

# SKIN AND SOFT TISSUE INFECTIONS



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## LEARNING OBJECTIVES

1. Given a patient's clinical presentation and risk factors, distinguish between the various types of skin and soft tissue infections.
2. Given a patient's profile, develop a pharmacotherapeutic plan to treat a skin or soft tissue infection.
3. Assess the safety profiles of antimicrobials commonly used for the treatment of skin and soft tissue infections.
4. Justify prevention measures to reduce the recurrence and transmission of a patient's skin and soft tissue infections.

## INTRODUCTION

Skin and soft tissue infections (SSTIs), also referred to as *skin and skin structure infections*, represent a group of infections that are diverse in their clinical presentations and degrees of severity. They are generally classified into two categories: purulent infections (e.g.,

furuncles, carbuncles, abscesses) nonpurulent infections (e.g., erysipelas, cellulitis, necrotizing fasciitis). They are then further classified into three subcategories: mild, moderate, and severe. Mild infections present with local symptoms only, whereas moderate to severe infections are associated with systemic signs of infection such as temperature higher than 38°C, heart rate higher than 90 beats/minute, respiratory rate higher than 24 breaths/minute, or WBC higher than  $12 \times 10^3$  cells/mm<sup>3</sup>. Patients with immunocompromising conditions, clinical signs of deeper infection, or infection that fails to improve with incision and drainage (I&D) plus oral antibiotics are also classified as severe cases. Purulent infections are treated with I&D and antibiotic administration in moderate and severe cases. Nonpurulent infections are treated with antibiotic administration, with the addition of surgical debridement in severe cases (Stevens 2014).

The majority of SSTIs are caused by bacteria and are referred to as acute bacterial skin and skin structure infections (ABSSSIs). Some cases are caused by viruses—most notably, varicella zoster virus (VZV), which is the causative

## BASELINE KNOWLEDGE STATEMENTS

Readers of this chapter are presumed to be familiar with the following:

- Basic knowledge of skin and soft tissue infections
- Pharmacology—including mechanisms of action, adverse effects, and drug interactions—of antimicrobials used in the treatment of skin and soft tissue infections

## ADDITIONAL READINGS

The following free resources are available for readers wishing additional background information on this topic.

- Infectious Diseases Society of America (IDSA). [Guidelines for skin and soft tissue infections](#), 2014.
- IDSA. [Guidelines for diabetic foot infections](#), 2012.
- IDSA. [Guidelines for methicillin-resistant \*Staphylococcus aureus\* infections](#), 2011.
- Centers for Disease Control and Prevention (CDC). [Methicillin-resistant \*Staphylococcus aureus\* \(MRSA\) infections](#), 2014 [homepage on the Internet].
- CDC. [Shingles \(herpes zoster\)](#), 2014 [homepage on the Internet].
- CDC. [Prevention of herpes zoster](#), 2008 [homepage on the Internet].

## ABBREVIATIONS IN THIS CHAPTER

ABSSSI	Acute bacterial skin and skin structure infection
CAMRSA	Community-associated methicillin-resistant <i>Staphylococcus aureus</i>
DFI	Diabetic foot infection
HAMRSA	Health care–associated methicillin-resistant <i>Staphylococcus aureus</i>
I&D	Incision and drainage
IDSA	Infectious Diseases Society of America
MIC	Minimum inhibitory concentration
MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
MSSA	Methicillin-sensitive <i>Staphylococcus aureus</i>
SSI	Surgical site infection
SSTI	Skin and soft tissue infection
VZV	Varicella zoster virus

organism of chickenpox and shingles. Similarities in clinical presentation and limitations in the ability to identify the causative organisms in a timely manner make the diagnosis and treatment of SSTIs initially challenging. Therefore, careful assessment of risk factors and degree of severity, as well as obtaining a detailed medical history and performing a physical examination are required to appropriately diagnose and manage a patient presenting with an SSTI. Antimicrobial regimens are often selected empirically based on host characteristics, most likely pathogens, and local susceptibility patterns, with streamlining according to microbiology culture and sensitivity if the causative organisms are isolated.

This chapter provides an update on the epidemiology, pathophysiology, risk factors, causative organisms, and clinical features of the most common ABSSSIs, as well as of herpes zoster, and focuses on the pharmacologic management of those infections in both the outpatient and inpatient settings. Antimicrobial stewardship, infection control, and prevention options are also discussed.

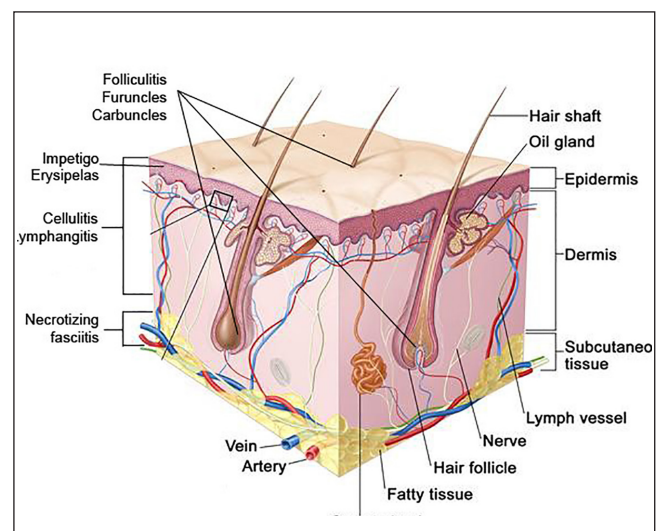
## EPIDEMIOLOGY

The true prevalence of SSTIs is unknown because mild infections are typically self-limiting and patients do not seek medical attention. Nonetheless, SSTIs are encountered often in both the outpatient and inpatient settings. According to the 2011 National Statistics of the Healthcare Cost and Utilization Project, SSTIs accounted for 3.4 million emergency department visits, or 2.6% of all emergency department visits, with 13.9% of visits resulting in hospitalization (DHHS 2011a). Skin and soft tissue infections also accounted for 500,000 hospital discharges, or 1.4% of total discharges, with a mean length of stay of 3.7 days and

a mean charge of \$18,299 per case (DHHS 2011b). Those numbers are on the rise because the prevalence of community-associated methicillin-resistant *Staphylococcus aureus* (CAMRSA) increased in the past decade (Merritt 2013; Talan 2011; Edelsberg 2009; Gerber 2009). A recent prospective study demonstrated that 1 in 5 patients presenting to a primary care clinic for an SSTI caused by methicillin-resistant *S. aureus* (MRSA) require additional interventions at an associated cost of almost \$2000 per patient (Labreche 2013). The incidence of herpes zoster is also increasing, and there are more than 1 million cases each year in the United States, with an annual rate of 3 to 4 cases per 1000 persons (Rimland 2010).

## Pathophysiology

Intact skin provides protection from the external environment by serving as a physical barrier and maintaining a normal flora that is not conducive to the growth of pathogenic organisms. *Primary SSTIs* occur when microorganisms invade otherwise healthy skin, whereas *secondary SSTIs* occur when, because of underlying disease or trauma, microorganisms infect already damaged skin. In both cases, pathogenic microorganisms cause damage to the surrounding tissues, which leads to an inflammatory response characterized by warmth, erythema, and pain. Such damage is more complicated in patients with diabetes because long-term hyperglycemia leads to motor and autonomic neuropathy, cellular and humoral immunopathy, and angiopathy. Reactivation of latent VZV at the spinal root or cranial nerve neurons causes the inflammatory response associated with herpes zoster. Figure 1-1 illustrates human skin structures and the corresponding locations of various SSTIs.



**Figure 1-1.** Skin structures.

Image from National Cancer Institute. [Skin anatomy](#) [homepage on the Internet].

## Risk Factors

Acute bacterial skin and skin structure infections occur when skin integrity is compromised as a result of high bacterial load on the skin, the availability of bacterial nutrients, excessive skin moisture, inadequate blood supply, immunosuppression, or damage to the corneal layer. Poor hygiene, the sharing of personal items, physical contact, and crowded living conditions facilitate the spread of contagious infections such as furuncles, carbuncles, and impetigo. Peripheral vascular disease and pre-existing skin diseases increase the risk of erysipelas and cellulitis. Poorly controlled diabetes often leads to diabetic foot infection (DFI). Traumatic events such as cuts and bites and injection drug use result in wounds that increase the risk of skin infections and abscesses. The risk of surgical site infection (SSI) depends on the category of operation, with clean and low-risk operations having the smallest risk of infections and contaminated and high-risk operations having the highest risk.

Colonization with *S. aureus* in the anterior nares and *Streptococcus pyogenes* on the skin increases the risk of those skin infections. Skin-to-skin contact from playing sports, attendance at day care or school, and living in close quarters (e.g., military barracks) are risk factors for CAMRSA skin infections. Risk factors for health care-associated methicillin-resistant *S. aureus* (HAMRSA) skin infections include recent exposure to antibiotics or the health care system (Herman 2008).

Herpes zoster is associated with advanced age and immunosuppressive conditions. The risk is higher for women, whites, and those with family histories of herpes zoster (Cohen 2013).

## CAUSATIVE ORGANISMS

Acute bacterial skin and skin structure infections are caused primarily by gram-positive cocci—particularly, *S. aureus* and *S. pyogenes*. *S. aureus* is the most common cause of furuncles, carbuncles, cutaneous abscesses, and impetigo. *S. pyogenes* is the most common cause of erysipelas, lymphangitis, and cellulitis in patients without penetrating trauma, evidence of MRSA infection elsewhere, nasal colonization with MRSA, injection drug use, or systemic inflammatory-response syndrome. Gram-negative rods and anaerobic bacteria can also cause ABSSSIs, particularly in patients with deep long-standing ulcers, immunocompromising conditions, or recent antibiotic exposure (Stevens 2014).

In the past decade, MRSA has become the most common identifiable cause of purulent SSTIs among patients presenting to emergency departments in the United States (Merritt 2013; Talan 2011). The CAMRSA isolates are predominantly pulsed-field type USA300 or USA400, with staphylococcal chromosome cassette type IV or V, and are most likely to be producers of Panton-Valentine leucocidin toxin (Herman 2008). These CAMRSA

isolates typically remain susceptible to trimethoprim/sulfamethoxazole, clindamycin, and tetracycline (Talan 2013; Herman 2008). The HAMRSA isolates are predominantly pulsed-field type USA100, USA500, or USA800, with staphylococcal chromosome cassette type I, II, or III, and are less likely to be producers of Panton-Valentine leucocidin toxin (Herman 2008). They are often resistant to older, non- $\beta$ -lactam antibiotics (Herman 2008). Figure 1-2 depicts a cutaneous abscess caused by MRSA.

