination and restoration of normal gut flora.[33] Fidaxomicin appears to be at least as effective for treatment of CDI as oral vancomycin with fewer recurrences in patients not infected with the epidemic hypervirulent strain.[34] No data are available on the effectiveness of fidaxomicin in patients who have had multiple recurrences of CDI after treatment with metronidazole or vancomycin.[35]

MENINGITIS

The organisms most commonly responsible for community-acquired bacterial meningitis in children and adults are *S. pneumoniae* (pneumococcus) and *Neisseria meningitidis* (meningococcus). Vaccines

have dramatically decreased the incidence of pediatric meningitis due to *H. influenzae* type b and pneumococci in children.[36] Enteric gram-negative bacteria can cause meningitis in neonates, the elderly, and in patients who have had recent nosocomial infections or neurosurgery, or are immunosuppressed.[37] Coagulase-negative staphylococci, *S. aureus* and, less commonly, diphtheroids such as *Propionibacterium acnes* can cause meningitis in patients who have had recent neurosurgery or have cerebrospinal fluid shunts or other CNS devices. Group B streptococcus often causes meningitis in neonates or in the elderly. Infection with *Listeria monocytogenes* can occur in pregnant women, neonates, immunosuppressed patients and patients who are >50 years old or abuse alcohol.[38]

For empiric treatment of meningitis in **adults and children >2 months old,** ceftriaxone or cefotaxime plus vancomycin (to cover highly penicillin- or cephalosporin-resistant pneumococci) is generally recommended. Some experts would add rifampin to empiric vancomycin in patients also receiving dexamethasone. Vancomycin should be stopped if the etiologic organism proves to be susceptible to ceftriaxone or cefotaxime. Ampicillin, sometimes in combination with gentamicin for severely ill patients, is added in patients in whom *L. monocytogenes* is a consideration.

Neonatal meningitis is most often caused by group B streptococci, gram-negative enteric organisms, or *L. monocytogenes.* For infants ≤2 months old, many pediatric specialists use ampicillin plus ceftriaxone, cefotaxime or cefepime, with or without gentamicin, while awaiting the results of culture and susceptibility tests. For empiric treatment of **nosocomial** meningitis, vancomycin and a cephalosporin with good activity against *P. aeruginosa*, such as ceftazidime, are appropriate. In hospitals where gram-negative bacilli that produce extended-spectrum ß-lactamases are common, use of meropenem or doripenem should be considered instead of a cephalosporin.

Ceftriaxone or cefotaxime can often be used safely to treat meningitis in **penicillin-allergic** patients.[39] For coverage of enteric gram-negative bacilli and *P. aeruginosa* in patients with significant penicillin and cephalosporin allergy, aztreonam could be considered. Trimethoprim/sulfamethoxazole can be used for treatment of *Listeria* meningitis in patients allergic to penicillin. As with nonallergic patients, vancomycin should be added initially to cover resistant pneumococci.

A corticosteroid, usually parenteral dexamethasone (*Decadron*, and generics), started before or at the same time as the first dose of antibiotics and continued for 4 days, has been reported to decrease the incidence of hearing loss in children, particularly with *H. influenzae* meningitis, and of neurological complications and mortality in adults.[40] The benefits in adults have been most striking in those with pneumococcal meningitis.

OTHER INFECTIONS

SEPSIS SYNDROME — For treatment of sepsis syndrome, the choice of drugs should be based on the probable source of infection, the causative organism, and the patient's immune status and recent antibiotic history. The choice should also reflect local patterns of bacterial resistance.[41]

For initial treatment of life-threatening sepsis in adults, a third- or fourth-generation cephalosporin (ceftazidime or cefepime), piperacillin/tazobactam, imipenem, doripenem or meropenem, each plus vancomycin, is recommended. Some experts would add an aminoglycoside or a fluoroquinolone for a brief period (2-3 days).[42] Linezolid can be used as an alternative to vancomycin.

BACTERIAL ENDOCARDITIS — *Staphylococcus* spp. and *Streptococcus* spp. are the most common pathogens in bacterial endocarditis.[43] A combination of ceftriaxone and vancomycin can be used if therapy must be started before the pathogen is identified. Many expert clinicians would also add low-dose gentamicin to cover *Enterococcus* spp. until cultures and susceptibility data are available.

FEVER AND NEUTROPENIA — Most fevers in patients with neutropenia are of unknown origin. Gram-positive bacteria account for the majority of microbiologically confirmed infections (especially in patients with central venous catheters), but enteric gram-negative organisms and *P. aeruginosa* pose the greatest threat to the neutropenic patient.

Empiric treatment with oral ciprofloxacin plus amoxicillin/clavulanate is recommended for neutropenic patients with a fever who are considered to be at low risk.[44] In higher-risk patients, ceftazidime, piperacillin/tazobactam, imipenem, doripenem, meropenem or cefepime, with or without an aminoglycoside, would be a reasonable first choice. Addition of vancomycin should be considered for patients at risk for infection with methicillin-resistant staphylococci or penicillin-resistant viridans streptococci, such as those with suspected catheter-related infection, pneumonia, or skin and soft tissue infection. When the response to antibacterials is poor, the possibility of fungemia, especially with *Candida* spp., should be considered.

