Skin and Soft Tissue Infections

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Skin and soft tissue infections result from microbial invasion of the skin and its supporting structures. Management is determined by the severity and location of the infection and by patient comorbidities. Infections can be classified as simple (uncomplicated) or complicated (necrotizing or nonnecrotizing), or as suppurative or nonsuppurative. Most community-acquired infections are caused by methicillin-resistant *Staphylococcus aureus* and beta-hemolytic streptococcus. Simple infections are usually monomicrobial and present with localized clinical findings. In contrast, complicated infections can be mono- or polymicrobial and may present with systemic inflammatory response syndrome. The diagnosis is based on clinical evaluation. Laboratory testing may be required to confirm an uncertain diagnosis, evaluate for deep infections or sepsis, determine the need for inpatient care, and evaluate and treat comorbidities. Initial antimicrobial choice is empiric, and in simple infections should cover *Staphylococcus* and *Streptococcus* species. Patients with complicated infections, including suspected necrotizing fasciitis and gangrene, require empiric polymicrobial antibiotic coverage, inpatient treatment, and surgical consultation for debridement. Superficial and small abscesses respond well to drainage and seldom require antibiotics. Immunocompromised patients require early treatment and antimicrobial coverage for possible atypical organisms. (*Am Fam Physician*. 2015;92(6):474-483. Copyright © 2015 American Academy of Family Physicians.)

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CME This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz Questions on page 441.

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▶ Patient information: A handout on this topic, written by the authors of this article, is available at http://www.aafp.org/ afp/2015/0915/p474-s1. html. kin and soft tissue infections (SSTIs) account for more than 14 million physician office visits each year in the United States, as well as emergency department visits and hospitalizations.¹ The greatest incidence is among persons 18 to 44 years of age, men, and blacks.^{1,2} Community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) accounts for 59% of SSTIs presenting to the emergency department.³

Classification

SSTIs are classified as simple (uncomplicated) or complicated (necrotizing or nonnecrotizing) and can involve the skin, subcutaneous fat, fascial layers, and musculotendinous structures.⁴ SSTIs can be purulent or nonpurulent (mild, moderate, or severe).⁵ To help stratify clinical interventions, SSTIs can be classified based on their severity, presence of comorbidities, and need for and nature of therapeutic intervention (*Table 1*).³

Simple infections confined to the skin and underlying superficial soft tissues generally respond well to outpatient management. Common simple SSTIs include cellulitis, erysipelas, impetigo, ecthyma, folliculitis, furuncles, carbuncles, abscesses, and traumarelated infections⁶ (*Figures 1 through 3*). Complicated infections extending into and involving the underlying deep tissues include deep abscesses, decubitus ulcers, necrotizing fasciitis, Fournier gangrene, and infections from human or animal bites⁷ (*Figure 4*). These infections may present with features of systemic inflammatory response syndrome or sepsis, and, occasionally, ischemic necrosis. Perianal infections, diabetic foot infections, infections in patients with significant comorbidities, and infections from resistant pathogens also represent complicated infections.⁸

Risk Factors

Older age, cardiopulmonary or hepatorenal disease, diabetes mellitus, debility, immunosenescence or immunocompromise, obesity, peripheral arteriovenous or lymphatic insufficiency, and trauma are among the risk factors for SSTIs (*Table 2*).⁹⁻¹¹ Outbreaks are more common among military personnel during overseas deployment and athletes participating in close-contact sports.^{12,13} Community-acquired MRSA causes infection in a wide variety of hosts, from healthy children and young adults to persons with comorbidities, health care professionals, and persons living in close quarters.

Table 1. Classification System for Skin and Soft Tissue Infections

Class	Description
1	Simple infection with no systemic signs or symptoms indicating spread* and no uncontrolled comorbidities that may complicate treatment; amenable to outpatient management with topical or oral antimicrobials
2	Infection with systemic signs or symptoms indicating spread* or with stable comorbidities, or infection without systemic spread but with uncontrolled comorbidities; may require inpatient management or parenteral antibiotics
3	Infection with signs or symptoms of systemic spread* or uncontrolled comorbidities; inpatient management with parenteral antibiotics required
4	Infection with signs of potentially fatal systemic sepsist requiring parenteral antibiotics; inpatient management (possibly in critical care unit) required, surgery may be indicated

*—Signs and symptoms indicating spread of infection: fever, tachycardia, diaphoresis, fatigue, anorexia, and vomiting.

†—Signs indicating systemic sepsis: mental status changes, tachycardia, tachypnea, and hypotension.

Information from reference 3.



Figure 1. Cellulitis anterior to abdominal wall.



Figure 2. Abscess over left gluteal region.

Predisposing factors for SSTIs include reduced tissue vascularity and oxygenation, increased peripheral fluid stasis and risk of skin trauma, and decreased ability to combat infections. For example, diabetes increases the risk of infection-associated complications fivefold.¹⁴ Comorbidities and mechanisms of injury can determine the bacteriology of SSTIs (*Table 3*).^{5,15} For instance,



Figure 3. Furuncle.



Figure 4. Pyoderma gangrenosum.

Table 2. Risk Factors for Skin and Soft Tissue Infections

Age (children,* older adults)	Human or animal bites	Obesity
Alcohol abuse†	Immunocompromise (e.g., human immunodeficiency	Peripheral arteriovenous insufficiency
Asplenia	virus infection, chemotherapy, antiretroviral	Peripheral neuropathy
Cardiopulmonary disease	therapy, disease-modifying antirheumatic drugs)	Poor nutrition†
Debility	Immunosenescence	Prolonged hospitalization‡
Diabetes mellitus†‡	Long-term care‡	Sports participation†
Dialysis (peritoneal, hemodialysis)‡	Long-term intravascular access‡	Subcutaneous or intravenous drug use
Health care professional*	Lymphedema or lymphatic insufficiency	Trauma (including surgery)†
Hepatorenal disease	Military personnel*	Water exposure (e.g., ocean, hot tubs)

*—Risk factor for community-acquired methicillin-resistant Staphylococcus aureus infection.

†—Also predisposes to necrotizing fasciitis.

‡-Risk factor for hospital-acquired methicillin-resistant S. aureus infection.

Information from references 9 through 11.