Infected dog and cat bite wounds are polymicrobial, with *Pasteurella* spp., *Streptococcus* spp., *Staphylococcus* spp., and *Moraxella* spp. as the most common aerobic organisms, and with *Fusobacterium* spp., *Porphyromonas* spp., *Prevotella* spp., and *Bacteroides* spp. as the most common anaerobic organisms. *Pasteurella* spp. is the most common etiology of dog and cat bite infections, and many infections are caused by both aerobic and anaerobic microorganisms. Such organisms often reflect the oral flora of the biting animal and, to a lesser extent, the victim's own skin flora (Abrahamian 2011). Infected human bite wounds are also polymicrobial, with *Streptococcus* spp., *Staphylococcus* spp., *Corynebacterium* spp., *Eikenella* spp., and oral anaerobic flora as the most common organisms (Pettitt 2012).

Necrotizing SSTIs are either monomicrobial or polymicrobial. Monomicrobial infections are often caused by hypervirulent strains of *S. pyogenes* and to a lesser extent by *S. aureus*, *Clostridium perfringens*, *Vibrio vulnificus*, or *Aeromonas hydrophila*. Infection with streptococci and staphylococci can occur simultaneously, and infection with *C. perfringens* is referred to as *clostridial gas gangrene* or *myonecrosis* (Stevens 2014). Polymicrobial infections are caused by a variety of organisms, with *Streptococcus*



**Figure 1-2.** Cutaneous abscess caused by methicillin-resistant *Staphylococcus aureus*.

Image from the Centers for Disease Control and Prevention. Methicillin-resistant *Staphylococcus aureus* (MRSA) infections [homepage on the Internet].



spp. and *Staphylococcus* spp. as the most common Gram-positive cocci; Enterobacteriaceae as the most common gram-negative rods; and *Bacteroides* spp., *Clostridium* spp., and *Peptostreptococcus* spp. as the most common anaerobic organisms (Anaya 2007).

## TREATMENT

The goals of therapy for ABSSSIs are to eradicate the causative organism(s), alleviate signs and symptoms, avoid complications, and prevent recurrences (Figure 1-3). Incision and drainage represents the mainstay of therapy for all purulent SSTIs. Table 1-1 lists dosing regimens in adults and children, adverse effects, and significant drug interactions for common antibiotics used in the treatment of SSTIs.

Mild purulent infections are treated with I&D and do not require systemic antibiotic therapy. Moderate purulent infections are treated with I&D and oral antibiotics. Severe purulent infections are treated with I&D and an initial course of intravenous antibiotics followed by oral antibiotics when appropriate.

Mild nonpurulent infections are treated with oral antibiotics. Moderate nonpurulent infections are treated with an initial course of intravenous antibiotics followed by oral antibiotics when appropriate. Severe nonpurulent infections are treated with surgical debridement and intravenous antibiotics (Stevens 2014).

The goals of therapy for herpes zoster are to alleviate signs and symptoms and avoid complications. Moderate to severe infections are often treated with antivirals that target VZV. Table 1-2 lists dosing regimens in adults, adverse effects, and significant drug interactions for antivirals commonly used in the treatment of herpes zoster.

## INFECTIONS IN THE OUTPATIENT SETTING

### Folliculitis, Furuncles, Carbuncles, and Cutaneous Abscesses

Folliculitis is an infection of one or more hair follicles that may affect any area of the body (excepting the palms and soles, where there is no hair). It presents as a red dot that ultimately becomes a white tip, and it may be associated with rash or pruritus. Furuncles are deeper than folliculitis and result in painful swollen boils on the skin. Carbuncles and cutaneous abscesses are larger than furuncles and have openings that drain pus; they are often associated with fever, swollen lymph nodes, and fatigue. Diagnosis of these SSTIs is based on clinical presentation. Gram stain and culture of the pus from carbuncles and abscesses are recommended, but treatment without those studies is reasonable in typical cases (Stevens 2014).

In mild cases, I&D is recommended without systemic antibiotic therapy. Conditions for which antibiotic therapy is recommended after I&D are summarized in Box 1-1. In moderate cases, oral antibiotics directed

against CAMRSA (e.g., trimethoprim/sulfamethoxazole, doxycycline, clindamycin) are recommended in addition to I&D. A recent multicenter randomized double-blind controlled trial of clindamycin versus trimethoprim/sulfamethoxazole in the treatment of uncomplicated SSTIs found no differences in efficacy and tolerability between the two agents (Miller 2013).

When methicillin-sensitive *S. aureus* (MSSA) is isolated, oral dicloxacillin or cephalexin is recommended. In severe cases, intravenous antibiotics directed against MRSA (e.g., vancomycin, daptomycin, linezolid) are recommended in addition to I&D. When MSSA is isolated, intravenous nafcillin, cefazolin, or clindamycin is recommended in severe cases (Singer 2014; Stevens 2014; Forcade 2012). The duration of therapy is 5–10 days for outpatients and 7–14 days for inpatients but should be individualized based on a patient's clinical response (Liu 2011).

In all cases, application of warm moist compresses facilitates pus elimination. Recurrent abscesses should be drained, cultured, and treated for 5–10 days with an antibiotic directed against the isolated organism. A decolonization regimen with mupirocin intranasally twice daily for 5 days, chlorhexidine washes daily, and decontamination of personal items should be considered (Stevens 2014). Patients in need of education about SSTIs caused by MRSA may be provided with a link to an [online video](#).

### Impetigo

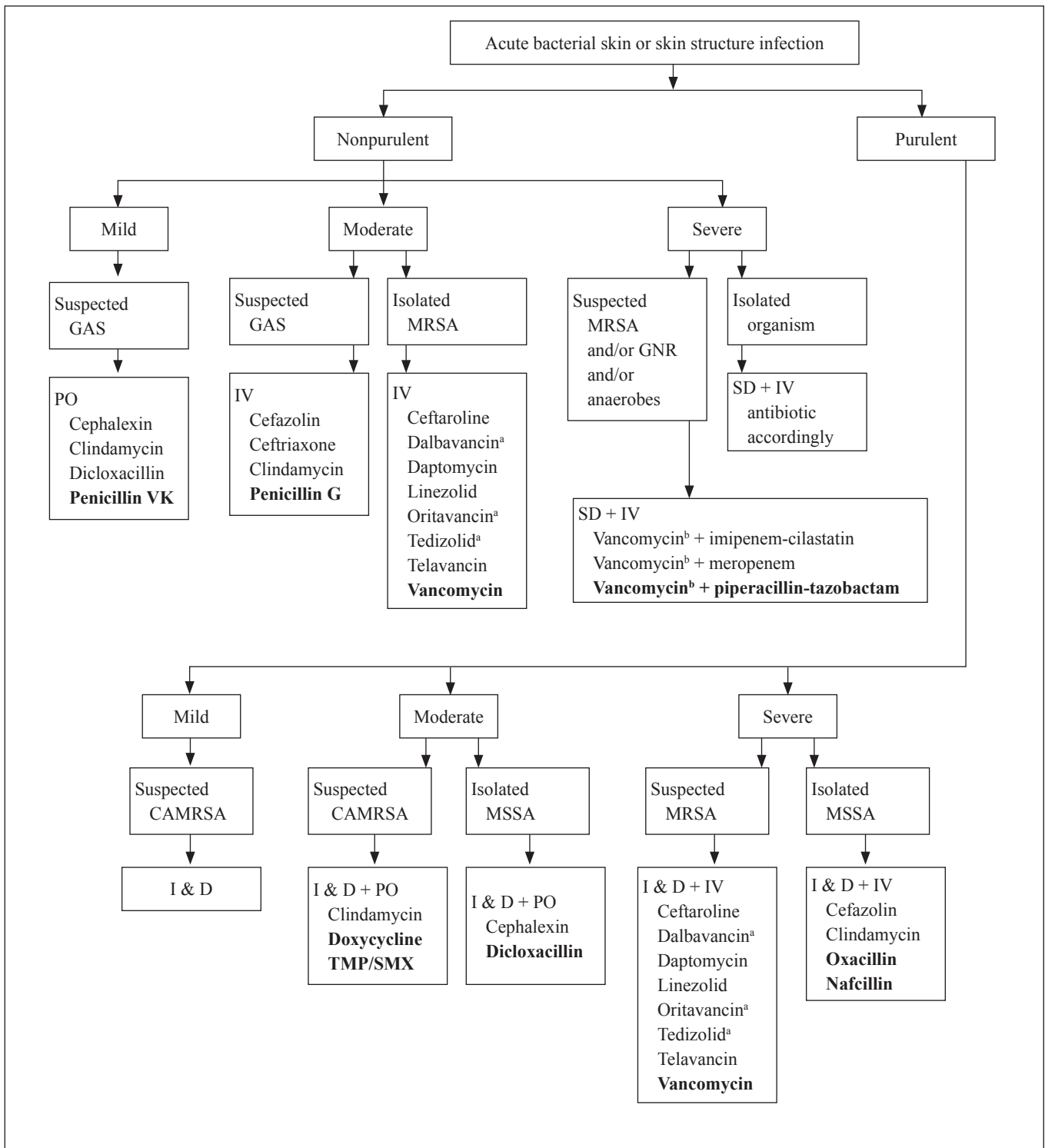
Impetigo occurs mostly in children and is characterized by multiple erythematous, vesicular, and pruritic lesions on the face and the extremities. Nonbullous impetigo presents with small fluid-filled vesicles that soon develop into pustules that rupture, leaving golden-yellow crusts. Bullous impetigo presents with vesicles that develop into yellow fluid-filled bullae that rupture, leaving brown crusts. Rarely, streptococcal impetigo leads to

*Continued on page 10*

#### Box 1-1. Conditions in Which Antibiotic Therapy is Recommended After Incision and Drainage

- Abscess in area difficult to drain completely
- Associated comorbidities or immunosuppression
- Associated septic phlebitis
- Extremes of age
- Lack of response to incision and drainage alone
- Severe or extensive disease
- Signs and symptoms of systemic illness

Information from: Liu C, Bayer A, Cosgrove SE, et al; Infectious Diseases Society of America. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. Clin Infect Dis 2011;52:e18-55.



**Figure 1-3.** General approach to the management of acute bacterial skin and skin structure infections. Bolding indicates antibiotic of choice.

<sup>a</sup>Not included in the 2014 IDSA guidelines for the management of skin and soft tissue infections.

