Chapter 133: Skin and Soft Tissue Infections

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CHAPTER SUMMARY FROM THE PHARMACOTHERAPY HANDBOOK

For the Chapter in the Schwinghammer Handbook, please go to Chapter 48, Skin and Soft-Tissue Infections.

KEY CONCEPTS

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1. Folliculitis, furuncles (boils), and carbuncles begin around hair follicles and are caused most often by *Staphylococcus aureus*. Folliculitis and small furuncles are generally treated with warm, moist heat to promote drainage; larger furuncles and carbuncles require incision and drainage. Purulent, moderately severe infections (eg, with fever or other systemic signs of infection) have a higher suspicion for community-associated methicillin-resistant *S. aureus* (MRSA) and empiric treatment should include trimethoprim–sulfamethoxazole or a tetracycline such as doxycycline.

2. Erysipelas, a superficial skin infection with extensive lymphatic involvement, is caused by *Streptococcus pyogenes*. The treatment of choice is penicillin, administered orally or parenterally, depending on the severity of the infection.

3. Impetigo is a superficial skin infection that occurs most commonly in children. It is characterized by fluid-filled vesicles that rapidly develop into pus-filled blisters that rupture to form golden-yellow crusts. Effective therapy includes penicillinase-resistant penicillins (dicloxacillin), first-generation cephalosporins (cephalexin), and topical mupirocin or retapamulin. *S. aureus* is the primary cause of impetigo, with MRSA becoming more common in recent years.

4. Lymphangitis, an infection of the subcutaneous lymphatic channels, is usually caused by *S. pyogenes*. Acute lymphangitis is characterized by the rapid development of fine, red, linear streaks extending from the initial infection site toward the regional lymph nodes, which are usually enlarged and tender. Penicillin is the drug of choice.

5. Cellulitis is an infection of the epidermis, dermis, and superficial fascia most commonly caused by *S. pyogenes* and *S. aureus*. Lesions generally are hot, painful, and erythematous, with nonelevated, poorly defined margins. Oral trimethoprim–sulfamethoxazole, doxycycline, or minocycline is used for initial treatment of suspected MRSA in patients with purulent, moderately severe cellulitis (ie, lesion with purulent drainage or exudate, or nondrainable abscess plus systemic signs of infection). Treatment of nonpurulent cellulitis generally consists of penicillin VK, a penicillinase-resistant penicillin (dicloxacillin), first-generation cephalosporin (cephalexin), or clindamycin for 5 days; coverage for MRSA may be added in certain patients. More severe infections in hospitalized and/or immunocompromised patients should receive empiric therapy with parenteral agents active against streptococci (nonpurulent infections) or both streptococci and MRSA (purulent infections).

6. Necrotizing fasciitis is an uncommon but life-threatening infection of subcutaneous tissue that results in progressive destruction of superficial fascia and subcutaneous fat. Early and aggressive surgical debridement is an essential part of therapy for treatment of necrotizing fasciitis. Mixed infections are treated with broad-spectrum regimens that cover streptococci, gram-negative aerobes, and anaerobes. Infections caused by *S. pyogenes* or *Clostridium* species should be treated with the combination of penicillin and clindamycin.

7. Diabetic foot infections are managed with a comprehensive treatment approach that includes both proper wound care and antimicrobial

therapy. Potential pathogens include staphylococci, streptococci, aerobic gram-negative bacilli, and obligate anaerobes. Antimicrobial regimens for diabetic foot infections are based on severity of the infection, expected treatment setting, and risk factors for infection with more resistant pathogens such as MRSA and *Pseudomonas aeruginosa*. Outpatient therapy with oral antimicrobials should be used whenever possible for less severe infections, while more severe infections initially require IV therapy.

8 Prevention is the single most important aspect in the management of pressure injuries. After an injury develops, successful local care includes a comprehensive approach consisting of relief of pressure, proper cleaning (debridement), disinfection, and appropriate antimicrobial therapy if an infection is present. Good wound care is crucial to successful management.

9 All bite wounds (animal or human) should be thoroughly irrigated with large volumes of sterile normal saline, and the injured area should be immobilized and elevated. Depending on the severity of the bite wound, amoxicillin–clavulanic acid or ampicillin–sulbactam is often used for treatment of animal bites because of their coverage of *Pasteurella* species, streptococci, *S. aureus*, and anaerobes typically present in the oral flora of dogs and cats.

10 Antimicrobial prophylaxis (early preemptive therapy) of animal bites is not routinely recommended; however, patients at high risk of infection (eg, immunocompromised, moderate-to-severe bite injuries especially to the hands and face, penetration of the periosteum or joint capsule) should be given prophylactic antimicrobial therapy for 3 to 5 days. Infected bite wounds should be treated for 7 to 14 days with oral or IV antibiotics having activity against *Eikenella corrodens*, streptococci, *S. aureus*, and β-lactamase–producing anaerobes.

BEYOND THE BOOK

BEYOND THE BOOK

Refer to "Chapter 126: Skin and Soft Tissue Infection: A Pain in the Butt Level II" in Pharmacotherapy Casebook: A Patient-Focused Approach, 11e (may be obtained online through AccessPharmacy). After studying the patient presentation, briefly answer Questions 1 through 5 and the Follow-Up Case Questions 1 through 9 regarding patient Jimmie Chipwood's skin and soft tissue infection (SSTI). The purpose of this exercise is to gain experience in applying knowledge regarding SSTI to assess infections in individual patients and develop an appropriate therapeutic plan based on clinical presentation, type and severity of infection, past treatment history, potential causative pathogens, and patient characteristics.

INTRODUCTION

Skin and soft-tissue infections (SSTIs) may involve any or all layers of the skin (epidermis, dermis, subcutaneous fat), fascia, and muscle. They may also spread far from the initial site of infection and lead to more severe complications, such as endocarditis, gram-negative sepsis, or streptococcal glomerulonephritis. Sometimes the treatment of SSTIs may necessitate both medical and surgical management. This chapter presents details of the pathogenesis and management of some of the most common infections involving the skin and soft tissues, ranging in severity from superficial to life-threatening.

EPIDEMIOLOGY

Bacterial infections of the skin can be classified as primary or secondary (Table 133-1).[1-4] Primary bacterial infections usually involve areas of previously healthy skin and are caused by a single pathogen. In contrast, secondary infections occur in areas of previously damaged skin and are frequently polymicrobic. SSTIs are also classified as complicated or uncomplicated. Complicated infections are those that involve deeper skin structures (eg, fascia, muscle layers), require significant surgical intervention, and/or occur in patients with compromised immune function (eg, diabetes mellitus, human immunodeficiency virus [HIV] infection).[3-5] Other categories that are crucial for successful treatment are the differentiation of necrotizing versus non-necrotizing, as well as purulent versus nonpurulent, SSTIs.[3-6] Acute bacterial skin and skin structure infections (ABSSSIs) are a subset of SSTI and specifically denote those more severe bacterial infections of the skin with a lesion size area of at least 75 cm^2 and for which

antibiotic therapy is generally considered to be required for successful resolution.[7] The subset of ABSSSI specifically includes cellulitis, erysipelas, wound infection, and major cutaneous abscess.[7]

TABLE 133-1

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, Enterobacterales)
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, Enterobacterales, *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*, Enterobacterales, *S. aureus*, streptococci

Data from References 1,2,8.

SSTIs are among the most common infections seen in community and hospital settings.[9,10] However, most infections are mild and are treated in an outpatient setting, making it difficult to accurately quantify community-acquired SSTIs. SSTIs occur in approximately 14 million persons each year, being more common among those 50 years of age and older.[8,9,10] Emergency room visits for SSTIs continue to increase each year, attributed primarily to an increase in community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) cellulitis and abscesses.[3-5,11] Both inpatient

admissions and outpatient office visits due to SSTIs increased by approximately 65% over a 9-year period in the early 2000s; during this same period the prevalence of MRSA among SSTIs increased from 29% to 64% in one emergency department.[10,12] In 2011 SSTIs were responsible for over 750,000 hospitalizations and represented approximately 2% of all admissions.[10] Additionally, the frequency of infections caused by drug-resistant gram-positive cocci (particularly *S. aureus*) has been increasing.[3-6,10,11] While the high incidence of healthcare-associated MRSA (HA-MRSA) has been a major concern for many years, the emergence of CA-MRSA is even more problematic.[3-6,13-20] CA-MRSA are characteristically isolated from patients lacking typical risk factors (eg, prior hospitalization, long-term care facility residence) and are often susceptible to antibiotics such as trimethoprim–sulfamethoxazole, doxycycline, and clindamycin.[13-20] They also differ genetically from HA-MRSA with methicillin resistance carried on the type IV or V staphylococcal chromosomal cassette *mec* (SCC*mec*) element of the *mecA* gene.[1,13,18] CA-MRSA strains often harbor genes for Panton-Valentine leukocidin (PVL), a cytotoxin causing leukocyte destruction and tissue necrosis. In contrast, HA-MRSA strains usually lack genes for PVL and are associated with SCC*mec* alleles I to III.[1,13,15,18] While the incidence of HA-MRSA has declined in recent years,[21] the incidence of CA-MRSA has dramatically increased; nearly half (46%) of all culture-positive SSTIs are caused by MRSA and nearly 50% of all CA-MRSA are isolated from SSTIs.[3-6,9,10,20] Clinicians should suspect CA-MRSA in geographic areas with a high prevalence of these strains, or in recurrent or persistent infections that are not responding to appropriate β-lactam therapy. In addition to the emergence of CA-MRSA, there is also concern about the use of clindamycin for CA-MRSA infections due to the risk of inducible clindamycin resistance in strains that are erythromycin-resistant, but clindamycin-susceptible.[8,15,18,21,23] A double-disk test (D-zone test) is recommended to identify erythromycin-resistant strains with inducible clindamycin resistance if treatment with clindamycin is desired.[4,6,13,15,18,24] A positive D-zone test, indicating the presence of inducible resistance conferred by the *erm* gene, suggests the possibility of the emergence of clindamycin resistance during therapy.[13,15,18,24]

ETIOLOGY

The majority of SSTIs are caused by gram-positive organisms present on the skin surface.[2,6,22] Gram-positive bacteria (coagulase-negative staphylococci, diphtheroids) are the predominant flora of healthy skin, with gram-negative organisms being relatively uncommon (Table 133-2).[1,2,8,22] *S. aureus*, as well as a variety of gram-negative bacteria, including *Acinetobacter* species, can be found in moist intertriginous areas (eg, axilla, groin, and toe webs) of the body.[1,2,22,23] Approximately 30% to 35% of healthy individuals are reported to be colonized with *S. aureus* on the skin or in the anterior nares.[1,8,22] Colonization, whether transient or permanent, provides a nidus for infection should the integrity of the epidermis be compromised.[1-3,5,6,8,22]

TABLE 133-2

Predominant Microorganisms of Normal Skin

Bacteria

- Gram-positive
  - Coagulase-negative staphylococci
  - Micrococci (*Micrococcus luteus*)
  - *Corynebacterium* species (diphtheroids)
  - *Propionibacterium* species
- Gram-negative
  - *Acinetobacter* species

Fungi

- *Malassezia* species
- *Candida* species

Data from References 1,2,8.