Table 3. Bacteriology and Clinical Features of Skin and Soft Tissue Infections

Infection	Microbiology	Clinical features
Abscess	Staphylococcus aureus, Streptococcus, anaerobes (often polymicrobial)	Collection of pus with surrounding granulation; painful swelling with induration and central fluctuance; possible overlying skin necrosis; signs or symptoms of infection*; features attenuated in cold abscess; recurrent abscesses with sinus tracts and scarring in axillae and groin occur in hidradenitis suppurativa
Bites (human, animal)	Polymicrobial (Bacteroides, Bartonella henselae, Capnocytophaga canimorsus, Eikenella corrodens, Pasteurella multocida, Peptostreptococcus, S. aureus, Streptobacillus moniliformis)	Cat bites become infected more often than dog or human bites (30% to 50%, up to 20%, and 10% to 50%, respectively); infection sets in 8 to 12 hours after animal bites; human bites may transmit herpes, hepatitis, or human immunodeficiency virus; may involve tendons, tendon sheaths, bone, and joints
Clostridial myonecrosis (gas gangrene)	Clostridium (usually C. perfringens, C. septicum)	Traumatic or spontaneous; severe pain at injury site followed by skin changes (e.g., pale, bronze, purplish red), tenderness, induration, blistering, and tissue crepitus; diaphoresis, fever, hypotension, and tachycardia
Erysipelas, cellulitis	Beta-hemolytic streptococci, Haemophilus influenzae (children), S. aureus	Erysipelas: usually over face, ears, or lower legs; distinctly raised inflamed skin Cellulitis: over areas of skin breakdown Signs or symptoms of infection,* lymphangitis or lymphadenitis, leukocytosis
Folliculitis	Candida, dermatophytes, Pseudomonas aeruginosa, S. aureus	Infection or inflammation of the hair follicles; tends to occur in areas with increased sweating; associated with acne or steroid use; painful or painless pustule with underlying swelling
Fournier gangrene	Polymicrobial	Genital, groin, or perineal involvement; cellulitis, and signs or symptoms of infection* followed by suppuration and necrosis of overlying skin
Furuncle, carbuncle (deep folliculitis)	S. aureus	Walled-off collection of pus; painful, firm swelling; systemic features of infection; carbuncles are larger, deeper, and involve skin and subcutaneous tissue over thicker skin of neck, back, and lateral thighs, and drain through multiple pores
Impetigo (non- bullous, bullous)	Beta-hemolytic streptococci, <i>S. aureus</i>	Common in infants and children; affects skin of nose, mouth, or limbs; mild soreness, redness, vesicles, and crusting; may cause glomerulonephritis; vesicles may enlarge (bullae); may spread to lymph nodes, bone, joints, or lung
Necrotizing fasciitis	Type 1: polymicrobial Type 2: monomicrobial	Spreading infection of subcutaneous tissue; usually affects genitalia, perineum, or lower extremities; severe, constant pain; signs or symptoms of infection*; overlying redness and cutaneous anesthesia; edema and induration of apparently uninvolved tissues; skin crepitus; progression despite antibiotics

*—Signs and symptoms of infection include fever, tachycardia, diaphoresis, fatigue, anorexia, nausea, and vomiting. Mental status changes and hypotension suggest worsening sepsis and hemodynamic compromise.

Information from references 5 and 15.

Pseudomonas aeruginosa infections are associated with intravenous drug use and hot tub use, and patients with neutropenia more often develop infections caused by gram-negative bacteria, anaerobes, and fungi.

Pathogenesis

Most SSTIs occur de novo, or follow a breach in the protective skin barrier from trauma, surgery, or increased tissue tension secondary to fluid stasis. The infection may also originate from an adjacent site or from embolic spread from a distant site. S. aureus and streptococci are responsible for most simple community-acquired SSTIs. In one prospective study, beta-hemolytic streptococcus was found to cause nearly three-fourths of cases of diffuse cellulitis.¹⁶ S. aureus, P. aeruginosa, enterococcus, and Escherichia coli are the predominant organisms isolated from hospitalized patients with SSTIs.17 MRSA infections are characterized by liquefaction of infected tissue and abscess formation; the resulting increase in tissue tension causes ischemia and overlying skin necrosis. Lymphatic and hematogenous dissemination causes septicemia and spread to other organs (e.g., lung, bone, heart valves). Diabetic lower limb infections, severe hospital-acquired infections, necrotizing infections, and head and hand infections pose higher risks of mortality and functional disability.9

Clinical Presentation

Patients with simple SSTIs present with erythema, warmth, edema, and pain over the affected site. Systemic features of infection may follow, their intensity reflecting the magnitude of infection. The lower extremities are most commonly involved.⁹ Induration is characteristic of more superficial infections such as erysipelas and cellulitis. Patients with necrotizing fasciitis may have pain disproportionate to the physical findings, rapid progression of infection, cutaneous anesthesia, hemorrhage or bullous changes, and crepitus indicating gas in the soft tissues.⁵ Tense overlying edema and bullae, when present, help distinguish necrotizing fasciitis from nonnecrotizing infections.¹⁸

Diagnosis

The diagnosis of SSTIs is predominantly clinical. A complete blood count, C-reactive protein level, and liver and kidney function tests should be ordered for patients with severe infections, and for those with comorbidities causing organ dysfunction. The Laboratory Risk Indicator for Necrotizing Fasciitis score uses laboratory parameters to stratify patients into high- and low-risk categories for necrotizing fasciitis (*Table 4*); a score of 6 or higher is indicative, whereas a score of 8 or higher is strongly predictive (positive predictive value = 93.4%).¹⁹