<sup>b</sup>An alternative new anti-MRSA antibiotic can also be used.

CAMRSA = community-associated methicillin-resistant *Staphylococcus aureus*; GAS = Group A  $\beta$ -hemolytic *Streptococcus*; GNR = gram-negative rods; I & D = incision and drainage; IV = intravenous; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-sensitive *Staphylococcus aureus*; PO = oral; SD = surgical debridement.

Information 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:e10-52.

**Table 1-1.** Common and New Antibiotics Used for Skin and Soft Tissue Infections

Agent	Clinically Useful Activity Against MRSA	Dosing Regimen <sup>a,b</sup>	Adverse Effects	Drug Interactions
<b>Topical Antibiotics</b>				
Mupirocin (ointment, cream)	Yes	Skin infections for adults and children $\geq 2$ months: Apply to affected area twice daily for 5 days MRSA decolonization for adults and children $\geq 12$ years: Apply to anterior nares twice daily for 5 days	Hypersensitivity reactions, skin irritation, pruritus, burning	None significant
Retapamulin (ointment)	Yes	Impetigo for adults and children $\geq 9$ months: Apply to affected area twice daily for 5 days	Hypersensitivity reactions, skin irritation, eczema, pruritus	None significant
<b>Systemic Antibiotics</b>				
Amoxicillin/clavulanic acid	No	Adults and children $\geq 40$ kg: 875 mg of amoxicillin PO twice daily Children $< 40$ kg: 25 mg/kg/day of amoxicillin PO divided into 2 doses	Hypersensitivity reactions, gastrointestinal upset	None significant
Cefazolin	No	Adults: 1 g IV three times daily Children: 50 mg/kg/day IV divided into 3 doses	Hypersensitivity reactions	None significant
Ceftaroline	Yes	Adults: 600 mg IV twice daily	Hypersensitivity reactions	None significant
Ceftriaxone	No	Adults: 1 g IV daily Children: 50–75 mg/kg/day IV divided into 1 to 2 doses	Hypersensitivity reactions	None significant
Cephalexin	No	Adults and children $> 15$ years: 250 to 500 mg PO 4 times daily Children $\leq 15$ years: 25 to 50 mg/kg/day PO divided into 3 to 4 times	Hypersensitivity reactions	None significant
Clindamycin	Yes <sup>c</sup>	Adults: 300–450 mg PO four times daily Adults: 600 mg IV three times daily Children: 20–40 mg/kg/day IV/PO divided into 3 doses	<i>Clostridium difficile</i> infection, gastrointestinal upset	None significant
Dalbavancin	Yes	Adults: 1000 mg on day 1 followed by 500 mg on day 8	Hypersensitivity reactions, infusion reactions, gastrointestinal upset	None significant
Daptomycin	Yes	Adults: 4 mg/kg IV daily	Elevated creatine phosphokinase, eosinophilic pneumonia	Statins
Dicloxacillin	No	Adults and children $\geq 40$ kg: 250–500 mg PO four times daily Children $< 40$ kg: 25–50 mg/kg/day PO divided into 4 doses	Hypersensitivity reactions	None significant

**Table 1-1.** Common and New Antibiotics Used for Skin and Soft Tissue Infections (*continued*)

<b>Agent</b>	<b>Clinically Useful Activity Against MRSA</b>	<b>Dosing Regimen<sup>a,b</sup></b>	<b>Adverse Effects</b>	<b>Drug Interactions</b>
Doxycycline <sup>d</sup>	Yes <sup>c</sup>	Adults and children > 45 kg: 100 mg PO twice daily Children ≥ 8 years and ≤ 45 kg: 2 mg/kg PO twice daily	Gastrointestinal upset, photosensitivity, permanent tooth discoloration in children < 8 years, not recommended for pregnant women and children < 8 years	Oral cations
Linezolid	Yes	Adults and children ≥ 12 years: 600 mg IV/PO twice daily Children < 12 years: 10 mg/kg/day IV/PO twice daily	Myelosuppression, neuropathy, serotonin syndrome	Serotonergic agents
Minocycline <sup>d</sup>	Yes <sup>c</sup>	Adults: 200 mg PO on day 1 followed by 100 mg twice daily Children ≥ 8 years: 4 mg/kg PO on day 1 followed by 2 mg/kg twice daily	Gastrointestinal upset, photosensitivity, permanent tooth discoloration in children < 8 years, not recommended for pregnant women and children < 8 years	Oral cations
Nafcillin	No	Adults: 1–2 g IV six times daily Children: 100–150 mg/kg/day divided into 4 doses	Hypersensitivity reactions	None significant
Oritavancin	Yes	Adults: 1200 mg IV single dose	Hypersensitivity reactions, infusion reactions, gastrointestinal upset	Warfarin, heparin, coagulation tests
Oxacillin	No	Adults: 1–2 g IV 6 times daily Children: 100–150 mg/kg/day divided into 4 doses	Hypersensitivity reactions	None significant
Penicillin G	No	Adults: 2–4 million units IV four to six times daily Children: 60,000 to 100,000 units/kg/dose IV four times daily	Hypersensitivity reactions	Probenecid
Penicillin VK	No	Adults: 250–500 mg PO four times daily Children: 25–50 mg/kg/day PO divided into 2 to 4 doses	Hypersensitivity reactions	Probenecid
Piperacillin-tazobactam	No	Adults and children > 40 kg: 3.375 g IV three or four times daily Children ≤ 40 kg: 100 mg/kg of piperacillin IV three times daily	Hypersensitivity reactions	None significant
Tedizolid	Yes	Adults: 200 mg IV/PO daily	Myelosuppression, neuropathy, serotonin syndrome	Serotonergic agents
Telavancin	Yes	Adults: 10 mg/kg IV daily	Infusion reactions, QT prolongation, nephrotoxicity, foamy urine, dysgeusia, gastrointestinal upset, headache, dizziness, not recommended for pregnant women	QT prolonging agents, nephrotoxic agents

**Table 1-1.** Common and New Antibiotics Used for Skin and Soft Tissue Infections (*continued*)

Agent	Clinically Useful Activity Against MRSA	Dosing Regimen <sup>a,b</sup>	Adverse Effects	Drug Interactions
Trimethoprim/sulfamethoxazole <sup>d</sup>	Yes <sup>c</sup>	Adults: 1 to 2 DS tablet(s) PO twice daily Children: 8–12 mg/kg/day of trimethoprim divided into 4 doses IV or 2 doses PO	Hypersensitivity reactions, nausea, vomiting, myelosuppression, hyperkalemia, hepatotoxicity, not recommended for women in the third trimester of pregnancy	Warfarin, renin-angiotensin-aldosterone system inhibitors
Vancomycin	Yes	Adults: 30 mg/kg/day divided into 2 doses Children: 40 mg/kg/day divided into 4 doses	Infusion reactions, red man syndrome, nephrotoxicity	Nephrotoxic agents

<sup>a</sup>Doses recommended for patients with skin and soft tissue infections and are based on normal kidney and liver functions.

<sup>b</sup>Pediatric regimens exclude dosing for neonates and infants.

<sup>c</sup>Commonly used to treat community-associated methicillin-resistant *Staphylococcus aureus* infections.

<sup>d</sup>Not active against *Streptococcus pyogenes*.

DS = double strength (160 mg of trimethoprim and 800 mg of sulfamethoxazole); IV = intravenously; MRSA = methicillin-resistant *Staphylococcus aureus*; PO = by mouth.

Information 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:e10-52; and Liu C, Bayer A, Cosgrove SE, 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. *Clin Infect Dis* 2011;52:285-92.

*Continued from page 6*

complications such as acute rheumatic fever and glomerulonephritis. Diagnosis of impetigo is based on clinical presentation. Gram stain and culture of the pus or exudates are recommended to identify whether *S. pyogenes* or *S. aureus* is the cause, but treatment without those studies is reasonable in typical cases (Stevens 2014).

The mainstay of therapy for both nonbullous and bullous impetigo is topical mupirocin or retapamulin twice daily for 5 days. Oral antibiotics directed against MSSA (e.g. dicloxacillin or cephalexin for 7 days) are recommended for patients with many lesions and in the setting of an outbreak. If the cultures reveal only streptococci, oral penicillin VK is recommended. When MRSA is suspected or confirmed, oral trimethoprim/sulfamethoxazole, doxycycline, or clindamycin is recommended (Stevens 2014). In all cases, soaking in soapy warm water facilitates crust removal.

### **Bite Wound Infections**

A comprehensive history, including how and when a bite occurred; the patient's medical history, allergies, and tetanus immunization status; immunization history of the animal; and medical history of the biter (for viral hepatitis, HIV, and other transmissible diseases) should be

obtained. Patients should be evaluated for type of wound, presence of damage to surrounding or underlying structures, and signs of infection (e.g., erythema, swelling, discharge), which may not develop until 24–72 hours after injury. Patients may also present with enlargement of the lymph nodes adjacent to the wound, fever, or leukocytosis. Gram stain and culture are usually not performed on wounds. Radiography is used to assess for septic arthritis or osteomyelitis when damage to a bone or joint is suspected (Brook 2009).

Preemptive early antibiotic therapy for 3–5 days is recommended for patients with immunocompromising conditions (e.g., asplenia, advanced liver disease). Preemptive therapy is also recommended in patients with edema in the affected area; injuries to the face, hands, or feet; or joint or bone injuries. Antibiotic therapy directed against both aerobic and anaerobic bacteria (e.g., amoxicillin/clavulanate) should be initiated. Alternative agents include second- or third-generation cephalosporin or fluoroquinolone or trimethoprim/sulfamethoxazole plus clindamycin or metronidazole. Doxycycline, moxifloxacin, or a carbapenem is also appropriate. Because of the high prevalence of *Pasteurella multocida*, antistaphylococcal



penicillins, first-generation cephalosporins, and macrolides are not recommended (Stevens 2014).

For infected animal or human bites in patients who can receive oral outpatient therapy, a 5- to 10-day course of antibiotic therapy is commonly used. Intravenous therapy for 7–14 days (extended to 4 weeks for septic arthritis and 6 weeks for osteomyelitis) is recommended for serious injuries, clenched-fist bite injuries, or injuries initially treated in the outpatient setting that have infection that progresses after 24 hours of oral therapy. Intravenous options include ampicillin/sulbactam, a cephamycin, or ertapenem. In patients allergic to penicillins, either doxycycline or a fluoroquinolone may be used in combination with metronidazole or clindamycin.

