Chapter 48: Skin and Soft-Tissue Infections

INTRODUCTION

- Bacterial infections of the skin can be classified as primary or secondary (**Table 48-1**). Primary bacterial infections are usually caused by a single bacterial species and involve areas of generally healthy skin (eg, impetigo and erysipelas). Secondary infections develop in areas of previously damaged skin and are frequently polymicrobic.
- The conditions that may predispose a patient to the development of skin and soft-tissue infections (SSTIs) include: (1) a high concentration of bacteria; (2) excessive moisture of the skin; (3) inadequate blood supply; (4) availability of bacterial nutrients; and (5) damage to the corneal layer, allowing for bacterial penetration.
- The majority of SSTIs are caused by gram-positive organisms on the skin surface. *Staphylococcus aureus* and *Streptococcus pyogenes* account for the majority of SSTIs. Other common nosocomial pathogens include *Pseudomonas aeruginosa* (11%), enterococci (9%), and *Escherichia coli* (7%).

TABLE 48-1

Bacterial Classification of Important Skin and Soft-Tissue Infections

Primary infections	
Erysipelas	Group A streptococci (*Streptococcus pyogenes*)
Impetigo	*Staphylococcus aureus* (including methicillin-resistant strains), group A streptococci
Lymphangitis	Group A streptococci; occasionally *S. aureus*
Cellulitis	Group A streptococci, *S. aureus* (potentially including methicillin-resistant strains); occasionally other gram-positive cocci, gram-negative bacilli, and/or anaerobes
Necrotizing fasciitis	
Type I	Anaerobes (*Bacteroides* spp., *Peptostreptococcus* spp.) and facultative bacteria (streptococci, Enterobacteriaceae)
Type II	Group A streptococci
Type III	*Clostridioides perfringens*
Secondary infections	
Diabetic foot infections	*S. aureus*, streptococci, Enterobacteriaceae, *Bacteroides* spp., *Peptostreptococcus* spp., *Pseudomonas aeruginosa*
Pressure sores	*S. aureus* including methicillin-resistant strains, streptococci, Enterobacteriaceae, *Bacteroides* spp., *Peptostreptococcus* spp., *P. aeruginosa*
Bite wounds	
Animal	*Pasteurella* spp., *S. aureus*, streptococci, *Bacteroides* spp.
Human	*Eikenella corrodens*, *S. aureus*, streptococci, *Corynebacterium* spp., *Bacteroides* spp., *Peptostreptococcus* spp.
Burn wounds	*P. aeruginosa*, Enterobacteriaceae, *S. aureus*, streptococci

ERYSIPELAS

- *Erysipelas* (Saint Anthony's fire) is a distinct form of cellulitis involving the superficial layers of the skin and cutaneous lymphatics. The infection is almost always caused by β-hemolytic streptococci, with *S. pyogenes* (group A streptococci) responsible for most infections.
- The lower extremities are the most common sites for erysipelas. Patients often experience flu-like symptoms (fever, chills, and malaise) prior to the appearance of the lesions. The infected area is painful, often a burning pain. The lesion is intensely erythematous and edematous, often with lymphatic streaking. It has a raised border, which is sharply demarcated from uninfected skin. Leukocytosis is common, and C-reactive protein is generally elevated.
- Mild-to-moderate cases of erysipelas in adults are treated with intramuscular **procaine penicillin G** or **penicillin VK** for 7–10 days. For more

serious infections, the patient should be hospitalized and **aqueous penicillin G** administered IV. Penicillin-allergic patients can be treated with **clindamycin**.

- Evidence-based recommendations for treatment of SSTIs are given in **Table 48-2**, and recommended drugs and dosing regimens for outpatient treatment of mild-to-moderate SSTIs are given in **Tables 48-3** and **48-4**.

TABLE 48-2

Evidence-Based Recommendations for Treatment of Skin and Soft-Tissue Infections

Recommendations	Recommendation Grade[a]
Folliculitis, furuncles, carbuncles	
Gram stain and culture of pus from carbuncles and abscesses are recommended, but treatment without cultures is reasonable in most patients	Strong, moderate
Carbuncles, abscesses, and large furuncles of mild severity should be treated with incision and drainage	Strong, high
Administration of antibiotics with activity against *Staphylococcus aureus* as an adjunct to incision and drainage should be based on presence or absence of systemic signs of infection	Strong, low
Antibiotics with activity against MRSA are recommended for patients with carbuncles or abscesses of higher severity who have failed initial antibiotic therapy, have severe systemic signs of infection, or are immunocompromised	Strong, low
Erysipelas	
Most infections are caused by *Streptococcus pyogenes*. Penicillin (oral or IV depending on clinical severity) is the drug of choice	A-I
If *S. aureus* is suspected, a penicillinase-resistant penicillin or first-generation cephalosporin should be used	A-I
Impetigo	
Gram stain and culture of pus or exudates should be obtained to help identify causative pathogens	Strong, moderate
Bullous and nonbullous impetigo should be treated with either mupirocin or retapamulin for 5 days	Strong, high
Impetigo should be treated with oral antibiotics active against *S. aureus* unless cultures show streptococci alone. Dicloxacillin or cephalexin is recommended for 7 days. Doxycycline, clindamycin, or sulfamethoxazole-trimethoprim should be used when MRSA is suspected or confirmed	Strong, moderate
Cellulitis	
Cultures of blood or cutaneous aspirates, biopsies, or swabs are not routinely recommended	Strong, moderate
Blood cultures are recommended, and cultures of cutaneous aspirates, biopsies, or swabs should be considered, in patients receiving chemotherapy for malignancies, neutropenia, severe cell-mediated immunodeficiency, immersion injuries, or animal bites	Strong, moderate (blood) Weak, moderate (other cultures)
Typical cases of mild nonpurulent cellulitis should be treated with antibiotics active against streptococci	Strong, moderate