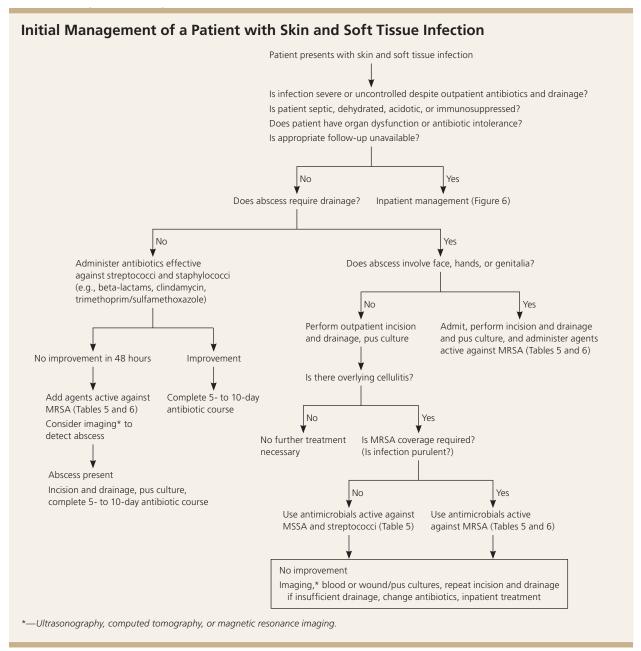
Blood cultures are unlikely to change the management of simple localized SSTIs in otherwise healthy, immunocompetent patients, and are typically unnecessary.²⁰ However, because of the potential for deep tissue involvement, cultures are useful in patients with severe infections or signs of systemic involvement, in older or immunocompromised patients, and in patients requiring surgery.^{5,21,22} Wound cultures are not indicated in most healthy patients, including those with suspected MRSA infection, but are useful in immunocompromised patients and those with significant cellulitis; lymphangitis; sepsis; recurrent, persistent, or large abscesses; or infections from human or animal bites.^{22,23} Tissue biopsies, which are the preferred diagnostic test for necrotizing SSTIs, are ideally taken from the advancing margin

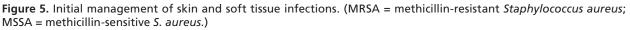
Table 4. Laboratory Risk Indicator for Necrotizing Fasciitis

Laboratory value	Score
C-reactive protein	
< 150 mg per L (< 1,430 nmol per L)	0
≥ 150 mg per L	4
Creatinine	
\leq 1.6 mg per dL (\leq 141 μ mol per L)	0
> 1.6 mg per dL	2
Glucose	
\leq 180 mg per dL (\leq 10 mmol per L)	0
> 180 mg per dL	1
Hemoglobin	
> 13.5 g per dL (> 135 g per L)	0
11 to 13.5 g per dL (110 to 135 g per L)	1
< 11 g per dL	2
Sodium	
\geq 135 mEq per L (\geq 135 mmol per L)	0
< 135 mEq per L	2
Total white blood cells	
< 15,000 per mm ³ (< 15.0 $ imes$ 10 ⁹ per L)	0
15,000 to 25,000 per mm³ (15.0 \times 109 to 25.0 \times 109 per L)	1
> 25,000 per mm ³	2

NOTE: Maximum score is 13. Scores of 6 or more are indicative of necrotizing fasciitis, and scores of 8 or more are highly predictive.

Adapted with permission from Wong CH, Khin LW, Heng KS, Tan KC, Low CO. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. Crit Care Med. 2004;32(7):1536.





of the wound, from the depth of bite wounds, and after debridement of necrotizing infections and traumatic wounds. Sterile aspiration of infected tissue is another recommended sampling method, preferably before commencing antibiotic therapy.²²

Imaging studies are not indicated for simple SSTIs, and surgery should not be delayed for imaging. Plain radiography, ultrasonography, computed tomography, or magnetic resonance imaging may show soft tissue edema or fascial thickening, fluid collections, or soft tissue air. Magnetic resonance imaging is highly sensitive (100%) for necrotizing fasciitis; specificity is lower (86%).²⁴ Extensive involvement of the deep intermuscular fascia, fascial thickening (more than 3 mm), and partial or complete absence of signal enhancement of the thickened fasciae on postgadolinium images suggest necrotizing fasciitis.²⁵ Adding ultrasonography to clinical examination in children and adolescents with clinically suspected SSTI increases the accuracy of diagnosing the extent and depth of infection (sensitivity = 77.6% vs. 43.7%; specificity = 61.3% vs. 42.0%, respectively).²⁶

Management

The management of SSTIs is determined primarily by their severity and location, and by the patient's comorbidities (*Figure 5*). According to guidelines from the

Infectious Diseases Society of America, initial management is determined by the presence or absence of purulence, acuity, and type of infection.⁵

MILD TO MODERATE INFECTIONS

Topical antibiotics (e.g., mupirocin [Bactroban], retapamulin [Altabax]) are options in patients with impetigo and folliculitis (*Table 5*).^{5,27} Beta-lactams are effective in children with nonpurulent SSTIs, such as uncomplicated cellulitis or impetigo.²⁸ In adults, mild to moderate SSTIs respond well to beta-lactams in the absence of sup-

puration.¹⁶ Patients who do not improve or who worsen after 48 hours of treatment should receive antibiotics to cover possible MRSA infection and imaging to detect purulence.¹⁶

Mild purulent SSTIs in easily accessible areas without significant overlying cellulitis can be treated with

Table 5. Antibiotic Choices for Mild to Moderate Skinand Soft Tissue Infections in Adults and Children

Antibiotic	Comments
Amoxicillin/clavulanate (Augmentin)	For impetigo; human or animal bites; and MSSA, Escherichia coli, or Klebsiella infections
Cefazolin*	For MSSA infections and human or animal bites
Cephalexin (Keflex)	For MSSA infections, impetigo, and human or animal bites
Clindamycin*	For impetigo; MSSA, MRSA, and clostridial infections; and human or animal bites
Dicloxacillin	For MSSA infections
Doxycycline or minocycline (Minocin)	For MRSA infections and human or animal bites; not recommended for children younger than 8 years
Fluoroquinolones	For human or animal bites; not useful in MRSA infections; not recommended for children
Mupirocin (Bactroban)*	For MRSA impetigo and folliculitis; not recommended for children younger than 2 months
Retapamulin (Altabax)*	For MSSA impetigo; not recommended for children younger than 9 months
Trimethoprim/ sulfamethoxazole	For MRSA infections and human or animal bites; contraindicated in children younger than 2 months

NOTE: This is a condensed version of this table. The full version is available online at http://www.aafp.org/afp.

MRSA = *methicillin-resistant* Staphylococcus aureus; *MSSA* = *methicillin-sensitive* S. aureus.

*—Higher dosages used in complicated infections caused by sensitive organisms. Information from references 5 and 27.