S. aureus and *S. pyogenes* account for the majority of community-acquired SSTIs.[1,12,15,22] Data from large surveillance studies showed *S. aureus* to be the most common cause of SSTIs in hospitalized patients, with often 30% to 50% of these being caused by MRSA.[8,10,12,13,17,20] Other common healthcare-associated pathogens included *Pseudomonas aeruginosa* (11%), enterococci (9%), and *Escherichia coli* (7%).[6,8,10,13]

PATHOPHYSIOLOGY

The skin serves as a barrier between humans and their environment, therefore functioning as a primary defense mechanism against infections. The skin and subcutaneous tissues normally are extremely resistant to infection but may become susceptible under certain conditions. Although the human skin supports an abundant and diverse microbiome of bacteria and fungi,[1,2,22] several host factors act together to confer protection against skin infections. Continuous renewal of the epidermal layer results in the shedding of keratocytes, as well as skin bacteria.[2,22] In addition, sebaceous secretions are hydrolyzed to form free fatty acids that strongly inhibit the growth of many bacteria and fungi. A normal commensal skin microbiome itself serves a protective function by not allowing space or environmental conditions favorable to colonization with more pathogenic strains.[1,2,22] Conditions that may predispose a patient to the development of skin infections include (a) high concentrations of bacteria (more than 10^5 microorganisms), (b) excessive moisture of the skin, (c) inadequate blood supply, (d) availability of bacterial nutrients, and (e) damage to the corneal layer allowing for bacterial penetration.[2,3,5,8,22,23,25]

The best defense against SSTI is intact skin.[2,22,25] The majority of SSTIs result from the disruption of normal host defenses by processes such as skin puncture, abrasion, or underlying diseases (eg, diabetes).[1-3,5,8,22,25] The nature and severity of the infection depend on both the type of microorganism present and the site of inoculation.

FOLLICULITIS, FURUNCLES, AND CARBUNCLES

1 Folliculitis is inflammation of the hair follicle and is caused by physical injury, chemical irritation, or infection. Infection occurring at the base of the eyelid is referred to as a stye. While folliculitis is a superficial infection with pus present only in the epidermis,[4,15,23] furuncles and carbuncles occur when a follicular infection around the hair shaft extends to involve deeper areas (subcutaneous tissue) of the skin.[4,15,23] A furuncle, commonly known as a *boil*, is a walled-off mass of purulent material arising from a hair follicle.[4,15,23] The lesions are called *carbuncles* when adjacent furuncles coalesce to form a single inflamed area.[4,15,23] This aggregate of infected hair follicles forms deep masses that generally open and drain through multiple sinus tracts.[15,23] *S. aureus* is the most common cause of folliculitis, furuncles, and carbuncles.[4,15,23] Outbreaks of furunculosis caused by *S. aureus* and CA-MRSA have been reported in settings involving close contact (eg, families, prisons), especially when skin injury was common (such as with athletes).[11] In addition, some individuals experience repeated episodes of furunculosis.[23] A major predisposing factor for recurrent infection is the presence of *S. aureus* in the anterior nares.[15,23]

CLINICAL PRESENTATION: Folliculitis, Furuncles, and Carbuncles

Folliculitis

- Clustering, pruritic papules localized to hair follicles.
- Generally develop in areas subject to friction and perspiration.
- Papules are generally 5 mm or less in diameter and erythematous.
- Papules evolve into pustules that generally spontaneously rupture in several days.
- Systemic signs (fever, malaise) are uncommon.

Furuncles

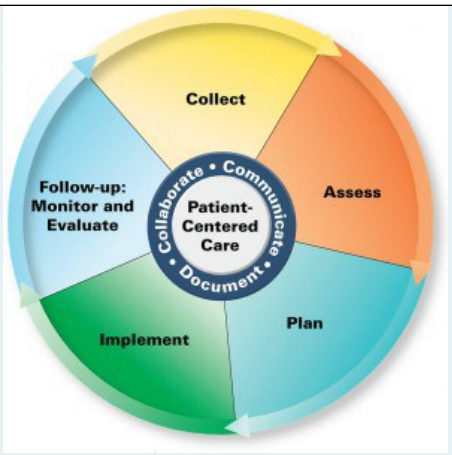
- Inflammatory, draining nodule involving a hair follicle.
- Develop in areas subject to friction and perspiration.
- Lesions are discrete, whether occurring as singular or multiple nodules.
- Lesion starts as a firm, tender, red nodule that becomes painful and fluctuant.
- Lesions often drain spontaneously.
- Lesions caused by CA-MRSA often have necrotic centers
- Systemic signs are uncommon.

Carbuncles

- Formed when adjacent furuncles coalesce to form a single inflamed area.
- Form broad, swollen, erythematous, deep, and painful follicular masses.
- Commonly develop on the back of the neck.
- Commonly associated with systemic signs (fever, chills, malaise).
- Bacteremia with secondary spread to other tissues is common.

Patient Care Process

Patient Care Process for the Treatment of Skin and Soft-Tissue Infections (SSTIs)



Collect

- Patient characteristics (eg, age, sex, pregnant)
- Patient medical history
- Social history (eg, drug/ethanol use), animal exposures (if bite injury)
- Current and prior medications (eg, antimicrobials, immunosuppressive agents)
- Objective data
  - Weight, temperature, blood pressure (BP), heart rate (HR), respiratory rate (RR), altered mental status (AMS), urine output (UO)
  - Laboratory findings including white blood cells (WBC) with differential, serum creatinine (SCr), liver function tests (LFT), blood glucose (especially for diabetic foot infection)
  - Culture and antimicrobial susceptibility data
  - Physical examination of skin lesions including location, size, appearance, presence of abscesses or ulcers, presence of purulence or drainage
  - Imaging studies (if suspicion for osteomyelitis, necrotizing fasciitis)

Assess

- Specific type of infection (see Clinical Presentation boxes for various SSTIs)
- Classification of infection severity, especially for cellulitis, diabetic foot infection, and pressure sores (see Tables 133-8 and 133-10)
- Risk for infection with specific pathogens (see Tables 133-1 and 133-9)
- Ability/willingness to be treated as outpatient, including potential adherence barriers
- Hemodynamic/clinical stability (eg, SBP <90 mm Hg, HR >100 bpm, RR >22, AMS, decreased UO)
- Contraindications to specific antibiotic therapy (eg, age, allergies, drug-drug/disease interactions)

Plan*

- Antibiotic regimen including specific antimicrobial(s), dose, route, frequency, and duration (see Figs. 133-1 to 133-3; Tables 133-3 to 133-5 and 133-9)

- Monitoring parameters including efficacy (eg, improvement and/or healing of infectious lesions and other symptoms [depending on specific SSTI]), and safety (eg, antibiotic side effects, *Clostridioides difficile*); frequency and timing of follow-up
- Monitoring parameters for specific antibiotics administered to hospitalized patients (see Table 133-6)
- Patient education (eg, purpose of treatment, lifestyle modification, drug- and infection-specific information, medication administration)
- Self-monitoring for resolution of SSTI signs and symptoms, signs of worsening or unresponsive SSTI, when to seek additional medical attention
- Referrals to other providers when appropriate (eg, surgeon, diabetes educator, wound care specialist)

Implement*

- Provide patient and caregiver education regarding all elements of treatment plan
- Use motivational interviewing and coaching strategies to maximize adherence to outpatient antibiotics
- Schedule follow-up as needed for more severe infections (eg, cellulitis, diabetic foot infection, pressure sores, bite wounds)

Follow-up: Monitor and Evaluate*

- Resolution of infectious symptoms (depending on specific type of SSTI)
- Presence of adverse effects specific to the antibiotic regimen
- Patient adherence to treatment plan using multiple sources of information
- Presence of drug-drug interactions potentially requiring changes in drug regimens or monitoring plans
- Therapeutic drug levels for specific agents used in hospitalized patients (see Table 133-6)

****Collaborate with patient, caregivers, and other healthcare professionals.***

Treatment: Folliculitis, Furuncles, and Carbuncles

Desired Outcomes

The goals of treatment include relieving discomfort, preventing further spread of the infection, and preventing recurrence. Controlling recurrent furunculosis is key due to the difficulty in treating chronic furunculosis. Treatments should be effective and inexpensive and have minimal adverse effects.

Pharmacologic Therapy

Table 133-3 summarizes evidence-based treatment recommendations from clinical guidelines for SSTIs.[3,4,8,15,26-28] Treatment of folliculitis generally requires only local measures, such as warm moist compresses or topical therapy (eg, clindamycin, erythromycin, mupirocin, retapamulin, or benzoyl peroxide).[8,23] Topical agents are typically applied two to four times daily for 7 days. Small furuncles generally can be treated with moist heat, which promotes localization and drainage of pus.[4,8,23] Large and/or multiple furuncles and carbuncles require incision and drainage.[4,5,8,13,15,23,27] Systemic antibiotics are usually not necessary unless accompanied by fever or extensive cellulitis.[4,5,15,23] Treatment of more severe infections (eg, accompanied by systemic signs of infection) should include oral trimethoprim–sulfamethoxazole or a tetracycline (doxycycline or minocycline) for 5 to 10 days due to a higher suspicion for MRSA (see Table 133-4 for adult and pediatric doses).[4,5,13,15,23,27] For individuals with nasal colonization, application of mupirocin ointment twice daily in the anterior nares for the first 5 days of each month decreases recurrent furunculosis by almost half.[13,15] Daily chlorhexidine washes and daily washing of personal items such as towels, bedding, and clothes may also be recommended.[15]

TABLE 133-3

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 the 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	Strong, moderate

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	
Broad-spectrum antibiotic therapy with vancomycin plus 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 patients with suspected or definitive serious MRSA infections, an individualized target of the AUC/MIC ratio of 400 to 600 (assuming a vancomycin MIC of 1 mg/L) should be advocated to achieve clinical efficacy while improving patient safety	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	Strong, low

linezolid plus piperacillin–tazobactam or a carbapenem, or vancomycin or linezolid plus ceftriaxone and metronidazole	
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	A II
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]Cited evidence-based guidelines utilize different systems for grading the strengths of recommendation and quality of the associated evidence. Qualitative (descriptive) recommendations are from Reference 15; letter- and roman numeral–based recommendations are from the other cited guidelines. Readers are advised to consult the original documents for full explanations of the grading systems and definitions used in individual guidelines.