Systemic antibiotics are recommended for moderate nonpurulent cellulitis with systemic signs of infection. Use of antibiotics active against methicillin-susceptible *S. aureus* could be considered	Weak, low
Patients with severe nonpurulent cellulitis associated with penetrating trauma, MRSA infection in another location, MRSA nasal colonization, injection drug use, or systemic signs of infection should be treated with vancomycin or other antibiotics active against both MRSA and streptococci	Strong, moderate
Broad-spectrum antibiotic therapy with vancomycin plus either piperacillin–tazobactam, imipenem, or meropenem may be considered for empiric treatment of severe nonpurulent cellulitis in severely immunocompromised patients	Weak, moderate (need for broad-spectrum therapy); strong, moderate (recommended broad-spectrum antibiotic regimen if used)
A treatment duration of 5 days is recommended for cellulitis, but may be extended if lack of clinical response within that time	Strong, high
Elevation of the affected area and treatment of predisposing factors are recommended for cellulitis	Strong, moderate
Systemic corticosteroids for 7 days can be considered for adjunctive treatment of cellulitis in nondiabetic patients	Weak, moderate
Patients with mild nonpurulent cellulitis who do not have systemic signs of infection, altered mental status, or hemodynamic instability should be treated as outpatients	Strong, moderate
Hospitalization is recommended for patients with moderate-to-severe nonpurulent cellulitis who have failed outpatient therapy, have poor adherence to therapy, are immunocompromised, or in whom there is a concern for deeper or necrotizing infection	Strong, moderate
Empiric antibiotics for outpatients with purulent cellulitis should provide activity against community-associated MRSA; coverage of β-hemolytic streptococci is likely not required. Mild-to-moderate infections can generally be treated with oral agents (dicloxacillin, cephalexin, clindamycin) unless resistance is high in the community	A-II
Recommended antibiotics for empiric coverage of MRSA in outpatients include orally administered trimethoprim–sulfamethoxazole, doxycycline, minocycline, clindamycin, and linezolid	A-II for all listed options
If coverage of both β-hemolytic streptococci and community-associated MRSA is desired, empiric antibiotic regimens for outpatient therapy include orally administered clindamycin alone; linezolid alone; or trimethoprim–sulfamethoxazole, doxycycline, or minocycline in combination with amoxicillin	A-II for all listed options
Hospitalized patients with complicated or purulent cellulitis should receive IV antibiotics with activity against MRSA pending culture data. Antibiotic options include vancomycin, linezolid, daptomycin, telavancin, and clindamycin	A-I for all except clindamycin; clindamycin A-III
In the treatment of *S. aureus* infections, trough serum vancomycin concentrations should always be maintained >10 mg/L (7 µmol/L) to avoid development of resistance	B-III
Necrotizing fasciitis	
Patients with severe nonpurulent cellulitis characterized by aggressive infection and associated with signs of systemic toxicity, necrotizing fasciitis, or gas gangrene should have prompt surgical consultation	Strong, low

Early and aggressive surgical debridement of all necrotic tissue is essential	A-III
Necrotizing fasciitis should be empirically treated with broad-spectrum antibiotics such as vancomycin or linezolid plus piperacillin–tazobactam or a carbapenem, or vancomycin or linezolid plus ceftriaxone and metronidazole	Strong, low
Necrotizing fasciitis caused by *S. pyogenes* should be treated with the combination of clindamycin and penicillin	Strong, low
In the treatment of necrotizing fasciitis caused by methicillin-resistant *S. aureus* infections, trough serum vancomycin concentrations of 15–20 mg/L (10–14 µmol/L) are recommended	B-II
Clostridial gas gangrene (myonecrosis) should be treated with clindamycin and penicillin	B-III
Diabetic foot infections	
Clinically uninfected wounds should not be treated with antibiotics	A-III
Empiric antibiotic regimens should be selected based on severity of infection and likely pathogens	A-III
Antibiotic therapy should target only aerobic gram-positive cocci in patients with mild-to-moderate infection who have not received antibiotics within the previous month	C-III
Broad-spectrum empiric antibiotic therapy should be initiated in most patients with severe infections, until culture and susceptibility data are available	A-III
Empiric antibiotics directed against *Pseudomonas aeruginosa* are usually unnecessary except in patients with specific risk factors for infection with this pathogen: patient has been soaking feet, patient has failed previous antibiotic therapy with nonpseudomonal agents, or clinically severe infection	A-III
Empiric antibiotics directed against MRSA should be considered in patients with specific risk factors, including prior history of infection or colonization with MRSA, high local prevalence of MRSA (eg, ≥50% for mild infections, ≥30% for severe infection), or clinically severe infection	C-III
Oral agents with high bioavailability may be used in the treatment of most mild, and many moderate, infections	A-II
Parenteral therapy is initially preferred for all severe, and some moderate, infections. After initial response, step-down therapy to oral agents can be considered	C-III
Definitive therapy should be based on results of appropriately collected cultures and sensitivities, as well as clinical response to empiric antimicrobial agents	A-III
Appropriate wound care, in addition to appropriate antimicrobial therapy, is often necessary for healing of infected wounds	A-III
Antibiotic therapy should only be continued until resolution of signs/symptoms of infection, but not necessarily until the wound is fully healed. The duration of therapy should initially be 1–2 weeks for mild infections and 2–3 weeks for moderate-to-severe infection	C-III
Pressure ulcers	