BEST PRACTICES IN INFECTIOUS DISEASE: RECOMMENDATIONS FROM THE CHOOSING WISELY CAMPAIGN		
Recommendation	Sponsoring organization	
Avoid antibiotics and wound cultures in emergency department patients with uncomplicated skin and soft tissue abscesses after successful incision and drainage and with adequate medical follow-up.	American College of Emergency Physicians	
Source: For more information on the Choosing Wisely choosingwisely.org. For supporting citations and to sea mendations relevant to primary care, see http://www.aaf, search.htm.	rch Choosing Wisely recom-	

incision and drainage alone.^{29,30} In children, minimally invasive techniques (e.g., stab incision, hemostat rupture of septations, in-dwelling drain placement) are effective, reduce morbidity and hospital stay, and are more economical compared with traditional drainage and wound packing.³¹

> Antibiotic therapy is required for abscesses that are associated with extensive cellulitis, rapid progression, or poor response to initial drainage; that involve specific sites (e.g., face, hands, genitalia); and that occur in children and older adults or in those who have significant comorbid illness or immunosuppression.³² In uncomplicated cellulitis, five days of treatment is as effective as 10 days.³³ In a randomized controlled trial of 200 children with uncomplicated SSTIs primarily caused by MRSA, clindamycin and cephalexin (Keflex) were equally effective.³⁴

SEVERE INFECTIONS

Inpatient treatment is necessary for patients who have uncontrolled infection despite adequate outpatient antimicrobial therapy or who cannot tolerate oral antibiotics (Figure 6). Hospitalization is also indicated for patients who initially present with severe or complicated infections, unstable comorbid illnesses, or signs of systemic sepsis, or who need surgical intervention under anesthesia.^{3,5} Broad-spectrum antibiotics with proven effectiveness against grampositive and gram-negative organisms and anaerobes should be used until pathogenspecific sensitivities are available; coverage can then be narrowed. Intravenous antibiotics should be continued until the clinical

picture improves, the patient can tolerate oral intake, and drainage or debridement is completed. The recommended duration of antibiotic therapy for hospitalized patients is seven to 14 days. A Cochrane review did not establish the superiority of any one pathogen-sensitive

Inpatient Management of a Patient with Skin and Soft Tissue Infection

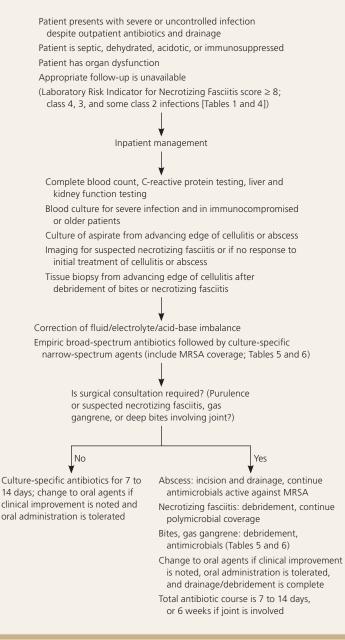


Figure 6. Inpatient management of skin and soft tissue infections. (MRSA = methicillin-resistant *Staphylococcus aureus*.)

antibiotic over another in the treatment of MRSA SSTI.³⁵ Intravenous antibiotics may be continued at home under close supervision after initiation in the hospital or emergency department.³⁶ Antibiotic choices for severe infections (including MRSA SSTI) are out-

lined in Table 6.5,27

Necrotizing Fasciitis. Treatment of necrotizing fasciitis involves early recognition and surgical consultation for debridement of necrotic tissue combined with empiric high-dose intravenous broad-spectrum antibiotics.⁵ The antibiotic spectrum can be narrowed once the infecting microbes are identified and susceptibility testing results are available. Monomicrobial necrotizing fasciitis caused by streptococcal and clostridial infections is treated with penicillin G and clindamycin; S. aureus infections are treated according to susceptibilities. Antibiotic therapy should be continued until features of sepsis have resolved and surgery is completed. Patients may require repeated surgery until debridement and drainage are complete and healing has commenced.

Special Considerations

Immunocompromised patients are more prone to SSTIs and may not demonstrate classic clinical features and laboratory findings because of their attenuated inflammatory response. Diagnostic testing should be performed early to identify the causative organism and evaluate the extent of involvement, and antibiotic therapy should be commenced to cover possible pathogens, including atypical organisms that can cause serious infections (e.g., resistant gramnegative bacteria, anaerobes, fungi).⁵

Specific types of SSTIs may result from identifiable exposures. Dog and cat bites in an immunocompromised host and those that involve the face or hand, periosteum, or joint capsule are typically treated with a beta-lactam antibiotic or beta-lactamase inhibitor (e.g., amoxicillin/clavulanate [Augmentin]).⁵ In patients allergic to penicillin, a combination of trimethoprim/ sulfamethoxazole or a quinolone with clindamycin or metronidazole (Flagyl) can be used. A recent article in *American Family Physician* provides further details about prophylaxis in patients with cat or dog bites (http://www.aafp.org/afp/2014/0815/p239.html).³⁷

Simple SSTIs that result from exposure to fresh water are treated empirically with a quinolone, whereas doxycycline is used for those that occur after exposure to salt water. The choice is based on the presumptive infecting organisms (e.g., *Aeromonas hydrophila*, *Vibrio vulnificus*, *Mycobacterium marinum*).⁵

In patients with at least one prior episode of cellulitis, administering prophylactic oral penicillin, 250 mg twice

Table 6. Antibiotic Choices for Necrotizing and Other Complicated Skin and Soft Tissue Infections in Adults and Children