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 1 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.

Data from References 3,4,8,15, and 26-29.

TABLE 133-4

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,b] • Clindamycin[a,b]
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.

Evaluation of Therapeutic Outcomes

Many follicular infections resolve spontaneously without medical or surgical intervention. Lesions should be incised if they do not respond to a few days of moist heat and nonprescription topical agents. Following drainage, most lesions begin to heal within several days without antimicrobial therapy. Any patient who is unresponsive to several days of systemic antibiotic therapy or suffers recurrent infection should have a culture and sensitivity test performed to guide continued antibiotic selection.

ERYSIPELAS

Erysipelas is a distinct form of cellulitis involving the more superficial layers of the skin and cutaneous lymphatics.[3,30,31] The intense red color and burning pain associated with erysipelas led to the common name of “St. Anthony’s fire.” The infection is almost always caused by β-hemolytic streptococci, with the organisms penetrating via small breaks in the skin. Group A streptococci (*S. pyogenes*) are responsible for most infections.[8,15,31] Infections are more common in infants, young children, older adults, and patients with nephrotic syndrome or who are immunocompromised.[4,8,30,31] Erysipelas also commonly occurs in areas of preexisting lymphatic obstruction or edema.[8,13,30,31] Diagnosis is made on the basis of the characteristic lesion.

CLINICAL PRESENTATION: Erysipelas

General

- Lower extremities are the most common sites.

Symptoms

- Flu-like symptoms (fever, chills, malaise) common prior to the appearance of the lesion.
- Infected area described as very painful or as a burning pain.

Signs

- Lesion is intensely erythematous and edematous, often with lymphatic streaking.
- Lesion has raised border, which is sharply demarcated from uninfected skin.
- Temperature is often mildly elevated.

Laboratory Tests

- Causative organism usually cannot be cultured from the skin surface.
- Needle aspiration or punch biopsies occasionally identify organism.
- Cultures considered for more severe cases (eg, atypical clinical findings such as fluid-filled blisters).

Other Diagnostic Tests

- Complete blood cell count is often performed, leukocytosis is common.
- C-reactive protein is also generally elevated.

Treatment: Erysipelas

Desired Outcomes

The goal of treatment of erysipelas is rapid eradication of the infection, thereby providing relief of symptoms (pain, tenderness, fever).[30] Preventing recurrent infection is also important as recurrence is a common complication, occurring in approximately 20% of patients.[30] Treatments should be effective and inexpensive, and have minimal adverse effects.

Pharmacologic Therapy

Mild-to-moderate cases of erysipelas are treated with intramuscular procaine penicillin G or oral penicillin VK for 7 to 10 days (see Table 133-4).[8,15,30] Recommended doses and monitoring parameters for selected antibiotics are given in Tables 133-5 and 133-6. Penicillin-allergic patients can be treated with clindamycin. For more serious infections, the patient should be hospitalized and administered IV aqueous penicillin G.[8,15] Marked improvement is seen within 48 hours, and the patient may be switched to oral penicillin to complete the course of therapy.

TABLE 133-5

Drug Dosing[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 orally in three to four divided doses[3]	May be used for oral 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	Pediatric: 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®	1,000 mg IV once on Day 1 of therapy, followed by 500 mg IV once on Day 8 of therapy; OR 1,500 mg IV once with no additional doses	Pediatric: 22.5 mg/kg (less than 6 years of age) or 18 mg/kg/day (6-18 years of age) IV in one dose	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® • Kimyrsa®	1,200 mg IV once with no additional doses (Orbactive® administered over 3 hours and		For MRSA infection

		Kimyrsa® over 1 hour)		
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 24-hour AUC/MIC ratios of 400-600 for serious MRSA infections	Pediatric: 60-80 mg/kg/day IV in three to four divided doses; doses guided by serum concentrations	For MRSA infection

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

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

TABLE 133-6

Drug Monitoring

Drug	Adverse Reaction	Monitoring Parameters	Comments
Aminoglycosides (tobramycin, gentamicin)	Nephrotoxicity	Serum creatinine, urine output, serum concentrations	Extended-interval ("once-daily") dosing potentially associated with less renal toxicity, similar efficacy to traditional dosing. Goal trough concentration <1 µg/mL (mg/L; 2 µmol/L) during extended-interval dosing
Daptomycin	Myopathy	Serum creatine phosphokinase	Most creatinine phosphokinase elevations will be asymptomatic; risk of myopathy may be increased with concomitant use of HMG-coA reductase inhibitors
Imipenem–cilastatin	CNS toxicities, seizures	Serum creatinine, mental status, CNS function	Increased incidence with higher dose, failure to adjust dose/interval for reduced renal function. Increased risk compared with meropenem or doripenem
Linezolid	Myelosuppression, thrombocytopenia, optic/peripheral neuropathy, serotonin syndrome	CBC, vision changes, serum lactate, heart rate, blood pressure, temperature, myoclonus	Myelosuppression and neuropathy more common with prolonged use. Weak MAO inhibitor, serotonin syndrome possible with other serotonergic drugs such as SSRIs and SNRIs
Nafcillin	Interstitial nephritis	Serum creatinine, urine output	Reversible, requires switch to alternative β-lactam
Vancomycin	Nephrotoxicity, infusion reactions	Serum creatinine, urine output, blood pressure, heart rate, serum concentrations	Dose adjustment required for renal dysfunction. Pretreatment and slow infusion may decrease incidence of infusion reaction. Drug concentrations monitored to achieve goal AUC/MIC ratio of 400-600 for serious infections, including necrotizing fasciitis

CBC, complete blood count; MAO, monoamine oxidase; SNRI, serotonin–norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

Evaluation of Therapeutic Outcomes

Erysipelas generally responds quickly to appropriate antimicrobial therapy. Temperature and white blood cell count should return to normal within 48 to 72 hours. Erythema, edema, and pain also should resolve gradually.

IMPETIGO

Impetigo is a superficial skin infection that is seen most commonly in children.[5,23,30,32,33] The infection is generally classified as bullous or nonbullous based on clinical presentation.[5,30,32,33] Impetigo is most common during hot, humid weather, which facilitates microbial colonization of the skin.[4,8,30,32] Minor trauma, such as scratches or insect bites, allows entry of organisms into the superficial layers of skin, and infection ensues.[8,23,30,32] Impetigo is highly communicable and readily spreads through close contact, especially among siblings and children in daycare centers and schools.[8,30,32]

Although historically caused by *S. pyogenes*, *S. aureus* has emerged as a principal cause of impetigo (either alone or in combination with *S.*

pyogenes).[23,30,32,33] The bullous form is caused by strains of *S. aureus* capable of producing exfoliative toxins.[23,32,33] The bullous form most frequently affects neonates and children less than 5 years of age,[33,34] and accounts for approximately 30% of all cases of impetigo.[8,32] Similar to other SSTIs, impetigo has been reported to be increasingly due to MRSA.[23,32,33]

CLINICAL PRESENTATION: Impetigo

General

- Exposed skin, especially the face, is the most common site.

Symptoms

- Pruritus is common.
- Systemic signs and symptoms of infection are minimal.
- Weakness, fever, and diarrhea occasionally seen with bullous form.

Signs

Nonbullous:

- Lesions start as small, fluid-filled vesicles.
- Vesicles rapidly develop into pustules that rupture readily.
- Purulent discharge dries to form characteristic golden-yellow crusts.

Bullous:

- Lesions start as vesicles that rapidly progress into bullae containing clear yellow fluid.
- Bullae soon rupture, forming thin, light brown crusts.
- Regional lymph nodes may be enlarged.

Laboratory Tests

- Cultures should be collected for pathogen identification in more severe cases.
- Crusted tops of lesions should be raised to obtain purulent material at the base for culture.
- Open, draining pustules should not be cultured as they may be colonized with skin flora.

Other Diagnostic Tests

- Complete blood cell count often performed, leukocytosis is common.

Treatment: Impetigo

Desired Outcomes

The goals of treatment include relieving discomfort, improving the cosmetic appearance of lesions, preventing further spread of the infection, and preventing recurrence. Preventing transmission to others is also important.[32] Treatments should be effective and inexpensive and have minimal

adverse effects.[30,32]

Pharmacologic Therapy

Although impetigo may resolve spontaneously, antimicrobial treatment is indicated to relieve symptoms, prevent formation of new lesions, and prevent complications such as cellulitis. A review of interventions for impetigo by the Cochrane Collaboration found that topical mupirocin and oral antibiotics (except penicillin and erythromycin) were equally effective for the treatment of impetigo[34]; topical mupirocin ointment or retapamulin ointment for 5 days are now recommended as first-line treatment of mild cases of impetigo not involving multiple lesions or the face.[15,23,30,32,33] Penicillinase-resistant penicillins (such as dicloxacillin) are preferred for oral treatment because of the increased incidence of infections caused by *S. aureus*.[15,23,32,33] First-generation cephalosporins (eg, cephalexin) are also commonly used.[15,23,30,32,33] Penicillin, administered as a single intramuscular dose of benzathine penicillin G or as oral penicillin VK, is effective for infections known to be caused by *S. pyogenes* but should not be used for empiric therapy of unknown etiology.[23] Penicillin-allergic patients, or those known to be infected with MRSA, can be treated with clindamycin, doxycycline, or trimethoprim–sulfamethoxazole. The duration of therapy is 7 days.[15,30,33] With proper treatment, healing of skin lesions is rapid and occurs without residual scarring. Removal of crusts by soaking in soap and warm water also may be helpful in providing symptomatic relief.[8,30,32]

Evaluation of Therapeutic Outcomes

Clinical response should be seen within 5 to 7 days of initiating antimicrobial therapy for impetigo. Treatment failures could be a result of noncompliance or antimicrobial resistance. A follow-up culture of exudates should be collected for culture and sensitivity, with treatment modified accordingly.

LYMPHANGITIS

4 Acute lymphangitis is an inflammation involving the subcutaneous lymphatic channels. Lymphangitis usually occurs secondary to puncture wounds, infected blisters, or other skin lesions. Most infections are caused by *S. pyogenes*.[35]

CLINICAL PRESENTATION: Lymphangitis

General

- Lymphadenitis (acute or chronic inflammation of the lymph nodes) may occur when microorganisms reach the lymph nodes.