Optimize the host response by evaluating nutritional status and addressing deficits; stabilizing glycemic control; improving arterial blood flow; and/or reducing immunosuppressant therapy if possible	A-III
Consider the use of topical antiseptics for pressure ulcers that are not expected to heal and are critically colonized/topically infected	B-III
Consider use of silver sulfadiazine in heavily contaminated or infected pressure ulcers until definitive debridement is accomplished	B-III
Consider the use of medical-grade honey in heavily contaminated or infected pressure ulcers until definitive debridement is accomplished	C-III
Limit the use of topical antibiotics on infected pressure ulcers, except in special situations where the benefit to the patient outweighs the risk of antibiotic side effects and resistance	B-III
Use systemic antibiotics for individuals with clinical evidence of systemic infection, such as positive blood cultures, cellulitis, fasciitis, osteomyelitis, systemic inflammatory response syndrome (SIRS), or sepsis	B-III
Animal bites	
Preemptive early antibiotics should be administered for 3–5 days in patients with any of the following: immunocompromised; asplenic; advanced liver disease; preexisting or resultant edema of the bitten area; moderate-to-severe bite-related injuries, especially to the hands or face; or bite injuries that have penetrated the periosteum or joint capsule	Strong, low
Amoxicillin–clavulanic acid or other antibiotics active against both aerobic and anaerobic bacteria should be used for treatment of infected animal bites	Strong, moderate
Serious infections requiring IV antimicrobial therapy can be treated with a β-lactam/β-lactamase inhibitor combination or second-generation cephalosporin with activity against anaerobes (eg, cefoxitin)	B-II
Penicillinase-resistant penicillins, first-generation cephalosporins, macrolides, and clindamycin should not be used for treatment of infected wounds because of their poor activity against *Pasteurella multocida*	D-III
Human bites	
Antimicrobial therapy should provide coverage against *Eikenella corrodens*, *S. aureus*, and β-lactamase–producing anaerobes	B-III

[a]Qualitative (descriptive) recommendations are from: 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:e10–e52.

Strength of recommendation: A, good evidence for use; B, moderate evidence for use; C, poor evidence for use, optional; D, moderate evidence to support not using; E, good evidence to support not using. *Quality of evidence*: I, evidence from ≥1 properly randomized controlled trials; II, evidence from ≥1 well-designed clinical trials without randomization, case–control analytic studies, multiple time series, or dramatic results from uncontrolled experiments; III, evidence from expert opinion, clinical experience, descriptive studies, or reports of expert committees.

Qualitative (descriptive) recommendations: *strong, high*: strong recommendation, high-quality evidence from well-performed randomized controlled trials (RCTs) or exceptionally strong evidence from unbiased observational studies; *strong, moderate*: strong recommendation, moderate quality evidence from RCTs with important limitations or exceptionally strong evidence from unbiased observational studies; *strong, low*: strong recommendation, low-quality evidence for at least

one critical outcome from observational studies, RCTs with serious flaws, or indirect evidence; *weak, moderate*: weak recommendation, moderate quality evidence from RCTs with important limitations or exceptionally strong evidence from unbiased observational studies; *weak, low*: weak recommendation, low-quality evidence for at least one critical outcome from observational studies, RCTs with serious flaws, or indirect evidence.

TABLE 48-3

Recommended Oral Drugs for Outpatient Treatment of Mild-to-Moderate Skin and Soft-Tissue Infections

Infection	Adults	Children
Folliculitis	None; warm saline compresses usually sufficient	
Furuncles and carbuncles	Trimethoprim–sulfamethoxazole[a,b] Doxycycline[a,b] Minocycline[a,b]	Trimethoprim–sulfamethoxazole[a,b] Clindamycin[a,b]
Erysipelas	Procaine penicillin G Penicillin VK Clindamycin[a] Erythromycin[a]	Penicillin VK Clindamycin[a] Erythromycin[a]
Impetigo	Mupirocin ointment[a] Retapamulin ointment[a] Dicloxacillin Cephalexin Trimethoprim–sulfamethoxazole[a,b] Clindamycin[a,b] Doxycycline[a,b]	Mupirocin ointment[a] Retapamulin ointment[a] Dicloxacillin Cephalexin Trimethoprim–sulfamethoxazole[a] Clindamycin[a]
Lymphangitis	Initial IV therapy, followed by penicillin VK Clindamycin[a]	Initial IV therapy, followed by penicillin VK Clindamycin[a]
Cellulitis	Penicillin VK[c] Cephalexin[c] Dicloxacillin[c] Clindamycin[b,c] Trimethoprim–sulfamethoxazole[b,d] Doxycycline[b,d] Minocycline[b,d] Linezolid[b]	Penicillin VK[c] Cephalexin[c] Dicloxacillin[c] Clindamycin[b,c] Trimethoprim–sulfamethoxazole[b,d] Linezolid[b]
Diabetic foot infections	Dicloxacillin Clindamycin Cephalexin Amoxicillin–clavulanate Levofloxacin ± metronidazole or clindamycin[a,e] Ciprofloxacin ± metronidazole or clindamycin[a,e]	

	Moxifloxacin	
Bite wounds (animal or human)	Amoxicillin–clavulanate Doxycycline[a] Moxifloxacin[a] Trimethoprim–sulfamethoxazole + metronidazole or clindamycin[a] Levofloxacin or ciprofloxacin + metronidazole or clindamycin[a] Cefuroxime axetil + metronidazole or clindamycin Dicloxacillin + penicillin VK	Amoxicillin–clavulanate Trimethoprim–sulfamethoxazole + metronidazole or clindamycin[a] Cefuroxime axetil + metronidazole or clindamycin Dicloxacillin + penicillin VK

[a]May be used in patients with penicillin allergy.

[b]Recommended if CA-MRSA is suspected.

[c]For nonpurulent cellulitis when CA-MRSA is not suspected, or purulent cellulitis when CA-MRSA not documented (not penicillin VK).

[d]May be combined with amoxicillin if additional coverage for streptococci is desired.

[e]Fluoroquinolone alone may be suitable for mild infections, while addition of drugs with antianaerobic activity may be recommended for more severe infections.