Antibiotic	Comments
Carbapenems (ertapenem [Invanz], imipenem/ cilastatin [Primaxin], meropenem [Merrem IV])	For polymicrobial necrotizing infections; safety of imipenem/cilastatin in children younger than 12 years is not known
Cefotaxime (Claforan)	Used with metronidazole (Flagyl) or clindamycin for initial treatment of polymicrobial necrotizing infections
Ceftaroline (Teflaro)	Dose adjustment required in patients with renal impairment; 5- to 14-day course
Ceftriaxone (Rocephin)	Useful in waterborne infections; used with doxycycline for <i>Aeromonas hydrophila</i> and <i>Vibrio vulnificus</i> infections
Dalbavancin (Dalvance)	For MSSA and MRSA infections; 2 doses, 1 week apart
Dalfopristin/quinupristin (Synercid)	For complicated MSSA and MRSA infections, especially in neutropenic patients and vancomycin-resistant infections
Daptomycin (Cubicin)	For MRSA infections; 7- to 14-day course in adults
Doxycycline	Useful in waterborne infections; used with ciprofloxacin (Cipro), ceftriaxone, or cefotaxime in <i>A. hydrophila</i> and <i>V. vulnificus</i> infections
Linezolid (Zyvox)	For MRSA infections; oral or intravenous dosing; 7- to 14-day course in adults; 10- to 14-day course in children
Metronidazole	Used with cefotaxime for initial treatment of polymicrobial necrotizing infections
Oritavancin (Orbactiv)	For MSSA, MRSA, and Enterococcus faecalis infections
Oxacillin or nafcillin	For necrotizing fasciitis caused by sensitive staphylococci
Penicillin plus clindamycin	Combined therapy for necrotizing fasciitis caused by streptococci; either drug is effective in clostridial infections
Piperacillin/tazobactam (Zosyn)	First-line antimicrobial for treating polymicrobial necrotizing infections
Telavancin (Vibativ)	For MSSA and MRSA infections; 7- to 14-day course; women of childbearing age should use 2 forms of birth control during treatment
Tigecycline (Tygacil)	For MRSA infections; 5- to 14-day course in adults; not recommended in children; increases mortality risk; considered medication of last resort
Vancomycin	Parenteral drug of choice for MRSA infections in patients allergic to penicillin; 7- to 14-day course for skin and soft tissue infections; 6-week course for bacteremia; maintain trough levels at 10 to 20 mg per L

Information from references 5 and 27.

Clinical recommendation	Evidence rating	References
Blood cultures seldom change treatment and are not required in healthy immunocompetent patients with SSTIs.	С	20
Uncomplicated purulent SSTIs in easily accessible areas without overlying cellulitis can be treated with incision and drainage only; antibiotic therapy does not improve outcomes.	С	29, 30
Inpatient treatment is recommended for patients with uncontrolled SSTIs despite adequate oral antibiotic therapy; those who cannot tolerate oral antibiotics; those who require surgery; those with initial severe or complicated SSTIs; and those with underlying unstable comorbid illnesses or signs of systemic sepsis.	С	3, 5
There is no evidence that any pathogen-sensitive antibiotic is superior to another in the treatment of MRSA SSTIs.	В	35
Treatment of necrotizing fasciitis involves early recognition and surgical debridement of necrotic tissue, combined with high-dose broad-spectrum intravenous antibiotics.	С	5

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.

daily for six months, reduces the risk of recurrence for up to three years by 47%.³⁸

Data Sources: A PubMed search was completed using the key term skin and soft tissue infections. The search included systematic reviews, metaanalyses, reviews of clinical trials and other primary sources, and evidence-based guidelines. Also searched were the Cochrane database, the National Institute for Health and Care Excellence guidelines, and Essential Evidence Plus. Search dates: May 7, 2014, through May 27, 2015.

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REFERENCES

- Hersh AL, et al. National trends in ambulatory visits and antibiotic prescribing for skin and soft-tissue infections. *Arch Intern Med.* 2008; 168(14):1585-1591.
- Pallin DJ, et al. Increased US emergency department visits for skin and soft tissue infections, and changes in antibiotic choices, during the emergence of community-associated methicillin-resistant *Staphylococcus aureus*. Ann Emerg Med. 2008;51(3):291-298.
- 3. Eron LJ, et al. Managing skin and soft tissue infections. J Antimicrob Chemother. 2003;52(suppl 1):i3-i17.

- 4. May AK. Skin and soft tissue infections. Surg Clin North Am. 2009; 89(2):403-420.
- 5. Stevens DL, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections. *Clin Infect Dis.* 2014;59(2):e10-e52.
- Jones ME, et al. Epidemiology and antibiotic susceptibility of bacteria causing skin and soft tissue infections in the USA and Europe. Int J Antimicrob Agents. 2003;22(4):406-419.
- 7. Stevens DL, et al. Practice guidelines for the diagnosis and management of skin and soft-tissue infections [published corrections appear in *Clin Infect Dis.* 2005;41(12):1830 and *Clin Infect Dis.* 2006;42(8):1219]. *Clin Infect Dis.* 2005;41(10):1373-1406.
- U.S. Food and Drug Administration. Uncomplicated and complicated skin and skin structure infections—developing antimicrobial drugs for treatment. http://www.fda.gov/ohrms/dockets/98fr/2566dft.pdf. Accessed May 24, 2014.
- 9. Ki V, et al. Bacterial skin and soft tissue infections in adults: a review of their epidemiology, pathogenesis, diagnosis, treatment and site of care. *Can J Infect Dis Med Microbiol.* 2008;19(2):173-184.
- 10. Gabillot-Carré M, et al. Acute bacterial skin infections and cellulitis. *Curr Opin Infect Dis.* 2007;20(2):118-123.
- Kowalski TJ, et al. Epidemiology, treatment, and prevention of community-acquired methicillin-resistant *Staphylococcus aureus* infections. *Mayo Clin Proc.* 2005;80(9):1201-1207.
- May L, et al. Self-reported incidence of skin and soft tissue infections among deployed US military. *Travel Med Infect Dis.* 2011;9(4):213-220.
- 13. Decker CF. Skin and soft tissue infections in the athlete. *Dis Mon.* 2010;56(7):414-421.
- 14. Suaya JA, et al. Skin and soft tissue infections and associated complications among commercially insured patients aged 0-64 years with and without diabetes in the U.S. *PLoS One*. 2013;8(4):e60057.
- 15. Habif TP. *Clinical Dermatology: A Color Guide to Diagnosis and Therapy.* 5th ed. New York, NY: Mosby; 2010:335-381.
- 16. Jeng A, et al. The role of beta-hemolytic streptococci in causing diffuse, nonculturable cellulitis. *Medicine (Baltimore)*. 2010;89(4):217-226.
- 17. Moet GJ, et al. Contemporary causes of skin and soft tissue infections in North America, Latin America, and Europe: report from the SENTRY Antimicrobial Surveillance Program (1998-2004). *Diagn Microbiol Infect Dis*. 2007;57(1):7-13.