All bite wounds should be thoroughly irrigated and cleansed with sterile normal saline. Primary closure of wounds is not recommended except for wounds to the face. Patients should be evaluated for rabies prophylaxis—particularly in geographic areas with high prevalence—and for bites from feral and wild animals. Patients should also be evaluated for tetanus prophylaxis, and tetanus toxoid should be administered to patients without toxoid vaccination in the previous 10 years. The tetanus, diphtheria, and acellular pertussis vaccine is preferred for patients who have not received a pertussis-containing vaccine as adults (Stevens 2014).

### Herpes Zoster

Herpes zoster is characterized by a unilateral rash localized to one or two adjacent dermatomes without

crossing the body's midline. It initially presents as an erythematous, maculopapular rash that transforms into vesicles and is followed by pustules that crust over and heal after 2–4 weeks. The rash may be preceded by a prodrome of episodic or continuous symptoms of pain, itching, and/or tingling. Patients with immunocompromising conditions may present with disseminated rash and the appearance of new lesions for up to 2 weeks. Postherpetic neuralgia—characterized by the persistence of pain for weeks, months, or several years after resolution of rash—is the most common complication of herpes zoster. Patients who scratch lesions are at risk of bacterial superinfection caused by skin flora, including *S. aureus* and *S. pyogenes*. Herpes zoster is usually diagnosed on the basis of its characteristic clinical presentation. Diagnostic testing (e.g., polymerase chain reaction to detect VZV DNA from skin lesions, direct fluorescent antibody staining of VZV-infected cells, serologic methods) may be used for patients with atypical presentations or to rule out infection with herpes simplex virus.

In addition to therapy for acute-pain control, the systemic antivirals listed in Table 1-2 are strongly recommended for the treatment of herpes zoster in patients with immunocompromising conditions or patients with one or more of the following: age 50 years or older, moderate or severe pain or rash, nontruncal involvement, or complications. An antiviral agent should be started as early as possible—ideally, within 72 hours of the onset of rash.

**Table 1-2.** Common Antivirals Used in the Treatment of Herpes Zoster

Drug	Clinically Useful Activity Against Acyclovir-Resistant VZV	Dosing Regimen <sup>a</sup>	Adverse Effects	Drug Interactions
Acyclovir	No	Immunocompetent: 800 mg PO 5 times daily Immunocompromised: 10 mg/kg IV three times daily	Malaise, nephrotoxicity	Nephrotoxic agents, zoster vaccine
Famciclovir	No	Immunocompetent: 500 mg PO three times daily	Headache, nausea	Zoster vaccine
Foscarnet <sup>b</sup>	Yes	Immunocompromised: 40 mg/kg IV three times daily	Fever, electrolyte disturbances, nausea, vomiting, diarrhea, headache, anemia, granulocytopenia	Nephrotoxic agents, QT prolonging agents
Valacyclovir	No	Immunocompetent: 1 g PO three times daily	Headache, nausea, abdominal pain, hepatotoxicity, nasopharyngitis	Zoster vaccine

<sup>a</sup>Doses recommended for patients with herpes zoster and are based on normal kidney and liver functions.

<sup>b</sup>Not approved for the treatment of herpes zoster by the FDA.

IV = intravenously; PO = by mouth; VZV = varicella zoster virus.

Information from: Cohen JI. Herpes zoster. *N Engl J Med* 2013;369:255-63.

There is still benefit to initiation of treatment after that time frame for those with continued formation of new lesions or complications. Famciclovir and valacyclovir are typically given for a 7-day course of treatment, whereas acyclovir is given for 7–10 days, with consideration given to extending treatment in those who experience continued formation of new lesions or complications after the recommended duration of therapy. Valacyclovir or famciclovir is preferred to acyclovir because of less frequent dosing, higher bioavailability, and higher and more consistent antiviral drug concentrations in the blood (Cohen 2013; McDonald 2012; Dworkin 2007). In a large randomized double-blind study, valacyclovir significantly accelerated the resolution of acute neuritis compared with acyclovir, and the proportion of patients with postherpetic neuralgia was lower in the valacyclovir arm compared with the acyclovir arm (Beutner 1995).

## INFECTIONS IN BOTH THE OUTPATIENT AND INPATIENT SETTINGS

### Erysipelas and Cellulitis

Erysipelas is characterized by a bright red erythematous lesion of the superficial layers of the skin; the lesion has a raised border and a well-demarcated margin. Erysipelas is often preceded by flu-like symptoms and is associated with burning pain. Cellulitis is an acute inflammation of the epidermis, dermis, and sometimes the superficial fascia, and it can be purulent or nonpurulent. The lesion is characterized by erythema and edema of the skin and has nonelevated and poorly defined margins. Cellulitis is considered a serious infection because of the propensity of the microorganism(s) to invade lymphatic tissue and blood. If left untreated, cellulitis can progress to adjacent tissue and cause an abscess, septic arthritis, or osteomyelitis. Diagnosis is based on clinical presentation, and cultures of blood or cutaneous aspirates, biopsies, or swabs are not routinely recommended, except in patients with immersion injuries or in those who with immunocompromising conditions (Stevens 2014).

Mild and typical cases with no focus of purulence are treated in the outpatient setting with oral antibiotics directed primarily against streptococci (e.g., penicillin VK) but could also include coverage against MSSA (e.g., dicloxacillin, cephalexin, or clindamycin). The recommended duration of therapy is 5 days, but treatment should be extended if the infection has not improved. Moderate cases with systemic signs of infection (e.g., fever, leukocytosis, extensive lesions) require a short hospitalization for administration of intravenous penicillin G, cefazolin, ceftriaxone, or clindamycin, with a switch to oral agents upon clinical response. For patients whose cellulitis is associated with penetrating trauma, evidence of MRSA infection elsewhere, nasal colonization with MRSA, injection drug use, or systemic inflammatory-response

syndrome, intravenous vancomycin or another antibiotic effective against both MRSA and streptococci is recommended.

Broad-spectrum antibiotic therapy with vancomycin plus either piperacillin-tazobactam or a carbapenem is a reasonable empiric regimen in severe cases, such as those occurring in patients whose cellulitis has failed oral antibiotic therapy, those occurring in immunocompromised patients, those with clinical signs of deeper infection, or those associated with systemic inflammatory-response syndrome. Other antibiotics commonly used in this setting are third- and fourth-generation cephalosporins, fluoroquinolones, and metronidazole. Because of increased risk of resistance among Enterobacteriaceae, ampicillin-sulbactam is rarely used, and aminoglycosides are considered less desirable alternative options because of their unfavorable adverse effect profiles. To hasten clinical improvement, the use of systemic corticosteroids such as prednisone 40 mg daily for 7 days could be considered in patients who do not have diabetes (Stevens 2014).

In all cases, immobilization and elevation of the affected extremity facilitate drainage. Treating fissuring, scaling, and maceration in the interdigital toe spaces reduces the incidence of recurrent lower-leg infections. Treating predisposing conditions such as obesity, edema, venous insufficiency, and eczema reduces the risk of recurrent infections. Lastly, prophylactic administration of penicillin VK or erythromycin orally twice daily or benzathine penicillin intramuscularly every 2 to 4 weeks should be considered in patients who have three or four episodes of cellulitis per year despite attempts to treat predisposing factors (Stevens 2014).

### Diabetic Foot Infections

Diabetic foot infection presents as a deep abscess, cellulitis of the dorsum, or a mal perforans ulcer after a history of penetrating trauma or extension of local infection. Although reports of swelling, edema, warmth, tenderness, and purulence are common, pain is often absent because of peripheral neuropathy. Diabetic foot infections are often much more extensive than they appear, and systemic signs of infection are rare, except in severe limb-threatening cases. Table 1-3 describes the classification of DFIs. Diagnosis is based on clinical presentation, medical history of diabetes, imaging, and cultures obtained from deep tissue samples post-debridement. Diabetic foot infection can be complicated by the presence of concomitant osteomyelitis, which must be assessed by bone imaging. Osteomyelitis is best diagnosed by bone culture and histology (Lipsky 2012).

### Treatment

The general approach to the management of DFI is highlighted in Figure 1-4. Wounds without evidence of soft tissue infection or bone infection do not require antibiotic therapy. Infected wounds require antibiotic therapy that targets aerobic

gram-positive cocci. Coverage for MRSA should be considered in patients with histories of MRSA infections, when the local prevalence of MRSA infection or colonization is high, or for severe infections. Broad-spectrum antibiotic therapy is prescribed for patients at risk of infection with antibiotic-resistant organisms, including patients with chronic, previously treated, or severe infections. Coverage for *Pseudomonas*

*aeruginosa* is usually unnecessary except when the local prevalence of *Pseudomonas* infection is high, in the setting of a warm climate, or in patients whose feet are frequently exposed to water. Anaerobic coverage is needed in patients with ischemic, necrotic, or foul-smelling wounds.

In addition to antibiotic therapy, most DFIs require surgical interventions ranging from debridement to

### Patient Care Scenario

Three days ago, a 50-year-old man was admitted to the hospital for the management of purulent left lower leg cellulitis. He has been receiving vancomycin 1000 mg intravenously every 12 hours. The lesion associated with cellulitis has shrunk, the erythema has improved, and the pain is much more manageable. His medical history is significant for hypertension, atrial fibrillation, and congestive heart failure. In addition to vancomycin, his home drugs include lisinopril 40 mg orally

daily, warfarin 5 mg orally daily, spironolactone 25 mg orally daily, furosemide 20 mg orally daily, carvedilol 25 mg orally twice daily, and oxycodone/acetaminophen 5 mg/325 mg 1 tab orally every 6 hours as needed for pain. Blood cultures are negative so far, but the culture obtained from aspiration of the edge of the lesion revealed *Staphylococcus aureus*, abundant growth, with the following microbiology and sensitivity report:

Antibiotic	MIC (mcg/mL)	Interpretation
Clindamycin	≥ 8	R
Oxacillin	≥ 4	R
Rifampin	≤ 0.5	S
Tetracycline	≤ 1	S
Trimethoprim/ sulfamethoxazole	≤ 10	S
Vancomycin	0.5	S

Upon admission, his temperature was 38°C, WBC count was 12,520 cells/mm<sup>3</sup>, and his INR was 2.6. Today, his temperature is 37.2°C, his WBC is 7.1 x 10<sup>3</sup> cells/mm<sup>3</sup>, and his INR is 2.9. What is the most appropriate antibiotic regimen for the patient to take upon discharge?