TABLE 48-4

Drug Dosing Table[a]

Drug	Brand Name	Usual Dosing Range	Special Population Dose	Other
Oral agents				
Amoxicillin–clavulanate	Augmentin	875/125 mg orally every 12 hours	Pediatric: 40 mg/kg (of the amoxicillin component) orally in two divided doses	
Cefaclor	Ceclor	500 mg orally every 8 hours	Pediatric: 20–40 mg/kg/day (not to exceed 1 g) orally in three divided doses	
Cefadroxil	Duricef	250–500 mg orally every 12 hours	Pediatric: 30 mg/kg orally in two divided doses	
Cefuroxime axetil	Ceftin	250–500 mg orally every 12 hours	Pediatric: 20–30 mg/kg orally in two divided doses	
Cephalexin	Keflex	250–500 mg orally every 6 hours	Pediatric: 25–50 mg/kg orally in four divided doses	
Ciprofloxacin	Cipro	500–750 mg orally every 12 hours		
Clindamycin	Cleocin	300–600 mg orally every 6–8 hours	Pediatric: 10–30 mg/kg/day	May be used for oral

			orally in three to four divided doses	treatment of MRSA infection
Delafloxacin	Baxdela	450 mg orally every 12 hours		May be used for oral treatment of MRSA infection
Dicloxacillin	Dynapen	250–500 mg orally every 6 hours	Pediatric: 25–50 mg/kg orally in four divided doses	
Doxycycline	Vibramycin	100–200 mg orally every 12 hours		May be used for oral treatment of MRSA infection
Erythromycin	E-Mycin Erythrocin	250–500 mg orally every 6 hours	Pediatric: 30–50 mg/kg orally in four divided doses[a]	
Levofloxacin	Levaquin	500–750 mg orally once daily		
Linezolid	Zyvox	600 mg orally every 12 hours	Pediatric: 20–30 mg/kg/day orally in two to three divided doses	For oral treatment of MRSA infection
Metronidazole	Flagyl	250–500 mg orally every 8 hours	Pediatric: 30 mg/kg orally in three to four divided doses	
Moxifloxacin	Avelox	400 mg orally once daily		
Mupirocin ointment	Bactroban	Apply to affected areas every 8 hours	Pediatric: apply to affected areas every 8 hours	
Penicillin VK	Veetids Pen-V	250–500 mg orally every 6 hours	Pediatric: 25,000–90,000 units/kg orally in four divided doses	
Retapamulin ointment	Altabax	Apply to affected area every 12 hours	Pediatric: apply to affected area every 12 hours	
Tedizolid	Sivextro	200 mg orally once daily		For oral treatment of MRSA infection
Trimethoprim–sulfamethoxazole	Bactrim Septra Cotrimoxazole	160/800 mg orally every 12 hours	Pediatric: 4–6 mg/kg (of the trimethoprim component) orally every 12 hours	Up to double the usual dose may be considered for oral treatment of MRSA infection
Parenteral agents				
Ampicillin	Omnipen Polycillin Principen	1–2 g IV every 6 hours	Pediatric: 200–300 mg/kg/day IV in four to six divided doses	

Aztreonam	Azactam	1 g IV every 6 hours	Pediatric: 100–150 mg/kg/day IV in four divided doses	
Cefazolin	Ancef Kefzol	1 g IV every 6–8 hours	Pediatric: 75 mg/kg/day IV in three divided doses	
Cefepime	Maxipime	1–2 g IV every 12 hours	Pediatric: 100 mg/kg/day IV in two divided doses	
Cefotaxime	Claforan	1–2 g IV every 6 hours	150–200 mg/kg/day in three to four divided doses	
Cefoxitin	Mefoxin	1–2 g IV every 6 hours	Pediatric: 30–40 mg/kg/day IV in four divided doses	
Ceftazidime	Fortaz	1–2 g IV every 8 hours	Pediatric: 150 mg/kg/day IV in three divided doses	
Ceftaroline	Teflaro	600 mg IV every 12 hours		For MRSA infection
Ceftriaxone	Rocephin	1 g IV once daily		
Cefuroxime	Zinacef	0.75–1.5 g IV every 8 hours	Pediatric: 150 mg/kg/day IV in three divided doses	
Ciprofloxacin	Cipro	400 mg IV every 8–12 hours		
Clindamycin	Cleocin	300–600 mg IV every 6–8 hours; 600–900 mg IV every 6–8 hours for necrotizing fasciitis	Pediatric: 30–50 mg/kg/day IV in three to four divided doses	
Dalbavancin	Dalvance	1000 mg IV once on day 1 of therapy, followed by 500 mg IV once on day 8 of therapy; OR 1500 mg IV once with no additional doses		For MRSA infection
Daptomycin	Cubicin	4 mg/kg IV once daily		For MRSA infection
Delafloxacin	Baxdela	300 mg IV every 12 hours		For MRSA infection
Doripenem	Doribax	500 mg IV every 8 hours		
Ertapenem	Invanz	1 g IV once daily	Pediatric: 30 mg/kg/day IV in one to two divided doses	
Gentamicin	Garamycin	Traditional: 2 mg/kg loading dose, followed by 1.5 mg/kg IV every 8 hours and guided by measured serum concentrations. Alternative: 5–7 mg/kg IV once daily	Pediatric: 5–7 mg/kg/day IV in three divided doses; doses guided by serum concentrations	
Imipenem–cilastatin	Primaxin	250–500 mg IV every 6–8 hours	Pediatric: 40–80 mg/kg/day IV in four divided doses	

Levofloxacin	Levaquin	500–750 mg IV once daily		
Linezolid	Zyvox	600 mg IV every 12 hours	Pediatric: 20–30 mg/kg/day IV in two to three divided doses	For MRSA infection
Meropenem	Merrem	1 g IV every 8 hours	Pediatric: 60 mg/kg/day IV in three divided doses	
Metronidazole	Flagyl	500 mg IV every 8 hours	Pediatric: 30–50 mg/kg/day IV in three divided doses	
Moxifloxacin	Avelox	400 mg IV once daily		
Nafcillin	Nafcil	1–2 g IV every 4–6 hours	Pediatric: 100–200 mg/kg/day IV in four to six equally divided doses	
Oritavancin	Orbactiv	1200 mg IV once with no additional doses		For MRSA infection
Penicillin G	Pfizerpen Bicillin Wycillin	1–2 million units IV every 4–6 hours	Pediatric: 100,000–200,000 units/kg/day IV in four divided doses[a]	
Piperacillin–tazobactam	Zosyn	3.375–4.5 g IV every 6 hours	Pediatric: 250–350 mg/kg/day IV in three to four divided doses	
Procaine penicillin G	Bicillin C-R	0.6–1.2 million units IM every 12 hours	Pediatric: 25,000–50,000 units/kg (maximum 1.2 million units) IM once daily	
Tedizolid	Sivextro	200 mg IV once daily		For MRSA infection
Telavancin	Vibativ	10 mg/kg IV once daily		For MRSA infection
Tigecycline	Tigacil	100 mg IV once, and then 50 mg IV every 12 hours		
Tobramycin	Nebcin	Traditional: 2 mg/kg loading dose, followed by 1.5 mg/kg IV every 8 hours and guided by measured serum concentrations. Alternative: 5–7 mg/kg IV once daily	Pediatric: 5–7 mg/kg/day IV in three divided doses; doses guided by serum concentrations	
Vancomycin	Vancocin	30–40 mg/kg/day IV in two divided doses; dosing guided by serum concentrations to achieve trough of 15–20 mg/L (10–14 µmol/L)	Pediatric: 40–60 mg/kg/day IV in three to four divided doses; doses guided by serum concentrations	For MRSA infection

[a]Dosing guidelines in patients with normal renal function.