- Wall DB, et al. Objective criteria may assist in distinguishing necrotizing fasciitis from nonnecrotizing soft tissue infection. *Am J Surg.* 2000; 179(1):17-21.
- Wong CH, et al. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. *Crit Care Med.* 2004;32(7):1535-1541.
- 20. Mills AM, et al. Are blood cultures necessary in adults with cellulitis? Ann Emerg Med. 2005;45(5):548-549.
- Perl B, et al. Cost-effectiveness of blood cultures for adult patients with cellulitis. *Clin Infect Dis.* 1999;29(6):1483-1488.
- 22. Baron EJ, et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases. *Clin Infect Dis.* 2013;57(4):e22-e121.
- Abrahamian FM, et al. Use of routine wound cultures to evaluate cutaneous abscesses for community-associated methicillin-resistant *Staphylococcus aureus*. Ann Emerg Med. 2007;50(1):66-67.
- 24. Schmid MR, et al. Differentiation of necrotizing fasciitis and cellulitis using MR imaging. *AJR Am J Roentgenol.* 1998;170(3):615-620.
- Malghem J, et al. Necrotizing fasciitis: contribution and limitations of diagnostic imaging. *Joint Bone Spine*. 2013;80(2):146-154.
- Marin JR, et al. Emergency ultrasound-assisted examination of skin and soft tissue infections in the pediatric emergency department. Acad Emerg Med. 2013;20(6):545-553.
- 27. Micromedex 2.0. http://www.micromedexsolutions.com (subscription required). Accessed May 25, 2014.
- Williams DJ, et al. Comparative effectiveness of antibiotic treatment strategies for pediatric skin and soft-tissue infections. *Pediatrics*. 2011;128(3):e479-e487.
- 29. Duong M, et al. Randomized, controlled trial of antibiotics in the management of community-acquired skin abscesses in the pediatric patient. *Ann Emerg Med.* 2010;55(5):401-407.

- Hankin A, et al. Are antibiotics necessary after incision and drainage of a cutaneous abscess? Ann Emerg Med. 2007;50(1):49-51.
- 31. Wright TN, et al. Minimally invasive drainage of subcutaneous abscesses reduces hospital cost and length of stay. *South Med J.* 2013;106(12): 689-692.
- 32. Liu C, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children [published correction appears in *Clin Infect Dis.* 2011;53(3):319]. *Clin Infect Dis.* 2011;52(3):e18-e55.
- Hepburn MJ, et al. Comparison of short-course (5 days) and standard (10 days) treatment for uncomplicated cellulitis. *Arch Intern Med.* 2004;164(15):1669-1674.
- Chen AE, et al. Randomized controlled trial of cephalexin versus clindamycin for uncomplicated pediatric skin infections. *Pediatrics*. 2011;127(3):e573-e580.
- 35. Gurusamy KS, et al. Antibiotic therapy for the treatment of methicillinresistant *Staphylococcus aureus* (MRSA) infections in surgical wounds. *Cochrane Database Syst Rev.* 2013;(8):CD009726.
- Corwin P, et al. Randomised controlled trial of intravenous antibiotic treatment for cellulitis at home compared with hospital. *BMJ*. 2005; 330(7483):129-135.
- Ellis R, et al. Dog and cat bites [published correction appears in Am Fam Physician. 2015;91(10):676]. Am Fam Physician. 2014;90(4):239-243.
- Thomas K, et al. Prophylactic antibiotics for the prevention of cellulitis (erysipelas) of the leg: results of the UK Dermatology Clinical Trials Network's PATCH II trial. *Br J Dermatol.* 2012;166(1):169-178.

Table 5. Antibiotic Choices for Mild to Moderate Skin and Soft Tissue Infections in Adults and Children

Antibiotic	Dosage	Comments
Amoxicillin/ clavulanate (Augmentin)	 Adults: 500 mg orally 2 times per day or 250 mg orally 3 times per day Children younger than 3 months and less than 40 kg (89 lb): 25 to 45 mg per kg per day (amoxicillin component), divided every 12 hours Children older than 3 months and 40 kg or more: 30 mg per kg per day, divided every 12 hours 	For impetigo; human or animal bites; and MSSA, <i>Escherichia coli</i> , or <i>Klebsiella</i> infections Common adverse effects: diaper rash, diarrhea, nausea, vaginal mycosis, vomiting Rare adverse effects: agranulocytosis, hepatorenal dysfunction, hypersensitivity reactions, pseudomembranous enterocolitis
Cefazolin*	Adults: 250 to 500 mg IV or IM every 8 hours (500 to 1,500 mg IV or IM every 6 to 8 hours for moderate to severe infections) Children: 25 to 100 mg per kg per day IV or IM in 3 or 4 divided doses	For MSSA infections and human or animal bites Common adverse effects: diarrhea, drug-induced eosinophilia, pruritus Rare adverse effects: anaphylaxis, colitis, encephalopath renal failure, seizure, Stevens-Johnson syndrome
Cephalexin (Keflex)	Adults: 500 mg orally 4 times per day Children: 25 to 50 mg per kg per day in 2 divided doses	For MSSA infections, impetigo, and human or animal bites; twice-daily dosing is an option Common adverse effect: diarrhea Rare adverse effects: anaphylaxis, angioedema, interstit nephritis, pseudomembranous enterocolitis, Stevens- Johnson syndrome
Clindamycin*	Adults: 150 to 450 mg orally 4 times per day (300 to 450 mg orally 4 times per day for 5 to 10 days for MRSA infection; 600 mg orally or IV 3 times per day for 7 to 14 days for complicated infections) Children: 16 mg per kg per day in 3 or 4 divided doses (16 to 20 mg per kg per day for more severe infections; 40 mg per kg per day in 3 or 4 divided doses for MRSA infection)	 For impetigo; MSSA, MRSA, and clostridial infections; a human or animal bites Common adverse effects: abdominal pain, diarrhea, nausea, rash Rare adverse effects: agranulocytosis, elevated liver enzyme levels, erythema multiforme, jaundice, pseudomembranous enterocolitis
Dicloxacillin	Adults: 125 to 500 mg orally every 6 hours (maximal dosage, 2 g per day) Children less than 40 kg: 12.5 to 50 mg per kg per day divided every 6 hours Children 40 kg or more: 125 to 500 mg every 6 hours	For MSSA infections Common adverse effects: diarrhea, impetigo, nausea, vomiting Rare adverse effects: anaphylaxis, hemorrhagic colitis, hepatorenal toxicity
Doxycycline or minocycline (Minocin)	Adults: 100 mg orally 2 times per day Children 8 years and older and less than 45 kg (100 lb): 4 mg per kg per day in 2 divided doses Children 8 years and older and 45 kg or more: 100 mg orally 2 times per day	For MRSA infections and human or animal bites; not recommended for children younger than 8 years Common adverse effects: myalgia, photosensitivity Rare adverse effects: <i>Clostridium difficile</i> colitis, hepatotoxicity, pseudotumor cerebri, Stevens-Johnson syndrome
Fluoroquinolones	Adults: ciprofloxacin (Cipro), 500 to 750 mg orally 2 times per day or 400 mg IV 2 times per day; gatifloxacin or moxifloxacin (Avelox), 400 mg orally or IV per day	 For human or animal bites; not useful in MRSA infection not recommended for children Common adverse effects: diarrhea, headache, nausea, rash, vomiting Rare adverse effects: agranulocytosis, arrhythmias, hepatorenal failure, tendon rupture