Symptoms

- Systemic signs and symptoms (ie, fever, chills, malaise, and headache) often develop rapidly before any sign of infection is evident at the initial site of inoculation, or after the initial lesion has subsided.
- Systemic signs and symptoms often are more profound than would be expected based on examination of the cutaneous lesion.

Signs

- Peripheral lesion associated with proximal red linear streaks directed toward the regional lymph nodes is diagnostic of acute lymphangitis.
- Lymph nodes are enlarged and tender.
- Peripheral edema of the involved extremity is present.
- Thrombophlebitis and acute lymphangitis in the lower extremities may be confused because both are associated with red linear streaking and tender areas; however, in thrombophlebitis, no portal of entry is identifiable.

Laboratory Tests

- Cultures of the affected lesions yield negative results.
- Pathogens identified by Gram stain of the initial lesion if done early in the course of the disease.

Other Diagnostic Tests

- Complete blood cell count is often performed as leukocytosis is common.

Treatment: Lymphangitis

Desired Outcomes

The goal of treatment of lymphangitis is rapid eradication of the infection, thereby providing relief of symptoms (pain, tenderness, fever). Prevention of systemic complications is also an important goal as thrombophlebitis and abscess formation are possible. Treatments should be effective and inexpensive and have minimal adverse effects.

Pharmacologic Therapy

Penicillin is the antibiotic of choice. Because these infections are potentially serious and rapidly progressive, initial treatment should be with IV penicillin G 1 to 2 million units every 4 to 6 hours. Parenteral treatment should be continued for 48 to 72 hours, followed by oral penicillin VK for a total of 10 days.[35] Nondrug therapy includes immobilization and elevation of the affected extremity and warm-water soaks every 2 to 4 hours.[35] For penicillin-allergic patients, clindamycin may be used.

Evaluation of Therapeutic Outcomes

Lymphangitis usually responds rapidly to appropriate therapy; signs and symptoms often are decreased markedly or absent within 24 hours of starting antibiotics.

CELLULITIS

Cellulitis is an acute infectious process that initially affects the epidermis and dermis and may spread subsequently within the superficial fascia.[3,5,12] Cellulitis is considered a serious disease because of the propensity of the infection to spread through lymphatic tissue and to the bloodstream. *S. pyogenes* and *S. aureus* are the most frequent bacterial causes.[3-6,13,21,30] However, many bacteria have been implicated in various types of cellulitis (Table 133-1). Approximately 4 million patients were hospitalized for cellulitis between 1998 and 2006, representing 10% of all infection-related admissions.[3,10,36] Additionally, hospitalizations and costs related to cellulitis and abscess doubled between 1998 and 2013; the number of visits to ambulatory care clinics and emergency rooms doubled from 4.6 million in 1997 to 9.6 million in 2005.[3,5] The rising incidence of infections caused by methicillin-resistant *S. aureus* (MRSA) is a major concern in both the community and hospital settings and is thought to be the major factor contributing to the dramatic increases in both outpatient visits and hospitalizations.[3,5,14,18,37]

Injection drug users are predisposed to several infectious complications, including abscess formation and cellulitis at the site of injection.[3,5,15] These SSTIs are often polymicrobic and originate from skin and/or oropharyngeal flora, as well as from contaminated needles, syringes, and diluents.[3,5,15] *S. aureus*, including MRSA, is the most common pathogen isolated from injection drug users.[3-5,37] Anaerobic bacteria, especially oropharyngeal anaerobes, are also found commonly, particularly in polymicrobic infections.[3,5,15] Outbreaks caused by *Clostridium* species have also been reported in injection drug users.[15]

Acute cellulitis with mixed aerobic and anaerobic pathogens may occur in persons with diabetes, following traumatic injuries, at sites of surgical incisions to the abdomen or perineum, or where host defenses have been otherwise compromised (eg, vascular insufficiency).[3-5,23] In older patients, cellulitis of the lower extremities also may be complicated by thrombophlebitis. Other complications of cellulitis include local abscess, myositis, osteomyelitis, septic arthritis, bacteremia, endocarditis, and sepsis.[3,5,15,23,30] Such complications of cellulitis may occur in approximately 1% of outpatients but as many as 17% of hospitalized patients.[9]

CLINICAL PRESENTATION: Cellulitis

General

- A history of an antecedent wound from minor trauma, abrasion, ulcer, or surgery is often present.

Symptoms

- Patients often experience fever, chills, or malaise and complain that the affected area feels hot and painful.
- Systemic findings such as hypotension, dehydration, and altered mental status are common.

Signs

- Characterized by erythema and edema of the skin.
- Lesions are nonelevated and have poorly defined margins.
- Affected areas are warm to touch.
- Inflammation is present with little or no necrosis or suppuration of soft tissue.
- Lesions may be associated with purulent drainage, exudates, and/or abscesses.
- Tender lymphadenopathy associated with lymphatic involvement is common.

Laboratory Tests

- Cultures of fluid should be collected when purulent drainage, exudates, or abscesses are present.
- Gram stain of fluid obtained by injection and aspiration of 0.5 mL of saline (using a small 22-gauge needle) into the advancing edge of the lesion may aid the microbiologic diagnosis but often yields negative results.
- Diagnosis usually is made on clinical grounds rather than by culture.

Other Diagnostic Tests

- Complete blood cell count is often performed as leukocytosis is common.
- Blood cultures often useful because bacteremia may be present in up to 30% of cases.

Treatment: Cellulitis

Desired Outcomes

The goals of therapy of acute bacterial cellulitis are rapid eradication of the infection and prevention of further complications. Effective treatment of cellulitis includes avoidance of unnecessary antimicrobials that contribute to increased resistance, and minimizing toxicities and cost of therapy.

Drug and Nondrug Management of Cellulitis

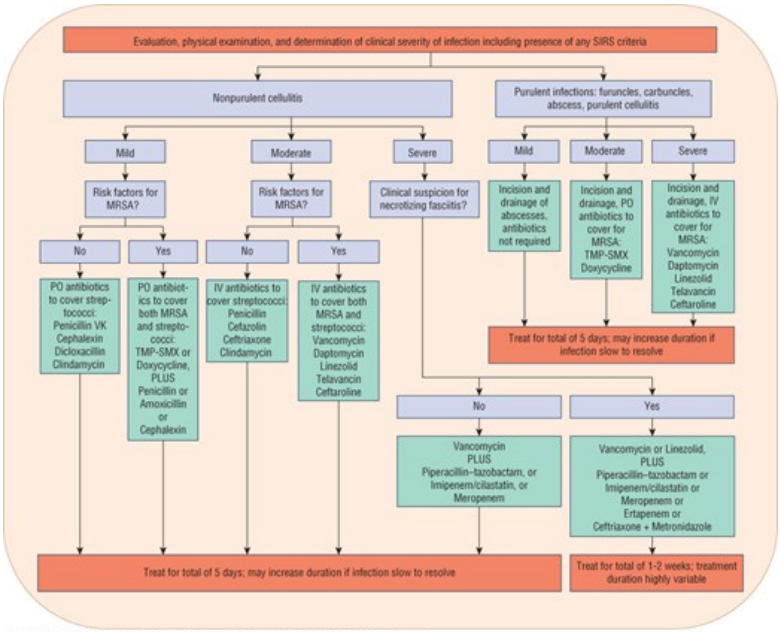
Local care of cellulitis includes elevation and immobilization of the involved area to decrease swelling.[3,5,15,23,30] Initial application of cool sterile saline dressings may decrease pain and swelling, and can be followed 1 to 3 days later with moist heat to aid in localization of the cellulitis. Surgical intervention (incision and drainage) is rarely indicated in the treatment of uncomplicated cellulitis, but may play an important role in management of more severe or complicated cases. Antimicrobial therapy is directed against the type of bacteria either documented or suspected to be present based

on the clinical presentation and risk factors. Particular attention must be paid to patients with risk factors for more atypical or resistant bacterial pathogens when selecting antibiotics for treatment of cellulitis. Such organisms include particularly MRSA, but also aerobic gram-negative bacteria and anaerobes.

Because staphylococcal and streptococcal cellulitis are indistinguishable clinically,[3-5,30] and because of concern regarding appropriate recognition and treatment of MRSA infections, guidelines from the Infectious Diseases Society of America (IDSA) provide detailed recommendations for empiric antibiotic therapy of cellulitis.[15,27] Antibiotic selection for treatment of cellulitis is chiefly determined by clinical findings such as appearance of the infected lesion and presence of more severe systemic illness. Cellulitis may be broadly classified as either purulent or nonpurulent for purposes of determining likely pathogens and appropriate empiric antibiotic therapy. Purulent cellulitis is defined as infection associated with purulent drainage or exudate in the absence of a simple drainable abscess; the presence of abscesses is also often associated with purulent cellulitis but by definition is the only clinical feature.[4,15,27] Incision and drainage of any abscesses and good wound care are the primary therapies for mild purulent infections when no systemic findings of infection are present. Systemic antibiotic therapy is often unnecessary in such cases.[3-5,27] Antibiotic therapy is recommended along with incision and drainage in patients with more complicated abscesses and/or moderately severe purulent cellulitis including the following: those with systemic signs of infection; multiple sites of infection; rapidly progressive infection in the presence of associated cellulitis; 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.[3-5,15,23,27] Patients with complicated abscesses and/or moderately severe purulent cellulitis are usually treated as outpatients using orally administered antibiotics with activity against MRSA; infection due to streptococci is less likely in this situation and specific coverage is not required.[3-5,27] Oral agents recommended for moderate purulent cellulitis include trimethoprim–sulfamethoxazole and doxycycline (Fig. 133-1).[3-5,15] Oral linezolid is also recommended in such cases but is more expensive and apparently no more efficacious than other treatment options.[3-5,27,37,38] Tedizolid, an oxazolidinone, is also indicated for the treatment of complicated SSTI. Compared to linezolid, tedizolid may have advantages related to a more convenient dosing schedule and fewer adverse effects and drug interactions. However, tedizolid is likely no more effective than linezolid for SSTI and its role relative to linezolid is still unclear.[15,37,38,39]

FIGURE 133-1

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.)