### Answer

The patient is hospitalized for the management of purulent cellulitis caused by methicillin-resistant *Staphylococcus aureus* sensitive to rifampin, tetracycline, trimethoprim/sulfamethoxazole, and vancomycin, but resistant to clindamycin. The patient responded favorably to a 3-day course of parenteral vancomycin as evidenced by improvement in signs and symptoms and normalization of temperature and WBC count. Therefore, the clinician should discharge the patient on an oral antibiotic regimen to complete the course of therapy. Clindamycin should not be used because the sensitivity report shows resistance to clindamycin. Although the sensitivity report is showing susceptibility to rifampin, rifampin should not be used as monotherapy for the management of staphylococcal infections because resistance can quickly develop during treatment. In addition, vancomycin should not be used orally for the treatment of staphylococcal infections because it is not systemically

absorbed. The only remaining options are trimethoprim/sulfamethoxazole, doxycycline, minocycline, tedizolid, and linezolid. Trimethoprim/sulfamethoxazole is known to interact with warfarin resulting in an increase in INR. In the absence of monitoring and dosage adjustment for warfarin, trimethoprim/sulfamethoxazole may not be the best option because it can increase the risk of bleeding particularly in this patient whose INR is already at the upper limit of the desired range of 2 to 3. Linezolid and tedizolid are considered expensive agents compared with generic antibiotics and may not be covered by this patient's insurance. This will leave minocycline or doxycycline orally twice daily for at least 4 days as the best options for the patient. This case illustrates the importance of taking into account the microbiology culture and sensitivity report as well as concomitant medications and patient-specific factors before switching to a different antibiotic regimen for a given patient.

1. 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:e10-52.
2. Liu C, Bayer A, Cosgrove SE, 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. Clin Infect Dis 2011;52:285-92.
3. Howard PA, Ellerbeck EF, Engelman KK, et al. The nature and frequency of potential warfarin drug interactions that increase the risk of bleeding in patients with atrial fibrillation. Pharmacoepidemiol Drug Saf 2002;11:569-76.

resection and amputation. Most DFIs also require wound care, including debridement to remove necrotic tissue, off-loading to redistribute pressure off the wound, and appropriate dressings to allow for moist wound healing. Bed rest and leg elevation are recommended initially to decrease swelling and edema, and glycemic control is crucial to the healing process and for the prevention of future infections. Although bioengineered skin equivalents, growth factors, granulocyte-colony-stimulating factors, hyperbaric oxygen therapy, and negative-pressure wound therapy have not been shown to consistently facilitate resolution of infection, they may be used on a case-by-case basis at the clinician's discretion (Lipsky 2012).

### Infections in the Inpatient Setting

#### Surgical Site Infections

Surgical site infections are divided into three categories: superficial incisional SSI, deep incisional SSI, and organ or space SSI. Diagnosis is based on purulent incisional discharge; positive culture of aseptically obtained material; local signs of pain, swelling, erythema, and tenderness; or assessment by the attending surgeon or an experienced physician. The majority of SSIs occur more than 4 days after operation (Stevens 2014).

Suture removal plus incision and drainage is the mainstay of therapy for SSIs. In addition, antibiotics are beneficial for patients presenting with erythema and induration extending more than 5 cm from the wound edge, temperature higher than 38.5°C, heart rate higher than 110 beats per minute, or WBC higher than  $12 \times 10^3$  cells/mm<sup>3</sup>. An antistaphylococcal penicillin or a first-generation

cephalosporin is recommended if MSSA is suspected or isolated. Vancomycin or another intravenous anti-MRSA antibiotic is recommended if MRSA is suspected (e.g., nasal colonization with MRSA, prior MRSA infection, recent hospitalization, recent antibiotic exposure). A cephalosporin or a fluoroquinolone in combination with metronidazole is recommended if gram-negative or anaerobic bacteria are suspected (e.g., surgery on the axilla, gastrointestinal or genital tracts, or perineum) (Stevens 2014).

#### Necrotizing fasciitis

Patients with necrotizing fasciitis present initially with erythema, tenderness, warmth, swelling, and pain out of proportion to physical findings. As the infection progresses, blistering, skin crepitus, skin discoloration, and necrosis occur. Polymicrobial necrotizing fasciitis presents with relatively intact skin and spreads in 3–5 days. Streptococcal necrotizing fasciitis (what the lay press terms *flesh-eating bacteria*) can progress quickly within 1–2 days. Clostridial gas gangrene is characterized by gas production and muscle necrosis. Diagnosis is based on clinical presentation, recent history of penetrating or blunt trauma, laboratory abnormalities, and surgical exploration. Cultures should be obtained from tissue samples and blood. Once the diagnosis is established, necrotizing fasciitis is considered a medical emergency (Lancero 2012).

Immediate and aggressive surgical debridement is essential in the management of necrotizing fasciitis. Polymicrobial infections must be empirically treated with broad-spectrum antibiotics such as vancomycin, linezolid, or daptomycin plus piperacillin-tazobactam or a

**Table 1-3.** Classification of Diabetic Foot Infections

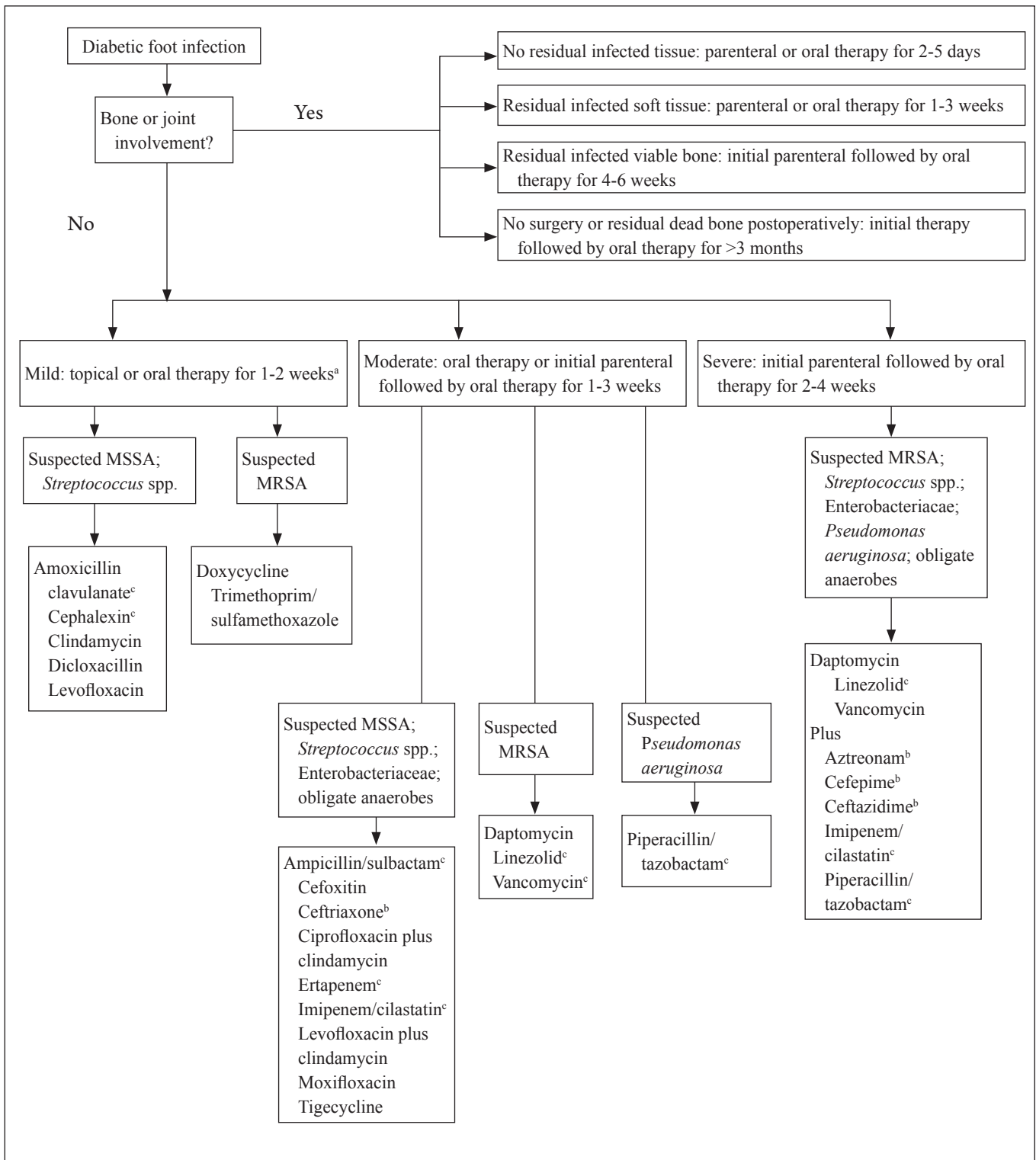
Clinical Manifestation of Infection	IDSA	PEDIS
No signs or symptoms of infection	Uninfected	1
Local infection <sup>a</sup> involving only the skin and the subcutaneous tissue If erythema is present, must be 0.5–2 cm around the ulcer Exclude other causes of an inflammatory response of the skin	Mild	2
Local infection <sup>a</sup> as described above with erythema >2 cm or involving structures deeper than skin and subcutaneous tissues No SIRS	Moderate	3
Local infection <sup>a</sup> as described above with signs of SIRS as manifested by $\geq 2$ of the following: • T 38°C to 36°C • HR >90 beats/minute • RR >20 breaths/minute or PaCO <sub>2</sub> <32 mm Hg • WBC count >12,000 or <4000 cells/mcL or $\geq 10\%$ bands	Severe	4

<sup>a</sup>Infection defined by the presence of at least two of the following: erythema, local swelling or induration, local tenderness or pain, local warmth, and purulent discharge.

HR = heart rate; IDSA = Infectious Diseases Society of America; PEDIS = perfusion, extent/size, depth/tissue loss, infection, and sensation; RR = respiratory rate; SIRS = systemic inflammatory response syndrome; T = temperature; WBC = white blood cells.

Information from: Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis* 2012;54:e132-73; and Chahine EB, Harris S, William II R. Diabetic foot infections: an update on treatment. *US Pharm* 2013;38:23-6.





**Figure 1-4.** General approach to the management of diabetic foot infection. Note: agents similar to those listed in this algorithm can be substituted based on clinical, epidemiologic, and financial considerations.

<sup>a</sup>May extend up to 4 weeks if slow to resolve.

<sup>b</sup>Consider adding an antibiotic with activity against obligate anaerobes

<sup>c</sup>Agents commonly used as comparators in clinical trials for the treatment of diabetic foot infections.