IM, intramuscularly; MRSA, methicillin-resistant *S. aureus*.

IMPETIGO

- *Impetigo* is a superficial skin infection that is seen most commonly in children. It is highly communicable and spreads through close contact. Most cases are caused by *S. pyogenes*, but *S. aureus* either alone or in combination with *S. pyogenes* has emerged as a principal cause of impetigo.

Clinical Presentation

- Exposed skin, especially the face, is the most common site for impetigo.
- Pruritus is common, and scratching of the lesions may further spread infection through excoriation of the skin. Other systemic signs of infection are minimal.
- Weakness, fever, and diarrhea are sometimes seen with bullous impetigo.
- Nonbullous impetigo manifests initially as small, fluid-filled vesicles. These lesions rapidly develop into pus-filled blisters that readily rupture. Purulent discharge from the lesions dries to form golden yellow crusts that are characteristic of impetigo.
- In the bullous form of impetigo, the lesions begin as vesicles and turn into bullae containing clear yellow fluid. Bullae soon rupture, forming thin, light brown crusts.
- Regional lymph nodes may be enlarged.

Treatment

- Although impetigo may resolve spontaneously, antimicrobial treatment is indicated to relieve symptoms, prevent formation of new lesions, and prevent complications such as cellulitis.
- Topical **mupirocin** ointment or **retapamulin** ointment for 5 days is recommended as first-line treatment of mild cases of impetigo not involving multiple lesions or the face.
- Penicillinase-resistant penicillins (eg, **dicloxacillin**) are the systemic agents of choice because of the increased isolation of *S. aureus*. First-generation cephalosporins (eg, **cephalexin**) are also used (see **Table 48-3**). **Penicillin** may be used for impetigo caused by *S. pyogenes*. It may be administered as either a single intramuscular dose of **benzathine penicillin G** (300,000–600,000 units in children, 1.2 million units in adults) or as oral penicillin VK given for 7 days. Penicillin-allergic patients can be treated with oral **clindamycin**, **doxycycline**, or **trimethoprim–sulfamethoxazole**. Recommended doses for antimicrobials are given in **Table 48-4**.

CELLULITIS

- Cellulitis is an acute, spreading infectious process that initially affects the epidermis and dermis and may subsequently spread within the superficial fascia. This process is characterized by inflammation but with little or no necrosis or suppuration of soft tissue.
- Cellulitis is most often caused by *S. pyogenes* or *S. aureus* (see **Table 48-1**).
- Acute cellulitis with mixed aerobic and anaerobic pathogens may occur in diabetics, following traumatic injuries, at sites of surgical incisions to the abdomen or perineum, or where host defenses have been otherwise compromised (vascular insufficiency).

Clinical Presentation

- Cellulitis is characterized by erythema and edema of the skin. The lesion, which may be extensive, is painful and nonelevated and has poorly defined margins. Tender lymphadenopathy associated with lymphatic involvement is common. Malaise, fever, and chills are also commonly present. There is usually a history of an antecedent wound from minor trauma, an ulcer, or surgery.
- A Gram stain of a smear obtained by injection and aspiration of 0.5 mL of saline (using a small-gauge needle) into the advancing edge of the

erythematous lesion may help in making the microbiologic diagnosis but often yields negative results. Blood cultures are useful, as bacteremia may be present in 30% of cases.

Treatment

- Goals of Treatment: Rapid eradication of the infection and prevention of further complications. Antimicrobial therapy of bacterial cellulitis is directed toward the type of bacteria either documented to be present or suspected. Local care of cellulitis includes elevation and immobilization of the involved area to decrease local swelling. Incision and drainage is the primary therapy for infections such as small abscesses and furuncles, and in otherwise uncomplicated patients with mild infections. Systemic antibiotic therapy is often unnecessary in such cases.

- Antibiotic therapy is recommended along with incision and drainage in patients with more complicated abscesses associated with the following: severe or extensive disease involving multiple sites of infection; rapidly progressive infection in the presence of associated cellulitis; signs and symptoms of systemic illness; complicating factors such as extremes of age, comorbidities, or immunosuppression; abscesses in areas that are difficult to drain, such as hands, face, and genitalia; or lack of response to previous drainage alone.

- Oral agents recommended for moderate purulent cellulitis include **trimethoprim–sulfamethoxazole** and **doxycycline** (**Figure 48-1**). Oral **linezolid** is also recommended in such cases but is significantly more expensive and apparently no more efficacious than other treatment options.

- Patients with severe purulent cellulitis should be hospitalized for empiric treatment with parenteral antibiotics having activity against MRSA. **Vancomycin, daptomycin, linezolid, telavancin**, and **ceftaroline** are all acceptable treatment options with comparable efficacy in adults (**Figure 48-1**). In children, **vancomycin, linezolid**, or **clindamycin** are the preferred treatment options.