Severe purulent cellulitis is defined as purulent infections occurring in patients who have failed incision and drainage plus oral antibiotic therapy,

patients with systemic signs of infection (defined as temperature greater than 38°C, heart rate greater than 90 beats/min, respiratory rate greater than 24 breaths/min, or white blood cell count greater than 12,000 [12×10^9/L] or less than 400 cells/μL [0.4×10^9/L]), or immunocompromised patients. Appropriate clinical specimens for culture and susceptibility testing should be collected whenever possible in such patients.[3-5,15,22,27] Patients with severe purulent cellulitis should be hospitalized for empiric treatment with parenteral antibiotics having activity against MRSA. Vancomycin, daptomycin, linezolid or tedizolid, televancin, and ceftaroline are all acceptable treatment options with comparable efficacy in adults (Fig. 133-1).[8,3-6,12,13,15,27,37,38] In children, vancomycin, linezolid, or clindamycin are the preferred treatment options.[3,15,33]

Linezolid, tedizolid, daptomycin, ceftaroline, and telavancin all exhibit excellent activity against resistant gram-positive pathogens.[6,12,37,38,39,40] However, significantly higher cost compared with vancomycin, as well as lack of clearly demonstrated advantages in efficacy, makes them most appropriate for the treatment of complicated or refractory infections, or those documented as caused by multidrug-resistant pathogens, rather than as initial therapy. The availability of orally administered linezolid and tedizolid may provide cost-effective "step-down" options as alternatives to prolonged treatment with parenteral agents for many patients with more complicated infections and/or those patients who require initial hospitalization.[4,6,12,13,37-39]

The appropriate roles of dalbavancin and oritavancin, two newer glycopeptide drugs indicated for the treatment of complicated SSTI and with good activity against MRSA, are not well-defined for the routine management of SSTIs. Dalbavancin exhibits a terminal elimination half-life of approximately 14 days and is administered as a single large dose or two smaller doses given one week apart. Oritavancin has a half-life of approximately 10 days and is administered as a single one-time dose. The ability to provide an entire course of therapy with only one or two doses is attractive in terms of convenience, improved adherence compared to oral therapy, facilitation of early discharge of hospitalized patients, and potential for avoidance of inpatient hospitalization costs through administration in the emergency department, infusion centers, or physician offices. However, drug acquisition costs are higher than other treatment options and there are concerns related to potential lack of patient follow-up for monitoring of severe infections. Although these agents are not routinely used as first-line therapy, they may be considered for individual patients on a case-by-case basis in order to optimize their use.[3-6,12,13,15,23,37,38]

Delafloxacin is a fluoroquinolone with activity against staphylococci including MRSA, streptococci, and gram-negative bacteria including *P. aeruginosa*. Although IV followed by oral delafloxacin is equivalent to vancomycin plus aztreonam in the treatment of ABSSSI, its role is not well-defined and delafloxacin is not routinely recommended for treatment of cellulitis. The ability to transition patients from IV to oral therapy and its broad spectrum of activity may make delafloxacin a potential treatment option for carefully selected patients, particularly those with severe polymicrobial infections.

Carbapenems (ie, imipenem, meropenem, ertapenem, and doripenem) and the penicillin–β-lactamase inhibitor combination antibiotics (ampicillin–sulbactam, piperacillin–tazobactam) are equivalent to standard therapies in adults.[3,8,15] However, the greater cost of these agents without increased efficacy compared with other reliable regimens, particularly given the increasing problem of MRSA, makes them less desirable for empiric therapy except in serious polymicrobic infections.[3,15] Newer β-lactam–β-lactamase inhibitor combination agents such as ceftolozane–tazobactam, ceftazidime–avibactam, and meropenem–vaborbactam have few clinical data in the treatment of SSTIs and should not be used for empiric treatment of severe infections.

Nonpurulent cellulitis is defined as cellulitis without purulent drainage or exudate and no associated abscess. The role of MRSA in these types of infection is not clear, so empiric therapy of nonpurulent cellulitis is directed primarily against Group A β-hemolytic streptococci.[3-5,23] 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 (Fig. 133-1).[3-5,15,21,27] Oral cephalosporins, such as cefadroxil, cefaclor, cefprozil, cefpodoxime proxetil, and cefdinir, are also effective in the treatment of cellulitis but are more expensive.[15,21,23] Oral clindamycin may be used in penicillin-allergic patients.[15,21,23,27] Alternatively, a cephalosporin may be used cautiously for patients without a history of immediate or anaphylactic reactions to penicillin. Patients with moderately severe nonpurulent cellulitis (ie, systemic evidence of infection) or poor adherence to oral therapy should be hospitalized and treated with parenteral antibiotics directed against Group A streptococci. Recommended agents include penicillin VK, ceftriaxone, cefazolin, and clindamycin.[3-5,15,21,33] 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 (as previously defined for purulent cellulitis), 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.[3,4,15,21,23] Empiric antibiotics for severe nonpurulent cellulitis should provide a broad spectrum of activity against MRSA and

streptococci, as well as gram-negative and anaerobic bacteria. Recommended regimens include vancomycin plus piperacillin–tazobactam, and vancomycin plus imipenem–cilastatin or meropenem.[3,5,15,21,23]

Empiric treatment of MRSA should be considered for patients with either moderate or severe nonpurulent cellulitis that is associated with penetrating trauma, evidence of MRSA infection at another site or nasal colonization with MRSA, injection drug use, or in patients meeting SIRS criteria (fever, tachycardia, tachypnea, or leukocytosis or leukopenia as previously defined).[3,13,15,21,27] Recommended drugs for the coverage of MRSA in this setting are the same as those for purulent cellulitis. Clindamycin has reasonably good activity against β-hemolytic streptococci, but the activities of trimethoprim–sulfamethoxazole and the tetracyclines against this organism are not well-defined.[3,15,23,27] Therefore, if empiric coverage of both MRSA and β-hemolytic streptococci is desired for patients with nonpurulent cellulitis, they should receive clindamycin alone or amoxicillin in combination with trimethoprim–sulfamethoxazole, doxycycline, or minocycline.[3,13,15,23,27] Hospitalized patients with nonpurulent cellulitis who are not initially treated for MRSA should have their antibiotic changed to an agent with activity against MRSA if there is unsatisfactory clinical response.[3,16,23,27] Although often used for treatment of uncomplicated outpatient cellulitis, fluoroquinolones (eg, levofloxacin, moxifloxacin) are not recommended for routine use due to their unnecessarily broad spectrum of activity, concerns for resistance and toxicities, and higher cost compared with other preferred options.

Patients in whom specific pathogens have been identified by culture should have empiric antibiotics narrowed according to susceptibility test results. If documented to be a mild cellulitis secondary to streptococci, oral penicillin VK or intramuscular procaine penicillin G may be administered. Since *S. aureus* susceptibilities are more variable, treatment of documented staphylococcal infections will depend on test results for specific isolates. The usual duration of therapy for outpatient treatment of cellulitis, either purulent or nonpurulent, is 5 days; a longer duration should be considered if the infection has not sufficiently improved within that time.[3,8,15,23,30] A 7 to 14 day course of antibiotics has been recommended for cellulitis in hospitalized patients, but shorter courses (5-7 days) are often as effective as longer courses and should be used whenever possible.[16] In all cases, duration of therapy should be individualized based on patient response.[3,4,15,27]

For cellulitis caused by gram-negative bacilli or a mixture of microorganisms, immediate antimicrobial therapy, as determined by Gram stain, is essential. Surgical debridement of necrotic tissue and drainage may also be appropriate. Gram-negative cellulitis may be treated appropriately with an aminoglycoside (ie, gentamicin or tobramycin), or a first- or second-generation cephalosporin (eg, cephalexin, cefaclor, or cefuroxime). Ceftriaxone, ceftazidime, and fluoroquinolones are also effective in the treatment of cellulitis caused by both gram-negative and gram-positive bacteria.[3,4,8,15] If gram-positive aerobic bacteria are also present on Gram stain, an additional agent such as penicillin G or a penicillinase-resistant penicillin may need to be added to provide coverage against streptococci or staphylococci, respectively, as appropriate.[3,4,27] Addition of an agent active against MRSA (eg, vancomycin) may need to be considered for severe, complicated infections in hospitalized patients.[3,4,6,8,27] Ceftaroline is potentially advantageous in this setting since it has activity against MRSA and streptococci as well as gram-negative aerobic bacteria.

Because some polymicrobic infections may involve anaerobic bacteria, antibiotic therapy may need to be broadened to include agents with good activity against these organisms. Many different treatment regimens are possible depending on the bacteriology of the lesion (Fig. 133-1). Orally administered antibiotics, as monotherapy or in combination regimens, may be appropriately used in the treatment of mild-to-moderate infections in outpatients. Monotherapy or combination regimens of IV antibiotics may be necessary for more severe infections in hospitalized patients. Therapy should be 5 to 7 days in duration, with longer durations potentially needed in patients who do not respond to therapy in that time.[8,3,4,15]

Because gram-negative and mixed aerobic–anaerobic cellulitis can progress quickly to serious tissue damage, therapeutic intervention should be immediate.[8,3,15] If treated early, a rapid response can be seen. Unfortunately, because these infections often occur in patients with compromised immune defenses, they may still progress, even with therapeutic intervention. If the infectious process is secondary to a systemic cause (eg, diabetes), the treatment course often is prolonged and may be associated with high morbidity and mortality.[3,4,8,23]

Infections in injection drug users are treated similar to those in other types of patients.[8,15] Blood cultures must be obtained in these cases because 25% to 35% of patients may be bacteremic.[8,15,22] Also, patients should be assessed for the presence of abscesses; incision, drainage, and culture of these lesions are of extreme importance.[15] Initial antimicrobial therapy while awaiting culture results of abscesses should include broad coverage for gram-negative and anaerobic organisms, in addition to MRSA and streptococci.[8,15,22]

Evaluation of Therapeutic Outcomes

If treated promptly with appropriate antibiotics, the majority of patients with cellulitis are cured rapidly. Culture and sensitivity results should be evaluated carefully for both the adequacy of culture material and the presence of resistant organisms. Additional high-quality samples for culture may be needed for microbiologic analysis. Failure to respond to therapy may also be indicative of an underlying local or systemic problem or a misdiagnosis.