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

Information from: Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis 2012;54:e132-73.

carbapenem or ceftriaxone plus metronidazole that are directed against gram-positive cocci, Enterobacteriaceae, and anaerobes. Group A streptococcal and clostridial infections are treated with parenteral aqueous penicillin G plus clindamycin. Adding clindamycin to  $\beta$ -lactam therapy provides several advantages, including additional coverage against streptococci and staphylococci, an immunomodulatory effect, and inhibition of toxin production. Pyomyositis caused by MSSA is treated with nafcillin or oxacillin or cefazolin. The recommended total duration of therapy is 2–3 weeks. Hyperbaric oxygen therapy is not recommended because it has not been proved effective and because it may delay resuscitation and surgical debridement (Stevens 2014).

## Monitoring

### Efficacy

For the majority of SSTIs, patients should note improvement in clinical symptoms of infection within 3 days of appropriate treatment; improvement may take up to 1 week for patients with impetigo. For any patient not responding to therapy within that period, additional culture and sensitivity testing should be performed, with therapy modified toward the specific infecting pathogen(s) and/or further surgical debridement for infections such as necrotizing fasciitis. Mild cases of folliculitis or furuncles without improvement after 2 to 3 days of moist heat or use of a topical agent likely require incision and drainage. Methicillin-resistant *Staphylococcus aureus* should be considered for any patient who has not had improvement after 3 days of antimicrobial therapy with an anti-staphylococcal penicillin or first-generation cephalosporin. When vancomycin is used, it should be dosed according to a patient's actual body weight to achieve a target trough of 10–15 mcg/mL for most SSTIs. A target trough of 15–20 mcg/mL is recommended for patients with necrotizing fasciitis or whose infection has progressed to osteomyelitis (Rybak 2009). Although this dosing strategy has not consistently correlated with improved outcomes, the traditional vancomycin dosing of 1 g every 12 hours is unlikely to achieve a sufficient concentration to eradicate MRSA in many patients and should no longer be recommended.

### Safety

See Table 1-1 for adverse effects and significant drug interactions of antibiotics commonly used in the treatment of SSTIs, and Table 1-2 for antiviral agents used for the treatment of herpes zoster. Clinicians are seeing more nephrotoxicity with the aggressive dosing of vancomycin. A recent large retrospective study showed that vancomycin trough concentrations higher than 12.1 mg/L were associated with increased risk of nephrotoxicity (Han 2014). Another retrospective study showed that the concomitant use of piperacillin-tazobactam was associated with increased risk of nephrotoxicity (adjusted odds ratio [OR] of 5.36; 95% confidence interval (CI) 1.41–20.5) (Meaney

2014). The main safety concerns with daptomycin are creatine phosphokinase elevation and myalgia. A recent meta-analysis of six randomized controlled trials of daptomycin versus other antibiotics for the treatment of SSTIs showed that patients receiving daptomycin had elevated creatine phosphokinase compared with control groups (OR 1.95; 95% CI, 1.04–6.65). However, this adverse event was reversible upon therapy discontinuation (Wang 2014).

Finally, the main safety concerns with linezolid are myelosuppression, neuropathy, and serotonin syndrome. A recent retrospective-analysis study showed that receiving linezolid therapy for 14 or more days was a significant risk factor for thrombocytopenia (OR 13.3; 95% CI, 3.2–55.6). Also, the incidence of thrombocytopenia was significantly higher in patients with CrCl less than 30 mL/minute than in patients with normal renal function ( $p=0.014$ ) (Hirano 2014). Because linezolid is a weak monoamine oxidase inhibitor, the U.S. Food and Drug Administration (FDA) recommends avoiding its use with other serotonergic drugs. In fact, the incidence of linezolid-associated serotonin toxicity is 0.5% to 18.2%, and most cases occurred in patients receiving selective serotonin reuptake inhibitors or multiple serotonergic drugs (Woytowish 2013).

## NEW ANTIBIOTICS

The FDA recently released guidance to assist sponsors in developing antibiotics for the treatment of ABSSSIs. For the purpose of this guidance, ABSSSIs include cellulitis/erysipelas, wound infection, and major cutaneous abscess and have a minimum lesion surface area of about 75 cm<sup>2</sup>. The FDA has designated more stringent efficacy end points and stricter timing of assessments. The primary end point is cessation of spread of skin lesion erythema and absence of fever at 48–72 hours after treatment initiation (FDA 2013). The FDA recently approved five antibiotics for the treatment of ABSSSIs: ceftaroline, dalbavancin, oritavancin, tedizolid, and telavancin.

### Ceftaroline

Ceftaroline is a fifth-generation cephalosporin active against MRSA, drug-resistant *Streptococcus pneumoniae*, and Enterobacteriaceae and was recently approved by the FDA for the treatment of ABSSSIs and community-acquired bacterial pneumonia. Results from two phase-3 multicenter randomized double-blind clinical trials, with clinical cure rates as primary outcome, have shown that ceftaroline 600 mg administered intravenously for 60 minutes is noninferior to vancomycin plus aztreonam administered intravenously for 5–14 days for the treatment of ABSSSIs (CANVAS 1: 91.1% with ceftaroline and 93.3% with vancomycin/aztreonam, 95% CI, –6.6–2.1; CANVAS 2: 92.2% with ceftaroline and 92.1% with vancomycin/aztreonam, 95% CI, –4.4–4.5). The most common adverse events associated with ceftaroline in

those trials were positive Coombs test without hemolysis and gastrointestinal upset (Corey 2010a, 2010b, Wilcox 2010). Ceftaroline is currently the only  $\beta$ -lactam antibiotic approved for the treatment of ABSSSIs caused by MRSA. Because of its broad spectrum of activity and because it can replace combination therapy in this setting, ceftaroline is particularly useful when used empirically for the treatment of SSTIs when both MRSA and Enterobacteriaceae are suspected.

### **Dalbavancin**

Dalbavancin is a new lipoglycopeptide antibiotic with activity against MRSA; it was recently approved by the FDA for the treatment of ABSSSIs. Results from two phase-3 multicenter randomized double-blind clinical trials with early clinical response as primary outcome showed that dalbavancin 1000 mg administered intravenously for 30 minutes on day 1 followed by 500 mg on day 8 is noninferior to vancomycin administered intravenously for at least 3 days, with an option to switch to oral linezolid for the treatment of ABSSSIs (DISCOVER 1: 83.3% with dalbavancin and 81.8% with vancomycin/linezolid, 95% CI, -4.6-7.9; DISCOVER 2: 76.8% with dalbavancin and 78.3% with vancomycin/linezolid, 95% CI, -7.4-4.6). The most common treatment-related adverse events associated with dalbavancin in these trials were nausea, diarrhea, and pruritus (Boucher 2014).

Dalbavancin is currently the only antibiotic with once-weekly dosing (2 total doses) for the treatment of SSTIs; this enables clinicians to avoid or shorten the hospitalization of selected patients and potentially reduce health care costs.

### **Oritavancin**

Oritavancin is a new lipoglycopeptide antibiotic active against MRSA; it was recently approved by the FDA for the treatment of ABSSSIs. Results from a phase-3 multicenter randomized double-blind clinical trial with early clinical response as primary outcome demonstrated that oritavancin 1200 mg administered intravenously as a single dose over a 3-hour infusion is noninferior to vancomycin administered intravenously twice daily for 7-10 days for the treatment of ABSSSIs (SOLO 1: 82.3% with oritavancin 78.9% with vancomycin, 95% CI, -1.6-8.4). Although the overall frequency of adverse events was similar between the two treatment arms, nausea was more common among those treated with oritavancin (Corey 2014).

Oritavancin is the first antibiotic with a single-dose formulation for the treatment of SSTIs, potentially enabling clinicians to avoid or shorten the hospitalization of selected patients and potentially reduce health care costs.

### **Tedizolid**

Tedizolid is a new oxazolidinone antibiotic active against MRSA. It was recently approved by the FDA for the treatment of ABSSSIs. Results from two phase-3

multicenter randomized double-blind clinical trials with early clinical response as primary outcome showed that tedizolid 200 mg administered intravenously or orally daily for 6 days is noninferior to linezolid administered intravenously or orally twice daily for 10 days for the treatment of ABSSSIs (ESTABLISH 1: 79.5% with tedizolid and 79.4% with linezolid, 95% CI, -6.1-6.2; ESTABLISH 2: 85% with tedizolid and 83% with linezolid, 95% CI, -3.0-8.2). Treatment-emergent adverse events were similar between the two treatment groups, with fewer gastrointestinal disorders reported in the tedizolid group than in the linezolid group (Moran 2014; Prokocimer 2013). Tedizolid is the second antibiotic with both oral and parenteral formulations to be indicated for the treatment of MRSA infections.

### **Telavancin**

Telavancin is a lipoglycopeptide antibiotic active against MRSA; it was recently approved by the FDA for the treatment of ABSSSIs and hospital-acquired and ventilator-associated bacterial pneumonia. Results from two phase-3 multicenter randomized double-blind clinical trials with clinical cure rates as primary outcome showed that telavancin 10 mg/kg administered intravenously for 60 minutes is noninferior to vancomycin administered intravenously for at least 7 days for the treatment of ABSSSIs (ATLAS 1: 84.3% with telavancin and 82.8% with vancomycin, 95% CI, -4.3-7.3; ATLAS 2: 83.9% with telavancin and 87.7% with vancomycin, 95% CI, -9.2-1.5). The most common adverse events associated with telavancin in these trials were taste disturbance, gastrointestinal upset, headache, and foamy urine (Stryjewski 2008). Telavancin was the first lipoglycopeptide antibiotic to be approved by the FDA for the treatment of ABSSSIs. It carries two boxed warnings: (1) new onset or worsening renal impairment and potential adverse developmental outcomes in pregnant women based on animal data; and (2) precautions related to QTc prolongation and potential for decreased efficacy in those with a CrCL of 50 mL/minute or greater. Because of its unfavorable safety profile, telavancin should be used as an alternative to vancomycin and other anti-MRSA agents for the treatment of SSTIs suspected to be caused by MRSA.

## **PREVENTION**

### **General Measures**

All patients with SSTIs should be counseled on hygiene and wound care measures to prevent the spread of infection. Patients should (1) cover any draining wounds with clean and dry bandages, (2) bathe regularly, (3) clean their hands regularly, (4) clean their hands after touching the area of infection or any item that has been in contact with a draining wound, and (5) avoid reusing or sharing any personal items that may have contacted the site of infection.