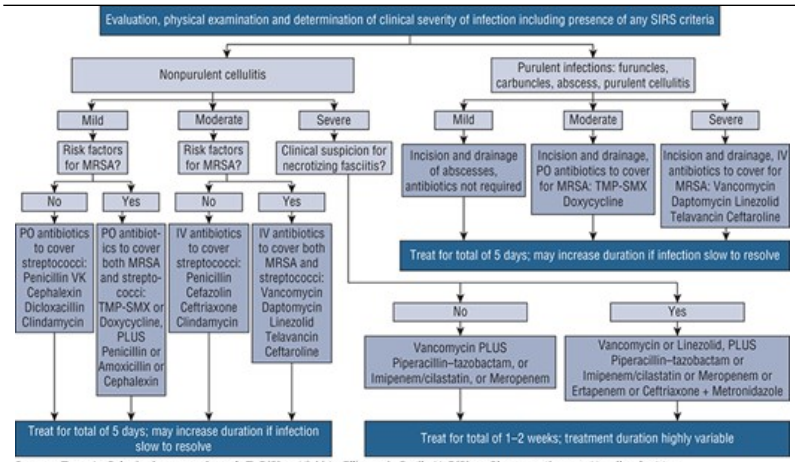
- Empiric therapy of nonpurulent cellulitis is directed primarily against group A β-hemolytic streptococci. Recommended empiric therapy of mild nonpurulent cellulitis (ie, no focus of purulence or systemic signs of infection) consists of an orally administered β-lactam such as **penicillin VK, cephalexin,** or **dicloxacillin**.

- Hospitalization and treatment with parenteral antibiotics are also recommended for patients with severe nonpurulent cellulitis as indicated by the presence of systemic findings of infection, failure of previous oral antibiotic therapy, immunocompromised states, or presence of clinical signs of deeper infection such as bullae, skin sloughing, hypotension, or organ dysfunction. Recommended regimens include vancomycin plus **piperacillin–tazobactam**, and **vancomycin** plus **imipenem–cilastatin** or **meropenem**.

FIGURE 48-1

Recommended treatment algorithm for initial empiric management of selected purulent and nonpurulent skin and soft-tissue infections.

(GNR, aerobic gram-negative rods; GPC, aerobic gram-positive cocci; IV, intravenous; MRSA, methicillin-resistant Staphylococcus aureus; PO, oral; SIRS, systemic inflammatory response syndrome; TMP-SMX, trimethoprim–sulfamethoxazole.)



Source: Terry L. Schwinghammer, Joseph T. DiPiro, Vicki L. Ellingrod, Cecily V. DiPiro: *Pharmacotherapy Handbook, 11e*

DIABETIC FOOT INFECTIONS

- Three key factors are involved in the causation of diabetic foot problems: neuropathy, ischemia, and immunologic defects. Any of these disorders can occur in isolation; however, they frequently occur together.
- There are three major types of diabetic foot infections (DFIs): deep abscesses, cellulitis of the dorsum, and mal perforans ulcers of the sole of the foot. Osteomyelitis may occur in 30%–40% of infections.
- Mild cases of DFIs are often monomicrobial. However, more severe infections are typically polymicrobic; up to 60% of hospitalized patients have polymicrobial infections. Staphylococci and streptococci are the most common pathogens, although gram-negative bacilli and anaerobes occur in 50% of cases.
- Patients with peripheral neuropathy often do not experience pain but seek medical attention for swelling or erythema. Lesions vary in size and clinical features. A foul-smelling odor suggests anaerobic organisms. Temperature may be mildly elevated or normal.

Treatment

- Goals of Treatment: (a) Successfully treat infected wounds by using effective nondrug and antibiotic therapy; (b) prevent additional infectious complications; (c) preserve as much normal limb function as possible; (d) avoid unnecessary use of antimicrobials that contribute to increased resistance; and (e) minimize toxicities and cost while increasing patient quality of life.
- Up to 90% of infections can be treated successfully with a comprehensive treatment approach that includes both wound care and antimicrobial therapy. After carefully assessing the extent of the lesion and obtaining necessary cultures, necrotic tissue must be thoroughly debrided, with wound drainage and amputation as required.
- Diabetic glycemic control should be maximized to ensure optimal healing.
- The patient should initially be restricted to bed rest, leg elevation, and control of edema, if present.
- Suggested antibiotic regimens for empiric treatment of DFIs are given in **Table 48-5**. Treatment algorithms for initial management of mild-to-moderate DFI and severe DFI are shown in **Figures 48-2** and **48-3**.

FIGURE 48-2

Recommended treatment algorithm for initial empiric management of mild-to-moderate diabetic foot infections.

(GNR, aerobic gram-negative rods; GPC, aerobic gram-positive cocci; MRSA, methicillin-resistant *Staphylococcus aureus*; TMP-SMX, trimethoprim–sulfamethoxazole.)

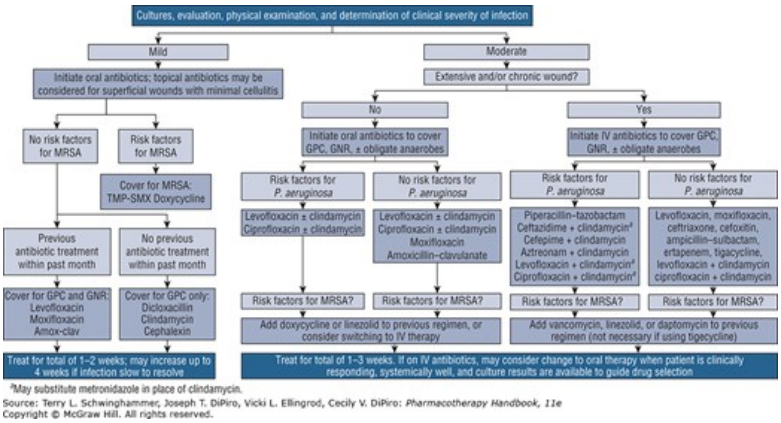


FIGURE 48-3

Recommended treatment algorithm for initial empiric management of severe diabetic foot infections.

(GNR, aerobic gram-negative rods; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillinsusceptible *S. aureus*.)