NECROTIZING SOFT-TISSUE INFECTIONS

Necrotizing soft-tissue infections consist of a group of extremely severe infections, associated with high morbidity and mortality, that require early and aggressive surgical debridement in addition to appropriate antibiotics and intensive supportive care.[4-6,23,41-45] Different terms have been used to classify necrotizing infections based on factors such as predisposing conditions, onset of symptoms, pain, skin appearance, etiologic agent, gas production, muscle involvement, and systemic toxicity.[3,4,23,42] However, while many types of necrotizing soft-tissue infections have been designated as unique infectious processes, they all share similar pathophysiologies, clinical features, and treatment approaches.[41-45] The major clinical entities of necrotizing infections are *necrotizing fasciitis* and *clostridial myonecrosis* (gas gangrene).[4,23,41-45]

6 Necrotizing fasciitis is a rare but severe infection of the subcutaneous tissue that may be caused by aerobic and/or anaerobic bacteria and results in progressive destruction of the superficial fascia and subcutaneous fat.[4,23,41-45] Type I necrotizing fasciitis is the most common and accounts for approximately 80% of necrotizing soft-tissue infections.[4,23,41-45] It generally occurs after trauma or surgery and involves a mixture of anaerobes (*Bacteroides*, *Peptostreptococcus*) and facultative bacteria (streptococci and Enterobacterales) that act synergistically to cause destruction of fat and fascia.[4,23,41,42] Type I necrotizing fasciitis is also reported more commonly among injection drug users.[41-44] In type I infections, the skin may be spared, and the speed at which the infection spreads (3-5 days) is somewhat slower than that in type II.[23,42] Necrotizing fasciitis affecting the male genitalia is termed *Fournier's gangrene*.[4,41,42] Type II necrotizing fasciitis is caused by virulent strains of *S. pyogenes* and is commonly referred to as *streptococcal gangrene*.[4,23,41-45] This type of infection has often been called "flesh-eating bacteria" by the lay press. Type II infections may occur in young, previously healthy individuals as well as older individuals with underlying diseases.[4,23,41-45] It differs from type I infections in its clinical presentation. Type II infections have rapidly extending necrosis (ie, 24-72 hours) of subcutaneous tissues and skin, gangrene, severe local pain, and systemic toxicity.[41-45] They are also highly associated with an early onset of shock and organ failure and are present in approximately half the cases of streptococcal toxic shock-like syndrome.[41-45] Of note, MRSA is increasingly reported in type II infections, either as a single organism or in combination with streptococci.[4,23,41-43]

Clostridial myonecrosis (type III necrotizing fasciitis) is a necrotizing infection that involves the skeletal muscle.[4,23,41-45] Type III infections account for less than 5% of necrotizing infections.[42] Gas production and muscle necrosis (myonecrosis) are prominent features of this infection, which readily explains why this infection is commonly referred to as *gas gangrene*.[4,23,41-43] The infection advances rapidly, often over a matter of a few hours.[41-45] Most infections occur after surgery or trauma, with *Clostridium perfringens* identified as the most common etiologic agent.[4,23,41-45]

CLINICAL PRESENTATION: Necrotizing Soft-Tissue Infections

General

- Most frequently involve the abdomen, perineum, and lower extremities.
- Predisposing factors such as diabetes mellitus, local trauma or infection, or recent surgery often present.
- Rapid diagnosis is critical due to the aggressive nature and high associated mortality (20%-50%).

Symptoms

- Systemic symptoms generally are marked (eg, fever, chills, and leukocytosis) and may include shock and organ failure, especially in patients with type II infections.
- Pain in the affected area and systemic toxicity are characteristically more pronounced than with cellulitis.

Signs

- May be difficult to differentiate between necrotizing fasciitis and cellulitis early in infection.
- Affected area is initially hot, swollen, and erythematous without sharply demarcated margins.
- Affected area is often shiny, exquisitely tender, and very painful.
- Diffuse swelling of the area is followed by the appearance of bullae filled with clear fluid.
- Rapidly progressive infection with the frequent development of a maroon or violaceous color of the skin after several days.
- Infection may rapidly evolve into a cutaneous gangrene, sometimes with myonecrosis.

Laboratory Tests

- Tissue samples should be obtained for histologic examination, and culture and susceptibility testing.
- Clostridial myonecrosis shows little inflammation on histologic examination.

Other Diagnostic Tests

- Surgical exploration is the best and most rapid means of diagnosing necrotizing infections; computed tomography and magnetic resonance imaging may also be helpful.
- Blood samples should be collected for complete blood cell count and chemistry profile, as well as for bacterial culture.
- Laboratory tests that may aid in the diagnosis of necrotizing infections (LRINEC score) include C-reactive protein, white blood cell count, hemoglobin, sodium, creatinine, and glucose.

Treatment: Necrotizing Soft-tissue Infections

Desired Outcomes

The goals of therapy of acute bacterial cellulitis are rapid eradication of the infection, prevention of further complications, and reduction in mortality. Effective treatment of necrotizing soft-tissue infections includes avoidance of unnecessary antimicrobials that contribute to increased resistance, and minimizing toxicities and cost of therapy.

Management of Necrotizing Infections

Immediate and aggressive surgical debridement of all necrotic tissues is essential in all patients with suspected or confirmed necrotizing fasciitis.[4,15,23,41-45] Initial surgical debridement performed greater than 14 hours after the diagnosis of necrotizing infection was independently associated with increased patient mortality, including a 34-fold increased risk of death in patients with septic shock.[41-45] Patients often require repeated surgical intervention following initial debridement to ensure that all necrotic tissue has been removed.[41-45] Type I necrotizing fasciitis must be empirically treated with broad-spectrum antibiotics that include coverage against streptococci, Enterobacterales, and anaerobes. Piperacillin–tazobactam plus vancomycin is specifically recommended as appropriate empiric therapy of necrotizing fasciitis, although a number of antibiotic regimens are also appropriate to successfully treat necrotizing soft-tissue infections (see Fig. 133-1).[4,15] These antibiotic regimens are generally similar to regimens used for polymicrobic cellulitis.[4,8,23,41-45] Antibiotic therapy can be modified after Gram stain and culture reports are available.

If a diagnosis of either type II (streptococcal) or type III (clostridial) necrotizing fasciitis is established, broad-spectrum empiric therapy should be replaced with the combination of penicillin plus clindamycin.[4,15,23,41-45] Although *S. pyogenes* remains susceptible to penicillin, the combination with clindamycin is more effective.[41,43] Several factors have been postulated to explain the greater efficacy of clindamycin, including a mechanism of action (inhibition of protein synthesis) that may cause decreased production of bacterial exotoxins.[4,23,41-45] In addition, clindamycin has immunomodulatory properties that may account for higher efficacy.[41-45] Clindamycin is also effective against some strains of MRSA.[4,23,42] Linezolid has also been suggested for necrotizing fasciitis due to mechanistic properties that are similar to those of clindamycin, but clinical data are fewer in comparison.[4,23,41,42] Hyperbaric oxygen is potentially beneficial for clostridial myonecrosis, but its use is not currently recommended due to lack of clear evidence of improved patient outcomes.[4,15,23,41-45] Likewise, the use of intravenous immunoglobulin (IVIG) has not yet been proven beneficial in the treatment of necrotizing streptococcal infections and its use is not routinely recommended.[4,15,23,41-45]

Evaluation of Therapeutic Outcomes

Because of the high mortality associated with necrotizing infections, rapid and complete debridement of all devitalized and necrotic tissue is essential. Surgical debridement, coupled with appropriate antimicrobial therapy and supportive measures for management of shock and organ failure, should stabilize the patient. Vital signs and laboratory tests should be monitored carefully for signs of resolution of the infection. Change in antimicrobial therapy or additional surgical debridement may be needed in patients who do not show signs of improvement.

DIABETIC FOOT INFECTIONS

Three major types of foot infections are seen in patients with diabetes: deep abscesses, cellulitis of the dorsum, and mal perforans ulcers.[46,47] Most deep abscesses involve the central plantar space (arch) and are caused by minor penetrating trauma or by an extension of infection of a nail or web space of the toes. Infections of the dorsal area generally arise from infections in the toes that are related to routine care of the nails, nail beds, and calluses of the toes. Mal perforans ulcer is a chronic ulcer of the sole of the foot. The ulcer develops on thickened, hardened calluses over the first or fifth metatarsal. Mal perforans ulcers are associated with neuropathic changes, which are responsible for the misalignment of the weight-bearing bones of the foot.[46,47] Osteomyelitis is one of the most serious complications of diabetic foot infection (DFI) and may occur in 30% to 40% of infections.[26,46,47]

Epidemiology

DFI is among the most common complications of diabetes, accounting for as many as 20% of all hospitalizations in patients with diabetes at an annual cost of $200 to $350 million.[26,46,48] Approximately 25% of patients with diabetes develop a foot ulcer during their lifetime; up to 60% of these ulcers involve significant soft-tissue infection and osteomyelitis is present in up to 40%.[26,46-48] Approximately 71,000 lower-extremity amputations, often sequelae of uncontrolled infection, are performed each year on patients with diabetes; this represents up to 80% of all nontraumatic amputations in the United States.[26,46,48] Approximately 40% of patients with diabetes will have recurrence of an ulcer within 12 months, and 20% of patients will undergo additional surgery or amputation of a second limb within 12 months of an initial amputation.[26,46-48]

Etiology

Mild cases of DFI are often monomicrobial. However, more severe infections are typically polymicrobic; up to 60% of hospitalized patients have polymicrobial infections (Table 133-7).[26,46,47,49,50-53] Wide ranges in the frequency of various bacteria in DFI reflect differences in culture techniques as well as variation among different types and severity of infections. Staphylococci and streptococci are the most common pathogens, although gram-negative bacilli and/or anaerobes occur in up to 50% of cases.[49-53] Although *P. aeruginosa* is an important pathogen in DFI, it is usually reported in less than 10% of wounds and is most commonly associated with more severe infections.[26,50] Obligate anaerobes are also more commonly associated with severe infections in patients with chronic foot ischemia.[26,49,50] MRSA is increasingly important in DFI and has been reported in 10% to 30% of infected wounds.[26,50,51,53-55] The presence of MRSA in DFI has been associated with increased risk of treatment failure and worse patient outcomes, but these findings have not been consistent among studies and the clinical relevance of MRSA in this setting is still unclear.[26,47,54]

TABLE 133-7

Bacterial Isolates from Foot Infections in Diabetic Patients

Organisms	Percentage of Isolates
Aerobes	63-100
Gram-positive	24-100
Staphylococcus aureus (all)	10-80
S. aureus (MRSA)	1-37
Streptococcus spp.	3-37
Enterococcus spp.	2-25
Coagulase-negative staphylococci	6-10
Other gram-positive aerobes	0-19
Gram-negative	16-73
Proteus spp.	3-7
Enterobacter spp.	1-9
Escherichia coli	3-10
Klebsiella spp.	1-6
Pseudomonas aeruginosa	1-48
Other gram-negative bacilli	3-13
Anaerobes	1-40
Peptostreptococcus spp.	4-28
Bacteroides fragilis group	2-9
Other *Bacteroides* spp.	3-6
Clostridium spp.	0-2
Other anaerobes	7-19

Data from References 26,46,47,49,50-54,56.