MULTI-DRUG RESISTANT ORGANISMS

ENTEROCOCCI — Many *Enterococcus* spp., particularly *E. faecium*, are resistant to penicillin and ampicillin, to gentamicin or streptomycin, or both, and to vancomycin. Some of these strains are susceptible *in vitro* to chloramphenicol, doxycycline or, rarely, fluoroquinolones, but clinical results with these drugs have been variable. Linezolid, daptomycin and tigecycline are active against many gram-positive organisms, including both *E. faecium* and *E. faecalis*; resistance to these drugs has been relatively rare. Quinupristin/dalfopristin, which is not commonly used because of its toxicity and drug interactions, is active against most strains of vancomycin-resistant *E. faecium*, but not *E. faecalis*.[45] Polymicrobial surgical infections that include antibiotic-resistant enterococci may respond to antibiotics aimed at other organisms. When antibiotic-resistant enterococci cause endocarditis, surgical replacement of the infected valve may be required. UTIs caused by resistant enterococci may respond nevertheless to ampicillin or amoxicillin, which reach very high concentrations in urine; nitrofurantoin or fosfomycin can also be used.

GRAM-NEGATIVE BACTERIA — Infections with multi-drug resistant gram-negative bacteria, including Enterobacteriaceae that produce extended-spectrum beta-lactamases (ESBL) or carbapenemases, *P. aeruginosa* and certain species of *Acinetobacter*, are increasingly common, particularly among hospitalized patients. These bacteria can cause a variety of clinical syndromes, including pneumonia (particularly in association with mechanical ventilation), skin and soft tissue infection, intra-abdominal infection, and urinary tract infection. The treatment of choice for serious infections with Enterobacteriaceae producing ESBL is a carbapenem, such as imipenem or meropenem.[46,47] Treatment options for carbapenemase-producing Enterobacteriaceae include polymyxin B, colistin, and tigecycline. Fosfomycin is an oral treatment option for urinary tract infections caused by carbapenemase-producing Enterobacteriaceae.[48,49] Multi-drug resistant isolates of *P. aeruginosa* may be susceptible to polymyxin B or colistin.[50] *Acinetobacter* spp. may be susceptible to ceftazidime, cefepime, imipenem, meropenem or ampicillin-sulbactam (the sulbactam component); addition of an aminoglycoside or fluoroquinolone may be considered. Multi-drug resistant isolates of *Acinetobacter* spp. may be susceptible to polymyxin B, colistin and tigecycline.[51] Combination therapy is recommended for all of these infections.

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2. Discuss the pharmacologic agents available for treatment of common bacterial infections and compare them based on their efficacy, dosage and administration and potential adverse effects.
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Issue 131 Questions

1. Uncomplicated skin and soft tissue infections in immunocompetent patients are commonly caused by:
   a. *Streptococcus pyogenes*
   b. *Pseudomonas aeruginosa*
   c. *Escherichia coli*
   d. anaerobes

2. A 53-year-old otherwise healthy woman presents with a simple abscess. Initial treatment should include:
   a. incision and drainage
   b. vancomycin
   c. moxifloxacin
   d. linezolid

3. Which of the following could be used for empiric treatment of serious skin and soft tissue infections suspected to be caused by methicillin-resistant *Staphylococcus aureus*:
   a. vancomycin
   b. linezolid
   c. daptomycin
   d. all of the above

4. The most common cause of acute osteomyelitis is:
   a. *Salmonella* spp.
   b. *Streptococcus pneumoniae*
   c. *Staphylococcus aureus*
   d. *Neisseria gonorrhoeae*

5. A 64-year-old woman with a complicated diabetic foot infection recently underwent surgical debridement of the involved bone. She is going on vacation and wants to know how long she will be on antibiotic therapy. Which of the following would you tell her?
   a. 1 week
   b. 2 weeks
   c. 3 weeks
   d. 4-6 weeks

6. Which of the following is recommended as monotherapy for empiric treatment of acute bacterial sinusitis?
   a. trimethoprim/sulfamethoxazole
   b. erythromycin
   c. clarithromycin
   d. none of the above

7. Which of the following is recommended for treatment of acute sinusitis due to *Streptococcus pneumoniae*?
   a. erythromycin
   b. clarithromycin
   c. azithromycin
   d. amoxicillin/clavulanate

8. The drug of choice for treatment of acute pharyngitis in children is:
   a. amoxicillin
   b. vancomycin
   c. clindamycin
   d. linezolid

9. Which of the following would be a reasonable choice for first-line treatment of community-acquired bacterial pneumonia in an otherwise healthy ambulatory adult?
   a. doxycycline
   b. penicillin
   c. ceftaroline
   d. tigecycline

10. Which of the following should not be used for treatment of a near-term pregnant woman with urinary tract infection because it can cause hemolytic anemia in the newborn?
    a. cephalexin
    b. nitrofurantoin
    c. amoxicillin
    d. trimethoprim/sulfamethoxazole

11. Which of the following is a reasonable choice for initial treatment of acute bacterial prostatitis in a patient who does not require hospitalization?
    a. ciprofloxacin
    b. nitrofurantoin
    c. amoxicillin
    d. metronidazole

12. Which of the following is often a cause of meningitis in pregnant women?
    a. *Salmonella* spp.
    b. *Propionibacterium acnes*
    c. *Listeria monocytogenes*
    d. *Neisseria gonorrhoeae*

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