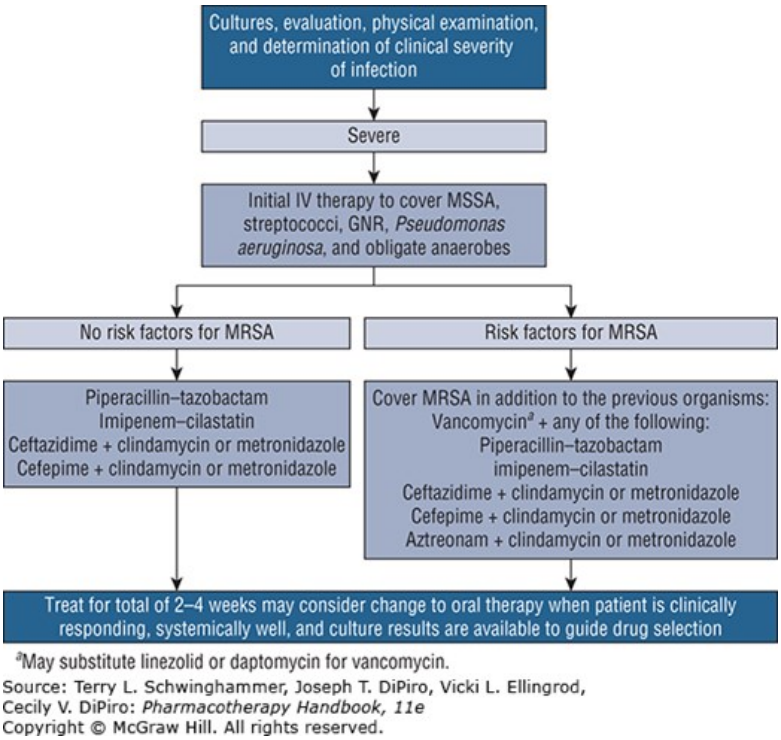


TABLE 48-5

Suggested Antibiotic Regimens for Empiric Treatment of Diabetic Foot Infections

Severity of Infection	Probable Pathogens	Drug(s)[a]	Duration of Therapy
Mild	*Staphylococcus aureus* (MSSA) *Streptococcus* spp. *S. aureus* (MRSA) • Patients with history of MRSA infection or colonization in past year	Amoxicillin–clavulanate Cephalexin Dicloxacillin Clindamycin Levofloxacin	1–2 weeks; may increase up to 4 weeks if infection slow to resolve

	• Prevalence of MRSA ≥50% in local geographic area • Recent hospitalization	Moxifloxacin[b]	
Moderate-to-severe (initially oral or IV antibiotics for moderately severe infections, IV antibiotics for severe infections)	MSSA *Streptococcus* spp. Enterobacteriaceae Obligate anaerobes	Ampicillin/Sulbactam Cefoxitin Ceftriaxone Imipenem/Cilastatin Ertapenem Levofloxacin Moxifloxacin Tigecycline Levofloxacin or ciprofloxacin + clindamycin	Moderately severe infection: 1–3 weeks; severe infection: 2–4 weeks
	MRSA • Patients with history of MRSA infection or colonization in past year • Prevalence of MRSA ≥30% in local geographic area • Recent hospitalization • Infection severe enough that not empirically covering MRSA poses unacceptable risk of treatment failure	Add to one of the above regimens: • Vancomycin • Linezolid • Daptomycin	
	Pseudomonas aeruginosa • Patient has been soaking feet • Patient has previously failed therapy with nonpseudomonal antibiotic regimen • Severe infection	Piperacillin/Tazobactam	
	Mixed infections potentially including all of the above	Cefepime, ceftazidime, or aztreonam + metronidazole or clindamycin + vancomycin[c] *or* Piperacillin–tazobactam or imipenem–cilastatin or meropenem[b] + vancomycin[c]	

[a]Agents not shown in any particular order of preference.

[b]Not specifically recommended in IDSA guidelines but may be appropriate treatment option.

[c]Linezolid or daptomycin may be used in place of vancomycin.

MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*.

INFECTED PRESSURE ULCERS

- A pressure sore is also called a “decubitus ulcer” or “bed sore.” A classification system for pressure sores is presented in **Table 48-6**. Many factors are thought to predispose patients to the formation of pressure ulcers: paralysis, paresis, immobilization, malnutrition, anemia, infection, and advanced age. Factors thought to be most critical to their formation are pressure, shearing forces, friction, and moisture; however, there is still debate as to the exact pathophysiology of pressure sore formation. The areas of highest pressure are generated over the bony prominences.
- Most pressure sores are heavily colonized by microorganisms. A large variety of aerobic gram-positive and gram-negative bacteria, as well as anaerobes, are frequently isolated from wound cultures.

TABLE 48-6

Pressure Injury Classification

Stage 1	Intact skin with a localized area of nonblanchable erythema. Presence of blanchable erythema or changes in sensation, temperature, or firmness may precede visual changes. Color changes do not include purple or maroon discoloration; these may indicate deep tissue pressure injury.
Stage 2	Partial-thickness loss of skin with exposed dermis. Wound bed is viable, pink or red, moist, and may also present as an intact or ruptured serum-filled blister. Adipose tissue is not visible and deeper tissues are not visible. Granulation tissue, slough, and eschar are not present.
Stage 3[a]	Full-thickness loss of skin, in which adipose tissue is visible in the ulcer and granulation tissue and epibole (rolled wound edges) are often present. Slough and/or eschar may be visible. Depth of tissue damage varies by anatomical location; areas of significant adiposity can develop deep wounds. Undermining and tunneling may occur. Fascia, muscle, tendon, ligament, cartilage, and/or bone are not exposed.
Stage 4[a]	Full-thickness skin and tissue loss with exposed or directly palpable fascia, muscle, tendon, ligament, cartilage, or bone in the ulcer. Slough and/or eschar may be visible. Epibole (rolled edges), undermining, and/or tunneling often occur. Depth varies by anatomical location.
Unstageable[a]	Full-thickness skin and tissue loss in which the extent of tissue damage within the ulcer cannot be confirmed because it is obscured by slough or eschar. If slough or eschar is removed, a stage 3 or stage 4 pressure injury will be revealed.
Deep-tissue pressure injury	Intact or nonintact skin with localized area of persistent nonblanchable deep red, maroon, purple discoloration or epidermal separation revealing a dark wound bed or blood-filled blister. Pain and temperature change often precede skin color changes. This injury results from intense and/or prolonged pressure and shear forces at the bone-muscle interface. The wound may evolve rapidly to reveal the actual extent of tissue injury, or may resolve without tissue loss.