Identifying causative pathogens from cultures of DFI is often difficult. The chronic nature of DFI means that these wounds are often heavily colonized by organisms not playing a role in the infection. Superficial swab cultures are not as reliable as culture specimens obtained from deep tissues or bone

via biopsy, tissue scraping (curettage), or needle aspiration of drainage or abscess fluid.[22,47,51,53] Therefore, cultures and sensitivity tests should be done with specimens obtained from a deep culture of the wound base whenever possible. Before the wound is cultured, it should be scrubbed vigorously with saline-moistened sterile gauze to remove any overlying necrotic debris and further debrided as necessary.[22,26,51] Bone cultures should also be performed when there is diagnostic uncertainty regarding the presence of osteomyelitis or when therapeutic decisions are dependent on knowing the exact etiology of infection.[22,26,47,51,53]

Pathophysiology

Three key factors are involved in the development of diabetic foot ulcers: neuropathy, angiopathy and ischemia, and immunologic defects. Any of these disorders can occur in isolation; however, they frequently occur together.[48]

Neuropathic changes to the autonomic nervous system as a consequence of diabetes may affect the motor nerve supply of small intrinsic muscles of the foot, resulting in muscular imbalance, abnormal stresses on tissues and bone, and repetitive injuries.[46,48] Diminished sensory perception causes an absence of pain and unawareness of minor injuries and ulceration. The sympathetic nerve supply may be damaged, resulting in the absence of sweating that may lead to dry cracked skin and secondary infection.[26,46,48]

Atherosclerosis is more common, appears at a younger age, and progresses more rapidly in the persons with diabetes compared with those without. Individuals with diabetes may have problems with both small vessels (microangiopathy) and large vessels (macroangiopathy) that can result in varying degrees of ischemia, ultimately leading to skin breakdown and infection. Peripheral artery disease is present in up to 50% of persons with diabetes and is strongly associated with impaired wound healing.[49]

Persons with diabetes typically have normal humoral immunity, normal levels of immunoglobulins, and normal antibody responses. Patients with diabetes, however, have impaired phagocytosis and intracellular microbicidal function as compared with nondiabetics; this may be related to angiopathy and low tissue levels of oxygen.[26,46,48] These defects in cell-mediated immunity make patients with diabetes more susceptible to certain types of infection and impair the patients' ability to heal wounds adequately.[46-48]

CLINICAL PRESENTATION: Diabetic Foot Infections

General

- Infections are much more extensive than they initially appear.

Symptoms

- Patients with peripheral neuropathy often do not experience pain; simple complaints of swelling or edema are common.

Signs

- Clinical signs of infection may not be present secondary to angiopathy and neuropathy.
- Lesions vary in size and clinical features (eg, erythema, edema, warmth, presence of pus, draining sinuses, pain, and tenderness).
- Foul-smelling odor suggests the presence of anaerobic organisms.
- Temperature may be mildly elevated or normal.

Laboratory Tests

- Specimens for culture and sensitivities should be collected.
- Deep-tissue samples obtained during surgical debridement are most useful for culture and susceptibility testing.
- Wounds must be cultured for both aerobic and anaerobic organisms.

Other Diagnostic Tests

- Possible presence of osteomyelitis must also be assessed via radiograph, bone scan, or both, as appropriate.

Treatment: Diabetic Foot Infections

Desired Outcomes

7 The goals of therapy in the management of DFI include the following: (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.

Management

Up to 90% of infections can be treated successfully with a comprehensive treatment approach that includes both wound care and antimicrobial therapy.[26,47,51] 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. Wounds must be kept clean and dressings changed frequently (two to three times daily). Because of the relationship between hyperglycemia and immune system defects, glycemic control must be maximized to ensure optimal wound healing. In addition, the patient's activities should be restricted initially to bed rest for leg elevation and control of edema, if present. Adequate pressure relief from a foot wound (ie, off-loading) is crucial to the healing process.[26,48,51] Finally, appropriate antimicrobials must be initiated.[26,47,48,51] However, the optimal antimicrobial therapy for DFI has yet to be defined. Broad-spectrum empiric therapy that provides coverage of all possible pathogens is not recommended unless the infection is life- or limb-threatening, assuming that adequate wound care is also being performed.[46-49,51,54] This is particularly true regarding MRSA, *P. aeruginosa*, and anaerobes; the perceived need for empiric coverage of these organisms often leads to use of excessively broad-spectrum drug regimens. Several studies have shown good antimicrobial treatment efficacy despite the fact that the regimens did

not have consistently good activity against these particular organisms and no specific regimen has shown clear superiority over another.[46-52,54-56]

Proper selection of empiric antibiotics for DFI begins with thorough patient assessment and classification of the severity of the infection. Specific drug regimens, route of administration, and duration of therapy are all then largely dependent on the severity of infection. Although a number of classification systems are available, the most recent DFI treatment guidelines use those summarized in Table 133-8.[26,46,51] Wounds with no local signs of infection often do not require antibiotic therapy, and the majority of mild, uncomplicated infections can be managed successfully on an outpatient basis with highly bioavailable oral antimicrobials and good wound care (Tables 133-8 and 133-9).[46-49,53] Antibiotics for treatment of mild infections should be largely limited to those with activity against skin flora such as streptococci and methicillin-susceptible *S. aureus* (MSSA), except in those patients with risk factors for infection with other types of pathogens (Fig. 133-2).[46-48,51] Patients with specific risk factors for MRSA (Table 133-9) should empirically receive trimethoprim–sulfamethoxazole or doxycycline orally, while those who have received antibiotics within the past month should also receive empiric antibiotics that provide activity against gram-negative bacilli. Oral antimicrobials should be used cautiously in DFI complicated by osteomyelitis, extensive ulceration, areas of necrosis, or a combination of these. The use of topical antimicrobials, including medical-grade honey, has been advocated for the treatment of DFI in an attempt to minimize the cost of therapy and systemic antibiotic exposure leading to adverse effects and resistance. Although the most recent guidelines allow for consideration of topical therapy in mild infection in selected patients, use of topical agents is quite controversial, inconsistent in proven benefits, and not routinely recommended.[26,47,51,57]

FIGURE 133-2

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.) [a]May substitute metronidazole in place of cylindamycin.

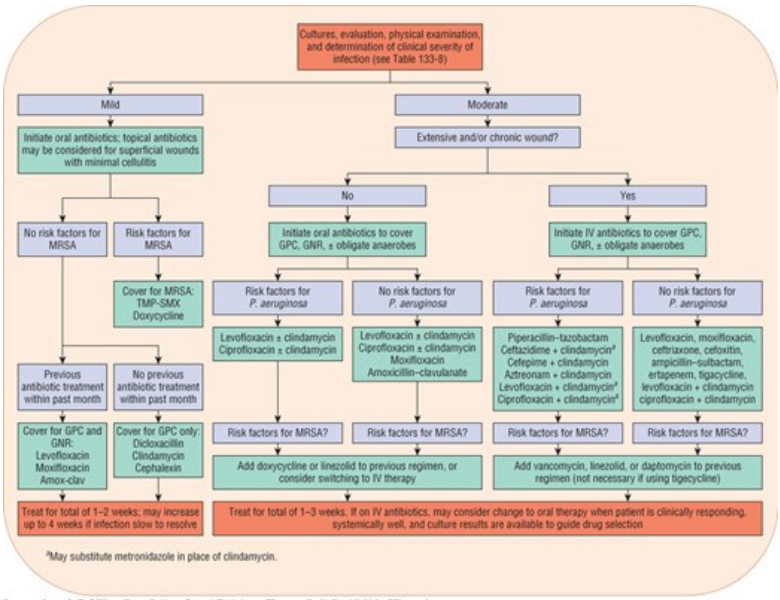


TABLE 133-8

Classifications and Treatment Strategies for Diabetic Foot Infections of Varying Severity

Clinical Signs/Symptoms of Infection	Infection Severity	Treatment Setting
None	Uninfected	Outpatient management; nonantibiotic wound management only
Local infection present (≥2 of the following): local swelling or induration, erythema, local tenderness or pain, local warmth, purulent discharge		Outpatient or inpatient management according to severity (mild, moderate, or severe) as assessed by additional criteria
Local infection involving only skin and subcutaneous tissue, without involvement of deeper tissues or SIRS criteria present; if erythema is present, must be >0.5 and ≤2 cm around ulcer	Mild	Outpatient management; topical or oral antibiotics
Local infection with erythema >2 cm around ulcer, or involving structures deeper than skin and subcutaneous tissue (eg, abscess, osteomyelitis, septic arthritis, fasciitis); no SIRS criteria present	Moderate	Outpatient (or initial inpatient) management; oral (or initial parenteral) antibiotics
Local infection with ≥2 SIRS criteria: • Temperature >38°C (100.4°F) or <36°C (96.8°F) • HR >90 • RR >20 • WBC >12,000/mm^3 (12×10^9/L) or <4,000/mm^3 (4×10^9/L), or >10% (0.10) bands	Severe	Inpatient, followed by outpatient, management; initial parenteral antibiotics, followed by switch to oral when possible

Data from Reference 26.

TABLE 133-9

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)	Amoxicillin–clavulanate	1-2 weeks; may increase up to 4 weeks if infection is slow to resolve
	Streptococcus spp.	Cephalexin	
	S. aureus (MRSA) • Patients with history of MRSA infection or colonization in past year • Prevalence of MRSA ≥50% in local geographic area • Recent hospitalization	• Dicloxacillin • Clindamycin • Levofloxacin • Moxifloxacin[b]	
Moderate-to-severe (initially oral or IV antibiotics for moderately severe infections,	• MSSA • *Streptococcus* spp.	• Ampicillin–Sulbactam • Cefoxitin	Moderately severe infection: 1-3 weeks;

IV antibiotics for severe infections)	• Enterobacterales • Obligate anaerobes	• Ceftriaxone • Imipenem/cilastatin • Ertapenem • Levofloxacin • Moxifloxacin • Tigecycline • Levofloxacin or ciprofloxacin + clindamycin	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.*

Data from Reference 26.