Because early recognition and management of risk factors for ulcers or amputations can prevent or delay adverse outcomes, all patients with diabetes mellitus should have an annual comprehensive foot examination, including inspection, assessment of foot pulses, and testing for loss of protective sensation. All patients with diabetes should also be educated on the importance of daily foot monitoring, proper nail and skin care of the foot, and the selection of appropriate footwear. Patients with loss of protective sensation should be counseled on alternative ways to assess for early foot problems, such as hand palpation, visual inspection, or assistance from another person (ADA 2014). A recently published update describes [the detection and prevention of SSTIs in acute-care hospitals](#) (Anderson 2014).

### Pharmacologic Measures

Because of an association between colonization and subsequent MRSA infection, different strategies for decolonization may be used in the outpatient setting for patients with recurrent infections (typically defined as two or more SSTIs at different body sites within 6 months) despite appropriate preventive measures (Liu 2011). A common decolonization strategy is intranasal mupirocin twice daily for 5–10 days, either alone or in combination with a skin antiseptic solution such as chlorhexidine or hexachlorophene for 5–14 days (Liu 2011). A recent study found that a 5-day regimen of hygiene, intranasal mupirocin, and 4% chlorhexidine body washes for all household members significantly reduced the incidence of self-reported recurrent SSTI in children during a 12-month period compared with decolonization of the index patient alone (72% vs. 52%,  $p=0.02$ ) (Fritz 2012).

Oral antibiotics are not routinely recommended for decolonization, but a 5- to 10-day course of rifampin in combination with trimethoprim/sulfamethoxazole or doxycycline may be considered for recurrent infections despite other preventive (appropriate personal and environmental hygiene) and decolonization measures (use of nasal and/or topical decolonization). A recent study showed a reduction in mean number of CAMRSA infections (0.03 vs. 0.84 infections/month,  $p < 0.0001$ ) when patients with recurrent infection were given 10-day regimens of intranasal mupirocin, daily hexachlorophene body wash, and an oral anti-MRSA agent (either trimethoprim/sulfamethoxazole, doxycycline, or minocycline) compared with placebo before the intervention (Miller 2012).

Several decolonization strategies have been used in the inpatient setting. Typically, patients undergoing surgical procedures, especially open-heart surgery or procedures involving implants, are preoperatively screened for MRSA; patients found to be carriers are given intranasal mupirocin and chlorhexidine baths. A recent study found that universal decolonization (intranasal mupirocin for 5 days plus daily bathing with 2% chlorhexidine-impregnated cloths for duration of ICU stay for all patients) was

more effective than either targeted decolonization (5 days of intranasal mupirocin and daily bathing with 2% chlorhexidine-impregnated cloths for those who screened positive for MRSA) or screening and isolation in preventing infections in the ICU setting (Huang 2013).

### Varicella Zoster Vaccine

To prevent shingles, the Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination with a single dose of zoster vaccine for all eligible persons 60 years and older, regardless of history with herpes zoster (CDC 2014). The ACIP's recommendation comes primarily from the Shingles Prevention Study, a double-blind, placebo-controlled trial designed to assess the efficacy of the zoster vaccine in 38,546 persons aged 60 years and older (Oxman 2005). The vaccine significantly reduced the incidence of herpes zoster by 51% overall, with reduction rates of 54% and 41% in those aged 60–69 years and 70–79 years, respectively. The zoster vaccine was also 66.5% effective overall at preventing postherpetic neuralgia.

Although the zoster vaccine is licensed by the FDA for use in persons aged 50 years and older, the ACIP does not recommend its routine use in patients younger than 60 years. Because it is a live, attenuated vaccine, its use is contraindicated in those who are pregnant, severely immunosuppressed, or severely immunodeficient, including those with malignancies, those who are HIV positive with a CD4<sup>+</sup> cell count less than 200 cells/mm<sup>3</sup>, or those who have been receiving the equivalent of 20 mg of prednisone daily for at least 2 weeks. In addition, the zoster vaccine is contraindicated in those with histories of anaphylaxis to gelatin, neomycin, or any other vaccine components. Because antivirals against VZV may interfere with replication of the live vaccine, clinicians should stop chronic antiviral treatment at least 24 hours before immunization if possible; and therapy should be restarted at least 14 days after vaccine administration. Vaccination should be deferred for at least 1 month after the discontinuation of immunosuppressive therapy and administered at least 14 days (with some recommending a delay of 1 month if possible) before the start of immunosuppressive therapy (Harpaz 2008).

## ANTIMICROBIAL STEWARDSHIP

Pharmacists play an integral role in antimicrobial stewardship programs, with the overall goal of selecting the most appropriate antimicrobial agent(s), dose, route, frequency, and duration of therapy to achieve clinical cure or prevention of infection while limiting the development of resistance, adverse drug events (e.g., *Clostridium difficile* infection), and cost (Dellit 2007). Because of the high incidence of SSTIs in both outpatient and inpatient settings, there are many opportunities for stewardship in the management of those infections.



In terms of selecting the most appropriate agent, although vancomycin is considered the gold standard for many types of SSTIs caused by MRSA, there is controversy over use of vancomycin for the treatment of certain systemic infections—particularly if they are caused by isolates that have a minimum inhibitory concentration (MIC) close to 2 mcg/mL, which is the upper limit of what is defined as sensitive (Van Hal 2013; Rybak 2009). For SSTIs caused by *S. aureus* with a vancomycin MIC of 2 or more mcg/mL, clinical response should be considered for determining whether its use should be continued. For patients who have had adequate debridement and any other foci of infection removed but who still have not had a clinical or microbiological response, it is recommended to change therapy to an alternate anti-MRSA agent. For the treatment of SSTIs caused by *S. aureus* isolates with a vancomycin MIC more than 2 mcg/mL, clinicians should use an alternative antimicrobial agent for treatment.

## CONCLUSION

Skin and soft tissue infections are commonly encountered in both outpatient and inpatient settings. Nonpharmacologic therapy such as cleansing and irrigation and I&D is just as important as pharmacologic therapy and can be used in mild purulent infections without any additional pharmacologic therapy. Pharmacists often assist prescribers in selecting the most-appropriate antimicrobial regimens for patients presenting with SSTIs. Pharmacists play an important role in educating both patients and health care professionals about the judicious and appropriate use of antimicrobials to optimize the outcomes of patients presenting with SSTIs. Pharmacists also assist in preventing DFIs by educating patients on the importance of optimal glycemic control and regular foot examination.

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## Practice Points

In determining the optimal management of a patient with a skin or soft tissue infection, the clinician must consider the following important points:

- Determine first whether the infection is purulent or nonpurulent, and second whether the infection is mild, moderate, or severe.
- Most purulent infections are treated with incision and drainage first, followed by administration of oral antibiotics directed against MRSA in moderate cases and intravenous antibiotics directed against MRSA in severe cases.
- Most nonpurulent infections are treated with oral antibiotics directed against GAS in mild cases and intravenous antibiotics directed against GAS in moderate cases. Severe nonpurulent infections are treated with surgical debridement and intravenous broad spectrum antibiotics that cover MRSA.
- Employ nonpharmacologic therapy particularly cleansing and irrigation and incision and drainage whenever possible. Nonpharmacologic therapy is sufficient alone without antibiotics to treat mild purulent infections.
- The type of SSTIs, extent and severity of the infection, risk factors for MRSA, and comorbid conditions contribute to the most likely cause(s) of the infection. These elements, along with host factors such as allergies, hepatic and renal functions, and concomitant medications, should serve as the basis for selecting an antibiotic regimen to treat SSTIs.
- Keep in mind safety and drug interaction concerns before selecting an antimicrobial regimen for the treatment of SSTIs.
- Monitor for the cessation of the spread of the infection and for the reduction of inflammation within 48 to 72 hours after antibiotic administration. Otherwise, re-evaluate the diagnosis and/or the antibiotic regimen.
- Educate patients presenting with diabetic foot infections about the importance of achieving optimal glycemic control and keeping the feet clean and dry to prevent foot ulcers and subsequent infections.
- In the absence of any contraindications, encourage patients aged 60 years and older to receive the zoster vaccine to decrease the risk of herpes zoster.

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# SELF-ASSESSMENT QUESTIONS

## Questions 1–3 pertain to the following case.

R.F., a 54-year-old man, presents to the emergency room with a 2-day history of left lower extremity edema, redness, and pain that limits his normal daily activities. The lesion is not elevated and has poorly defined margins. His weight has not changed. His physical examination is notable for temperature 38°C, blood pressure 148/92 mm Hg, heart rate 88 beats/minute, respiratory rate 18 breaths/minute, and 1+ lower extremity edema. His laboratory values include sodium 138 mEq/L, potassium 4.4 mEq/L, BUN 18 mg/dL, SCr 0.9 mg/dL, WBC  $16 \times 10^3$  cells/mm<sup>3</sup>, hemoglobin 13 g/dL, hematocrit 39%, and platelet count 240,000 cells/mm<sup>3</sup>. R.F.'s medical history includes hypertension (HTN), dyslipidemia, and depression. His home drugs include hydrochlorothiazide 25 mg/day, atorvastatin 20 mg/day, fluoxetine 40 mg/day, and duloxetine 60 mg/day. R.F. is admitted to the hospital for intravenous antibiotic administration and nasal swab is positive for methicillin-resistant *Staphylococcus aureus* (MRSA).

- Which one of the following is the most likely cause of R.F.'s lesions?
  - Cellulitis.
  - Erysipelas.
  - Furuncle.
  - Impetigo.
- Which one of the following regimens is the best empiric therapy for R.F.?
  - Ciprofloxacin 400 mg intravenously every 12 hours.
  - Linezolid 600 mg intravenously every 12 hours.
  - Penicillin G 2 million units intravenously every 6 hours.
  - Vancomycin 15 mg/kg intravenously every 12 hours.
- Which one of the following topical antibiotics is the best option to decolonize R.F. from nasal MRSA carriage?
  - Clindamycin.
  - Retapamulin.
  - Metronidazole.
  - Mupirocin.
- A 65-year-old man was bitten in his leg by a dog while walking in the park. His wounds are infected. He has had uncontrolled type 2 diabetes mellitus for the past 5 years, for which he takes metformin 1000 mg PO twice daily. He developed hives when he received sulfa

drugs. He received the full primary vaccine series of tetanus immunization and had a tetanus toxoid-containing booster 12 years ago. In addition to cleansing and irrigation, which one of the following is the most appropriate treatment for this patient?