[a]Stage 3, stage 4, and unstageable lesions are unlikely to resolve on their own and often require surgical intervention.

Clinical Presentation

- Most pressure sores are in the pelvic region and lower extremities. The most common sites are the sacral and coccygeal areas, ischial tuberosities, and greater trochanter.
- A dark red color on the surface of a pressure sore may indicate local infection. Surrounding erythema, swelling, and heat are commonly present with infection. Purulent discharge, foul odor, and systemic signs (fever and leukocytosis) may be present.
- Pressure sores vary greatly in their severity, ranging from an abrasion to large lesions that can penetrate into the deep fascia involving both bone and muscle.

Prevention and Treatment

- Goals of Treatment: The primary goal for pressure sores is prevention. Once a pressure sore has developed, the goals of therapy are prevention of complications (ie, infections), preventing sores from growing larger, and preventing the development of sores in other locations.
- Prevention is the single most important aspect in managing pressure sores. Friction and shearing forces can be minimized by proper positioning. Skin care and prevention of soilage are important, with the intent being to keep the surface relatively free from moisture. Relief for a period of only 5 minutes once every 2 hours gives protection against pressure sore formation.
- The goal of therapy is to clean and decontaminate the ulcer in order to permit formation of healthy granulation tissue that promotes wound healing or prepares the wound for an operative procedure. The main factors to be considered for successful wound care are: (1) relief of pressure; (2) debridement of necrotic tissue; (3) wound cleansing; (4) dressing selection; and (5) prevention, diagnosis, and treatment of infection.
- Medical management is generally indicated for lesions that are of moderate size and of relatively shallow depth (stage 1 or 2 lesions) and are not located over a bony prominence.
- Debridement can be accomplished by surgical, mechanical (wet-to-dry dressing changes), or chemical means. Other effective therapies are hydrotherapy, wound irrigation, and dextranomers. Pressure sores should be cleaned with normal saline.
- A short, 2-week trial of topical antibiotic (**silver sulfadiazine** or **triple antibiotic**) is recommended for a clean ulcer that is not healing or is producing a moderate amount of exudate despite appropriate care.

INFECTED BITE WOUNDS

- Patients at risk of acquiring an infection after a bite have had a puncture wound, have not sought medical attention within 8 hours of injury, or are older than 50 years.
- An infected dog or cat bite is usually characterized by erythema, and clear or purulent discharge at the wound site. If *Pasteurella multocida* is present, a rapidly progressing cellulitis is observed within 24–48 hours of initial injury.
- Most infections from dog and cat bites are polymicrobial. *Pasteurella* is the most frequent isolate.
- Bite wounds should be irrigated thoroughly with a copious volume of sterile water or saline, and the wound washed vigorously with soap or povidone–iodine in order to reduce the bacterial count in the wound. Surgical debridement and immobilization of the affected area are often required in dog and human bites associated with more extensive tissue injury.
- The role of antimicrobials for non-infected dog bite wounds remains controversial. A 3–5 day antibiotic prophylaxis regimen is recommended in patients with the following factors associated with increased risk for infection: immunocompromised; asplenic; advanced liver disease; preexisting or resultant edema of the affected area; moderate-to-severe bite-related injuries, especially to the hands or face; or bite injuries that have penetrated the periosteum or joint capsule.
- Empiric antibiotics for the treatment of established infection of dog and cat bite wounds should be directed at a variety of aerobic and anaerobic flora. **Amoxicillin–clavulanic** acid is commonly recommended for oral outpatient therapy. Alternative oral agents include **doxycycline** alone, or **trimethoprim–sulfamethoxazole, levofloxacin, ciprofloxacin**, or a second- or third-generation cephalosporin in combination with **metronidazole** or **clindamycin** to provide activity against oropharyngeal anaerobes.
- Treatment options for patients requiring IV therapy include β-lactam–β-lactamase inhibitors (**ampicillin–sulbactam** and **piperacillin–tazobactam**), second-generation cephalosporins with antianaerobic activity (**cefoxitin**), and **ertapenem**. Therapy should generally be continued from 7 to 14 days.
- If the immunization history of a patient with anything other than a clean minor wound is not known, tetanus/diphtheria toxoids (TD) should be administered. Both TD and tetanus immunoglobulin should be administered to patients who have never been immunized.

- If a patient has been exposed to rabies, the treatment objectives consist of thorough irrigation of the wound, tetanus prophylaxis, antibiotic prophylaxis (if indicated), and immunization. Postexposure prophylaxis immunization consists of both passive antibody administration and vaccine administration.

HUMAN BITES

- Infections caused by these injuries are most often caused by the normal oral flora, which includes both aerobic and anaerobic microorganisms. Human bite wounds are notable for potential involvement of *Eikenella corrodens* in approximately 30% of infections.
- Management of bite wounds consists of aggressive irrigation and topical wound dressing, surgical debridement, and immobilization of the affected area. Primary closure for human bites is not generally recommended. Tetanus toxoid and antitoxin may be indicated.
- All patients with human bite injuries should receive prophylactic antibiotic therapy (“early preemptive therapy”) for 3–5 days due to high infection risk.
- **Amoxicillin–clavulanic** acid (500 mg every 8 hours) is commonly recommended. Alternatives for penicillin-allergic patients include fluoroquinolones or **trimethoprim–sulfamethoxazole** in combination with **clindamycin** or **metronidazole**.
- Patients with serious injuries or clenched-fist injuries should be started on IV antibiotics. Treatment options for patients requiring IV therapy include β-lactam–β-lactamase inhibitor combinations (**ampicillin–sulbactam**, **piperacillin–tazobactam**), second-generation cephalosporins with antianaerobic activity (eg, **cefoxitin**), and **ertapenem**.

See Chapter 128, Skin and Soft-Tissue Infections, authored by Douglas N. Fish, for a more detailed discussion of this topic.