IM = intramuscularly; IV = intravenously; MRSA = methicillin-resistant Staphylococcus aureus; MSSA = methicillin-sensitive S. aureus.

*—Higher dosages used in complicated infections caused by sensitive organisms.

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Table 5. Antibiotic Choices for Mild to Moderate Skin and Soft Tissue Infections in Adults and Children (continued)

Antibiotic	Dosage	Comments
Mupirocin (Bactroban)*	2% ointment applied 3 times per day for 3 to 5 days	For MRSA impetigo and folliculitis; not recommended for children younger than 2 months Rare adverse effects: burning over application site, pruritus
Retapamulin (Altabax)*	1% ointment applied 2 times per day for 5 days	For MSSA impetigo; not recommended for children younger than 9 months Rare adverse effects: allergy, angioedema, application site irritation
Trimethoprim/ sulfamethoxazole	Adults: 1 or 2 double-strength tablets 2 times per day Children: 8 to 12 mg per kg per day (trimethoprim component) orally in 2 divided doses or IV in 4 divided doses	 For MRSA infections and human or animal bites; contraindicated in children younger than 2 months Common adverse effects: anorexia, nausea, rash, urticaria, vomiting Rare adverse effects: agranulocytosis, <i>C. difficile</i> colitis, erythema multiforme, hepatic necrosis, hyponatremia, rhabdomyolysis, Stevens-Johnson syndrome

IM = intramuscularly; IV = intravenously; MRSA = methicillin-resistant Staphylococcus aureus; MSSA = methicillin-sensitive S. aureus.

*-Higher dosages used in complicated infections caused by sensitive organisms.

Information from references 5 and 27.

Table 6. Antibiotic Choices for Necrotizing and Other Complicated Skin and Soft Tissue Infections in Adults and Children

Adults: 1 g IV per day children 3 months to 12 years: 15 mg per kg IV every 12 hours, up to 1 g per day dults: 1 g IV every 6 to 8 hours children: 25 mg per kg IV every 6 to 12 hours, up to 4 g per day adults: 1 g IV every 8 hours children: 10 mg per kg (up to 500 mg) IV every 8 hours; increase to 20 mg per kg (up to 1 g) IV every 8 hours for <i>Pseudomonas</i> infections adults: 2 g IV every 6 hours children: 50 mg per kg IV every 6 hours	For polymicrobial necrotizing infections; safety of imipenem/cilastatin in children younger than 12 years is not known Common adverse effects: anemia, constipation, diarrhea, headache, injection site pain and inflammation, nausea, vomiting Rare adverse effects: acute coronary syndrome, angioedema, bleeding <i>Clostridium difficile</i> colitis, congestive heart failure, hepatorenal failure, respiratory failure, seizures, vaginitis Used with metronidazole (Flagyl) or clindamycin for initial treatment or polymicrobial necrotizing infections Common adverse effects: diarrhea, pain and thrombophlebitis at
	polymicrobial necrotizing infections Common adverse effects: diarrhea, pain and thrombophlebitis at
	injection site, vomiting Rare adverse effects: agranulocytosis, arrhythmias, erythema multiforme
dults: 600 mg IV every 12 hours for 5 to 14 days Inknown safety in children	Dose adjustment required in patients with renal impairment Rare adverse effects: abdominal pain, arrhythmias, C. <i>difficile</i> colitis, diarrhea, dizziness, fever, hepatitis, rash, renal insufficiency, seizures thrombophlebitis, urticaria, vomiting
dults: 1 to 2 g IV every 24 hours hildren: 50 to 75 mg per kg IV or IM once per day or divided every 12 hours, up to 2 g per day	Useful in waterborne infections; used with doxycycline for Aeromonas hydrophila and Vibrio vulnificus infections Common adverse effects: diarrhea, elevated platelet levels, eosinophilia, induration at injection site Rare adverse effects: <i>C. difficile</i> colitis, erythema multiforme, hemolytic anemia, hyperbilirubinemia in newborns, pulmonary injury, renal failure
dults: 1,000 mg IV initial dose, followed by 500 mg IV 1 week later lot recommended in children	For MSSA and MRSA infections Common adverse effects: constipation, diarrhea, headache, nausea Rare adverse effects: <i>C. difficile</i> colitis, gastrointestinal hemorrhage, hepatotoxicity, infusion reaction
dults and children 12 years and older: 7.5 mg per kg IV every 12 hours	 For complicated MSSA and MRSA infections, especially in neutropenic patients and vancomycin-resistant infections Common adverse effects: arthralgia, diarrhea, edema, hyperbilirubinemia, inflammation at injection site, myalgia, nausea, pain, rash, vomiting Rare adverse effects: arrhythmias, cerebrovascular events, encephalopathy, hemolytic anemia, hepatitis, myocardial infarction, pancytopenia, syncope
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IM = *intramuscularly; IV* = *intravenously; MRSA* = *methicillin-resistant* Staphylococcus aureus; *MSSA* = *methicillin-sensitive* S. aureus. *Information from references 5 and 27.*