- Amoxicillin-clavulanate.
- Amoxicillin-clavulanate plus a tetanus toxoid-containing vaccine.
- Ciprofloxacin plus clindamycin.
- Moxifloxacin plus a tetanus toxoid-containing vaccine.

## Questions 5 and 6 pertain to the following case.

F.R., a 64-year-old woman, presents to the emergency room with a 2-week history of left lower extremity edema, redness, and pain that limits her normal daily activities. She has a lesion close to her small toes that is macerated and foul-smelling. The erythema is close to 3 cm around the ulcer. She thinks she might have stepped on a nail while walking on the beach in South Florida. Her physical examination is notable for temperature 38.2°C, blood pressure 145/90 mm Hg, heart rate 92 beats/minute, respiratory rate 19 breaths/minute, and 1+ lower extremity edema. Her laboratory values include sodium 139 mEq/L, potassium 4.3 mEq/L, BUN 19 mg/dL, SCr 0.9 mg/dL, glucose 180 mg/dL, A1C 8%, WBC  $14 \times 10^3$  cells/mm<sup>3</sup>, hemoglobin 12 g/dL, hematocrit 36%, and platelet count 290,000 cells/mm<sup>3</sup>. F.R.'s medical history is significant for HTN, type 2 diabetes, painful diabetic neuropathy, and a recent history of diabetic foot infection (DFI). Her home drugs include hydrochlorothiazide 25 mg/day, lisinopril 20 mg/day, glyburide 10 mg/day, metformin 1000 mg twice daily, pregabalin 75 mg twice daily, and aspirin 81 mg/day. F.R. is admitted to the hospital for intravenous antibiotic administration and nasal swab is positive for MRSA.

- In addition to cleansing, irrigation, and surgical debridement, which one of the following is the most appropriate empiric antibiotic treatment for F.R.'s DFI?
  - Levofloxacin plus vancomycin.
  - Piperacillin-tazobactam.
  - Piperacillin-tazobactam plus metronidazole.
  - Piperacillin-tazobactam plus vancomycin.
- Which one of the following treatment durations would be best for F.R.'s DFI?
  - 5 days
  - 7 days
  - 21 days
  - 42 days



7. A 61-year-old woman presents to your clinic with a 3-day history of rash. She has vesicles and pustules on the left side of the forehead, a few lesions on the left side of the nose, and blurry vision in the left eye. The rash is associated with moderate to severe burning pain and was preceded by a tingling sensation on the left side of the face. She has diabetes and hypothyroidism for which she takes glyburide 5 mg/day and levothyroxine 25 mcg/day. Which one of the following is the most likely cause of this patient's lesions?
- Cellulitis.
  - Erysipelas.
  - Impetigo.
  - Shingles.
8. A 66-year old man presents to your clinic with a moderate to severe case of herpes zoster. The primary care physician decides to treat the patient with antivirals and is asking you to recommend the most appropriate regimen. The patient is currently taking aspirin 81 mg/day, naproxen 500 mg twice daily, and oxycodone/acetaminophen 10 mg/325 mg 2 tablets three times daily. His CrCl is 60 mL/minute. Which one of the following is best to recommend for this patient?
- Acyclovir 400 mg orally five times daily for 7 days.
  - Acyclovir 800 mg orally five times daily for 5 days.
  - Famciclovir 500 mg orally three times daily for 5 days.
  - Valacyclovir 1 g orally three times daily for 7 days.
9. A 48-year-old woman is in your pharmacy asking if she is a candidate for the herpes zoster vaccine. She had an episode of severe herpes zoster 3 years ago. She also has asthma for which she takes fluticasone propionate and salmeterol 100 mcg/50 mcg per inhalation 1 inhalation twice daily and levalbuterol 2 puffs q4–6h PRN shortness of breath. She is currently on day 5 (last day) of a tapered dose of oral methylprednisolone for an acute asthma exacerbation. Which one of the following best explains why this patient is not a candidate for herpes zoster vaccination?
- She has asthma and is currently on fluticasone and salmeterol.
  - She has had an episode of severe herpes zoster in the past.
  - She is currently on methylprednisolone for asthma exacerbation.
  - She is too young for herpes zoster vaccination.

**Questions 10 and 11 pertain to the following case.**

M.I. is an 18-year-old man who presents to your clinic with a small purulent tender mass on his thigh that looks like a spider bite. The middle of the lesion is filled with pus and debris. The area is painful and warm to touch. M.I. has no chills and no other complaints. He is very active and exercises on a daily basis with a group of athletes. Physical examination reveals the following: temperature 37°C, blood pressure 120/70 mm Hg, heart rate 60 beats/minute, and respiratory rate 16 breaths/minute.

10. Which of the following is the most likely cause of M.I.'s clinical presentation?
- Clostridium perfringens*.
  - Methicillin resistant *Staphylococcus aureus*.
  - Methicillin sensitive *Staphylococcus aureus*.
  - Streptococcus pyogenes*.
11. Which one of the following is best to recommend for M.I.?
- Clindamycin.
  - Incision and drainage.
  - Penicillin G plus clindamycin.
  - Penicillin VK.

**Questions 12 and 13 pertain to the following case.**

M.N., a 40-year-old man, is admitted to the hospital for the management of an infection on the right side of his face. The area is red, elevated, and clearly demarcated. He thinks he may have scratched his face a couple of days ago. His physical examination is notable for temperature 38.6°C, blood pressure 135/80 mm Hg, heart rate 80 beats/minute, and respiratory rate 17 breaths/minute. M.N.'s laboratory values include sodium 140 mEq/L, potassium 4.2 mEq/L, BUN 20 mg/dL, SCr 1.1 mg/dL, WBC  $17 \times 10^3$  cells/mm<sup>3</sup>, hemoglobin 14 g/dL, hematocrit 42%, and platelet count 310,000 cells/mm<sup>3</sup>. M.N. has a history of anaphylactic shock caused by penicillin VK when he was 11 years old.

12. Which one of the following is the most likely cause of M.N.'s lesions?
- Cellulitis.
  - Cutaneous abscess.
  - Erysipelas.
  - Impetigo.
13. Which of the following is best to recommend for M.N.?
- Aztreonam 1 g intravenously three times daily
  - Cefazolin 1 g intravenously three times daily.
  - Trimethoprim/sulfamethoxazole 1 double-strength tablet orally twice daily.
  - Vancomycin 15 mg/kg intravenously twice daily.

14. A 30-year-old man presents to the emergency department with fever and severe pain in his right hand with erythema, tenderness, warm skin, and swelling. Two days ago, he had a minor scratch to his hand while gardening. He is admitted to the hospital for further evaluation and management. Twenty-hours later, blisters, crepitus, and necrosis become apparent on his right hand, and the patient is rushed to the operating room for surgical debridement and removal of necrotic tissues. Pertinent laboratory values are WBC  $19 \times 10^3$  cells/mm<sup>3</sup>, creatine kinase 301 IU/L, and albumin 3 g/dL. Blood cultures reveal group A  $\beta$ -hemolytic streptococci susceptible to all antibiotics tested. Nasal swab is negative for MRSA. Which one of the following is the most appropriate antibiotic treatment for this patient?
- Imipenem-cilastatin.
  - Imipenem-cilastatin plus vancomycin.
  - Penicillin G.
  - Penicillin G plus clindamycin.
15. A 65-year-old woman is in the hospital for management of an infected wound, a complication of a surgery on the trunk. She is currently receiving telavancin 10 mg/day pending microbiology culture and sensitivity report. Her other hospital medications include methadone 20 mg three times daily, oxycodone/acetaminophen 10 mg/325 mg 1 tablet three times daily PRN pain, bisacodyl 5 mg/day, docusate 100 mg twice daily, enoxaparin 40 mg subcutaneously daily, and omeprazole 20 mg/day. Which one of the following is this patient most at risk of because of her medications?
- Hepatotoxicity.
  - Hypothyroidism.
  - QTc prolongation.
  - Seizures.
16. You wish to measure the degree of patient satisfaction in the prevention of herpes zoster in patients who were referred to the pharmacist-run immunization clinic and those who received standard care. Patients are asked to indicate their satisfaction level using a Likert scale (1 = strongly dissatisfied, 5 = strongly satisfied). Which one of the following statistical tests would be best to compare these data?
- McNemar's test.
  - Paired t test.
  - Wilcoxon rank sum.
  - Wilcoxon signed rank.
17. You are asked to implement an antimicrobial stewardship initiative to decrease the incidence of *Clostridium difficile* infection (CDI) after several patients who were treated with clindamycin for skin and soft tissue infections (SSTIs) came back to the emergency department with CDI. Physicians in your department have recently switched from cephalexin to clindamycin because of the sharp increase in the incidence of community-associated MRSA (CAMRSA) infections. In addition to incision and drainage, which one of the following would be best to recommend for the treatment of moderate purulent SSTIs?
- Continue the use of clindamycin if the double disk diffusion test is positive.
  - Use cephalexin instead of clindamycin.
  - Use linezolid instead of clindamycin.
  - Use trimethoprim/sulfamethoxazole instead of clindamycin.
18. You are asked to implement a strategy to reduce the incidence of recurrent SSTIs caused by MRSA in a long-term care facility. Despite emphasizing personal and environmental hygiene, a large percentage of residents still present with MRSA infections. After treating the infections, which one of the following would be best to administer to residents to prevent recurrences?
- Mupirocin intranasally twice daily for 5 days.
  - Retapamulin intranasally twice daily for 7 days.
  - Rifampin 600 mg orally daily for 5 days.
  - Trimethoprim/sulfamethoxazole 1 DS tablet orally twice daily for 7 days.
19. A 7-year-old girl was ready to be discharged after a 2-day course of vancomycin therapy for the treatment of a carbuncle in her right buttock. The culture from the abscess grew MRSA sensitive to all antibiotics tested except erythromycin and oxacillin, and the double disk diffusion test was positive. Which one of the following would best complete the course of antibiotic therapy for this patient?
- Clindamycin.
  - Doxycycline.
  - Levofloxacin.
  - Trimethoprim/sulfamethoxazole.
20. A 51-year-old man is expected to receive a 3-week-course of outpatient daptomycin therapy for the treatment of DFI. He has a history of myocardial infarction for which he has been taking aspirin 81 mg/day, lisinopril 40 mg/day, metoprolol 25 mg twice daily, and simvastatin 20 mg/day at bedtime for 5 years with no complaints. His SCr is 0.8 mg/dL. Which one of the following monitoring parameters would best ensure the safety of this patient's antibiotic regimen?
- Creatine kinase.
  - Liver function tests.
  - QTc interval.
  - Serum creatinine.