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Table 6. Antibiotic Choices for Necrotizing and Other Complicated Skin and Soft Tissue Infections in Adults and Children (continued)

Antibiotic	Dosage	Comments
Daptomycin (Cubicin)	Adults: 4 mg per kg IV per day for 7 to 14 days Not recommended in children	For MRSA infections Common adverse effects: diarrhea, throat pain, vomiting Rare adverse effects: gram-negative infections, pulmonary eosinophilia, renal failure, rhabdomyolysis
Doxycycline	Adults: 100 mg IV every 12 hours Children 8 years and older and less than 45 kg (100 lb): 4 mg per kg IV per day in 2 divided doses Children 8 years and older and 45 kg or more: 100 mg IV every 12 hours	 Useful in waterborne infections; used with ciprofloxacin (Cipro), ceftriaxone, or cefotaxime in <i>A. hydrophila</i> and <i>V. vulnificus</i> infections Common adverse effects: diarrhea, photosensitivity Rare adverse effects: <i>C. difficile</i> colitis, erythema multiforme, liver toxicity, pseudotumor cerebri
Linezolid (Zyvox)	 Adults: 600 mg IV or orally every 12 hours for 7 to 14 days Children 12 years and older: 600 mg IV or orally every 12 hours for 10 to 14 days Children younger than 12 years: 10 mg per kg IV or orally every 8 hours for 10 to 14 days 	For MRSA infections Common adverse effects: diarrhea, headache, nausea, vomiting Rare adverse effects: C. <i>difficile</i> colitis, hepatic injury, lactic acidosis, myelosuppression, optic neuritis, peripheral neuropathy, seizures
Metronidazole	Adults: 600 to 900 mg IV every 8 hours Children: 10 to 13 mg per kg IV every 8 hours	Used with cefotaxime for initial treatment of polymicrobial necrotizing infections Common adverse effects: abdominal pain, altered taste, diarrhea, dizziness, headache, nausea, vaginitis Rare adverse effects: aseptic meningitis, encephalopathy, hemolytic- uremic syndrome, leukopenia, optic neuropathy, ototoxicity, peripheral neuropathy, Stevens-Johnson syndrome
Oritavancin (Orbactiv)	Adults: 1,200-mg infusion over 3 hours Not indicated in children	For MSSA, MRSA, and <i>Enterococcus faecalis</i> infections Common adverse effects: headache, nausea, vomiting Rare adverse effects: C. <i>difficile</i> colitis, clotting abnormalities, hypersensitivity, infusion complications (thrombophlebitis), osteomyelitis
Oxacillin or nafcillin	Adults: 1 to 2 g IV every 4 hours Children: 25 mg per kg IM 2 times per day	For necrotizing fasciitis caused by sensitive staphylococci Rare adverse effects: anaphylaxis, bone marrow suppression, hypokalemia, interstitial nephritis, pseudomembranous enterocolitis
Penicillin plus clindamycin	 Adults: 2 to 4 million units penicillin IV every 6 hours plus 600 to 900 mg clindamycin IV every 8 hours Children: 60,000 to 100,000 units penicillin per kg IV every 6 hours plus 10 to 13 mg clindamycin per kg IV per day in 3 divided doses For MRSA infections in children: 40 mg per kg IV per day in 3 or 4 divided doses 	Combined therapy for necrotizing fasciitis caused by streptococci; either drug is effective in clostridial infections Adverse effects from penicillin are rare in nonallergic patients Common adverse effects of clindamycin: abdominal pain, diarrhea, nausea, rash Rare adverse effects of clindamycin: agranulocytosis, elevated liver enzyme levels, erythema multiforme, jaundice, pseudomembranous enterocolitis

IM = intramuscularly; IV = intravenously; MRSA = methicillin-resistant Staphylococcus aureus; MSSA = methicillin-sensitive S. aureus.

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Table 6. Antibiotic Choices for Necrotizing and Other Complicated Skin and Soft Tissue Infections in Adults and Children (continued)

Antibiotic	Dosage	Comments
Piperacillin/ tazobactam (Zosyn)	Adults: 3.375 g IV every 6 to 8 hours Children: 60 to 75 mg per kg (piperacillin component) IV every 6 hours	First-line antimicrobial for treating polymicrobial necrotizing infections Common adverse effects: constipation, diarrhea, fever, headache, insomnia, nausea, pruritus, vomiting Rare adverse effects: agranulocytosis, <i>C. difficile</i> colitis, encephalopathy, hepatorenal failure, Stevens-Johnson syndrome
Telavancin (Vibativ)	Adults: 10 mg per kg IV per day for 7 to 14 days Not recommended in children	For MSSA and MRSA infections; women of childbearing age should use 2 forms of birth control during treatment Common adverse effects: altered taste, nausea, vomiting Rare adverse effects: hypersensitivity, prolonged QT interval, renal insufficiency
Tigecycline (Tygacil)	Adults: 100 mg IV followed by 50 mg IV every 12 hours for 5 to 14 days Not recommended in children	 For MRSA infections; increases mortality risk; considered medication of last resort Common adverse effects: abdominal pain, diarrhea, nausea, vomiting Rare adverse effects: anaphylaxis, C. difficile colitis, liver dysfunction, pancreatitis, pseudotumor cerebri, septic shock
Vancomycin	Adults: 15 mg per kg IV every 12 hours Children: 10 mg per kg IV every 6 hours	 Parenteral drug of choice for MRSA infections in patients allergic to penicillin; 7- to 14-day course for skin and soft tissue infections; 6-week course for bacteremia; maintain trough levels at 10 to 20 mg per L Common adverse effects: abdominal pain, diarrhea, nausea, vomiting Rare adverse effects: agranulocytosis, anaphylaxis, <i>C. difficile</i> colitis, hypotension, nephrotoxicity, ototoxicity

IM = *intramuscularly; IV* = *intravenously; MRSA* = *methicillin-resistant* Staphylococcus aureus; *MSSA* = *methicillin-sensitive* S. aureus. *Information from references 5 and 27.*