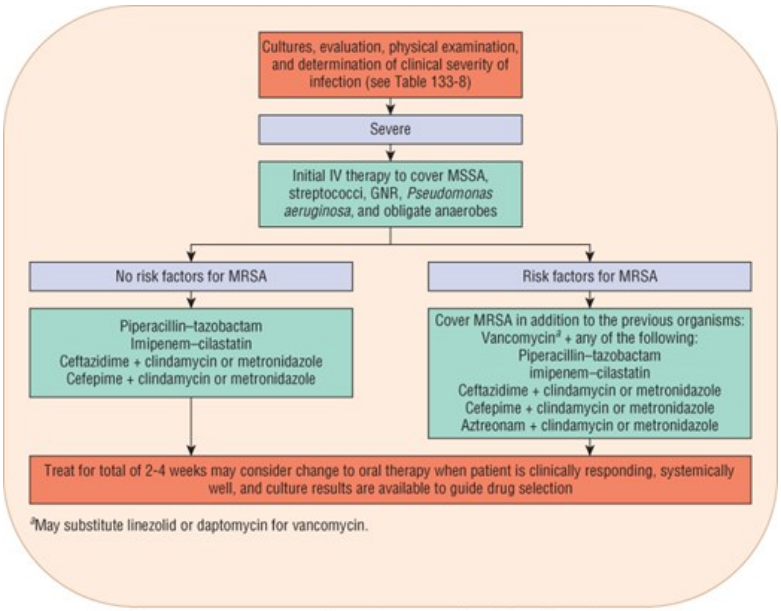
Appropriate initial therapy for patients with moderate-to-severe infection is also dependent on the presence of specific risk factors that increase the

likelihood of infection with more resistant pathogens such as *P. aeruginosa* and MRSA (Table 133-9).[26,46,48,51] Many moderate infections can be successfully treated with orally administered antibiotics that provide activity against MSSA, streptococci, and gram-negative aerobic bacilli; coverage of obligate anaerobes may also be considered in patients with chronic or previously treated wounds (Fig. 133-3).[26,46,48,51] The addition of orally administered agents with activity against MRSA is recommended in patients with moderate or severe infection and specific risk factors for MRSA; such patients may also be considered for hospitalization and initial treatment with parenteral antibiotics in order to ensure adequate antibiotics for potentially more complex infections.[26,46,48,50,51] Patients with more extensive or chronically unhealed wounds, even though assessed as moderate in severity, may also be more appropriately treated initially with parenteral antibiotics in the hospital setting.[47-52]

FIGURE 133-3

Recommended treatment algorithm for initial empiric management of severe diabetic foot infections. (GNR, aerobic gram-negative rods; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S. aureus*.)

[a]May substitute linezolid or daptomycin for vancomycin.



All patients with severe DFI should be hospitalized initially and treated with broad-spectrum IV antibiotics (Table 133-9 and Fig. 133-3).[46-52] Severe infection is considered a risk factor for *P. aeruginosa*, so most patients with severe DFI will be initially started on antipseudomonal antibiotics.[48-51] Many patients will also be initially started on antibiotics that provide activity against MRSA due to risk-versus-benefit considerations, but assessment of risk factors in individual patients is important in order to minimize the use of excessively broad-spectrum antibiotics when possible.

Guidelines for management of DFI include options for both monotherapy and combination regimens (Table 133-9).[26] Monotherapy, along with appropriate medical or surgical management, or both, is often effective in treating DFI, including those in which osteomyelitis is present.[46-52,56] Monotherapy is particularly attractive because of the potential advantages of convenience, cost, and avoidance of toxicities. Microbiologic and clinical cure rates ranging from 60% to 90% may be expected from any of these agents.[46-52,56] Selection of a specific regimen is determined by patient-specific factors including allergies, renal function, history of previous antibiotic use, and cost. In penicillin-allergic patients, metronidazole or clindamycin plus a fluoroquinolone, aztreonam, or possibly a third- or fourth-generation cephalosporin is appropriate.[46-52,56] Vancomycin is also used frequently in severe infections because of its good activity against gram-positive pathogens, with linezolid, daptomycin, and tigecycline specifically recommended as alternatives to vancomycin.[46-52] Tigecycline may be particularly useful in this setting because of its activity against gram-negative aerobes and anaerobic bacteria, thus allowing it to be used as monotherapy for the treatment of mixed infections in patients where coverage of *P. aeruginosa* is not of great concern. Ceftaroline fosamil also has in vitro activity suitable for DFI but has not been studied for this indication. Because many patients

already have some degree of diabetic nephropathy that may place them at higher risk of nephrotoxicity, strong recommendations have been made against the use of aminoglycoside antibiotics unless no alternative agents are available.[26,47] When an aminoglycoside is used, care must be taken to avoid further compromising renal function. All antibiotic regimens should be adjusted as necessary for renal dysfunction. There is no defined role for newer broad-spectrum agents such ceftolozane–tazobactam, ceftazidime–avibactam, meropenem–vaborbactam, eravacycline, and delafloxacin; their use in DFI is not recommended.

Duration of therapy for DFI depends on the severity of the infection, ranging from 1 to 2 weeks for mild infections up to 2 to 4 weeks or more for severe infections.[46-52] In the cases of underlying osteomyelitis, treatment should continue for 6 to 12 weeks.[46-52] After healing of the infection has occurred, a well-designed program for the prevention of further infections should be instituted. The use of adjunctive agents such as colony-stimulating factors, growth factors, and hyperbaric oxygen for either prevention or treatment of DFIs is controversial and not widely recommended.[26]

Evaluation of Therapeutic Outcomes

Therapy should be reevaluated carefully after 48 to 72 hours to assess favorable response. Change in therapy (or route of administration, if oral) should be considered if clinical improvement is not observed at this time. For optimal results, drug therapy should be appropriately modified according to information from deep-tissue culture and the clinical condition of the patient. Infections in patients with diabetes often require extended courses of therapy because of impaired host immunity and poor wound healing.

PRESSURE INJURIES

The terms *decubitus ulcer*, *bed sore*, *pressure sore*, and *pressure injury* are often used interchangeably, althought pressure injury is now the preferred term.[29,58-60] The decubitus ulcer and the bed sore are types of pressure injuries. The term *decubitus ulcer* is derived from the Latin word *decumbere*, meaning “lying down.” Pressure injuruie, however, can develop regardless of a patient’s position.

Numerous systems for classification of pressure injuries have been described. The 2016 recommendations of the National Pressure Ulcer Advisory Panel (NPUAP) are shown in Table 133-10. The NPUAP classification system is most commonly used and illustrates various stages of progression through which a pressure injury may pass.[60]

TABLE 133-10

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.

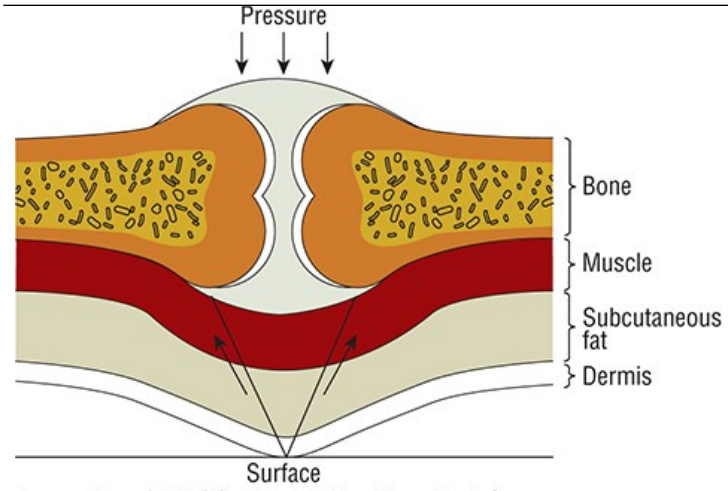
[a]Stage 3, stage 4, and unstageable lesions are unlikely to resolve on their own and often require surgical intervention.

Data from Reference 60.

Complications of pressure injuries are common and may be life-threatening. Infection is one of the most serious and most frequently encountered complications of pressure injuries.[58,59] Although most pressure injury wounds are heavily colonized, the majority of these eventually heal.[58,59,61] When true infection is present, however, there is bacterial invasion of previously healthy tissue. Without treatment, an initial small, localized area of ulceration can rapidly progress to large ulcers within days. The visible ulcer is just a small portion of the actual wound[29]; up to 70% of the total wound is below the skin. A pressure-gradient phenomenon is created by which the wound takes on a conical nature; the smallest point is at the skin surface, and the largest portion of the defect is at the base of the ulcer (Fig. 133-4).

FIGURE 133-4

Distribution of forces involved with sore formation in a conical fashion.



Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*

Epidemiology

Pressure injuries are most common among chronically debilitated persons, older adults (70% involve persons older than 70 years), and persons with serious spinal cord injury.[29,58,59] Generally, patients who are at risk for pressure injuries are older adults or chronically ill young patients who are immobilized, in either bed or a wheelchair, and who may have altered mental status and/or incontinence.[58,59]

Etiology

Similar to DFIs, a large variety of aerobic gram-positive and gram-negative organisms, as well as anaerobes, frequently are isolated from wound cultures.[24,62] Most pressure injury–related ulcers are heavily colonized with microorganisms, making assessment for infection a clinical challenge.[24,62] Curettage of the ulcer base after debridement provides more reliable culture information than does needle aspiration.[61,62] Biopsy specimens give the most reliable data but may not be practical to obtain. Deep-tissue cultures from different sites may give different results. Cultures collected from pressure ulcers reveal polymicrobial growth. A culture collected by swab is likely to identify surface bacteria colonizing the wound rather than to diagnose the infection.[29,62]

Pathophysiology

Many factors apparently predispose patients to the formation of pressure injuries: 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[29,58,59]; however, there is still a debate as to the exact pathophysiology of pressure injury development.[58,59]

Pressure is the essential element in the formation of pressure injuries.[24,58,59] The areas of highest pressure are generated most often over the bony prominences.[24,58,59] Both the degree of pressure and the length of time that the pressure is applied are important.[58,59]

Shearing occurs when two surfaces move in opposite directions.[24,58,59] This situation can occur when the head of a bed is raised, causing the upper torso to slide downward, transmitting pressure to the sacrum and other areas. This effect results in occlusion or distortion of vessels, leading to compromise of the dermis. At the same time, sitting and gravity create shearing forces; the posterior sacral skin area can become fixed secondary to friction with the bed. The effects of friction and shearing forces combine, resulting in transmission of force to the deep portion of the superficial fascia and leading to further damage of soft-tissue structures.[24,58,59]

Compounding the problems of shearing and friction forces are the macerating effects of excessive moisture in the local environment, resulting from incontinence and perspiration. This factor is of critical importance because when combined with the other forces, it increases the risk of pressure sore

formation fivefold.[29,58,59]

CLINICAL PRESENTATION: Pressure Injuries

General

- Most pressure injuries are in the pelvic region and lower extremities; see Fig. 133-5.
- Most common sites: sacral and coccygeal areas, ischial tuberosities, and greater trochanter.

Symptoms

- Patients commonly have other medical problems that may mask signs and symptoms of infection.
- Pain may be present with or without infection; continuous pain may indicate infection.

Signs

- A dark red color on the surface of a pressure injury–related ulcer may indicate local infection.
- Surrounding erythema, swelling, and heat are commonly present with infection.
- Purulent discharge, foul odor, and systemic signs (eg, fever and leukocytosis) of infection may be present.

Laboratory Tests

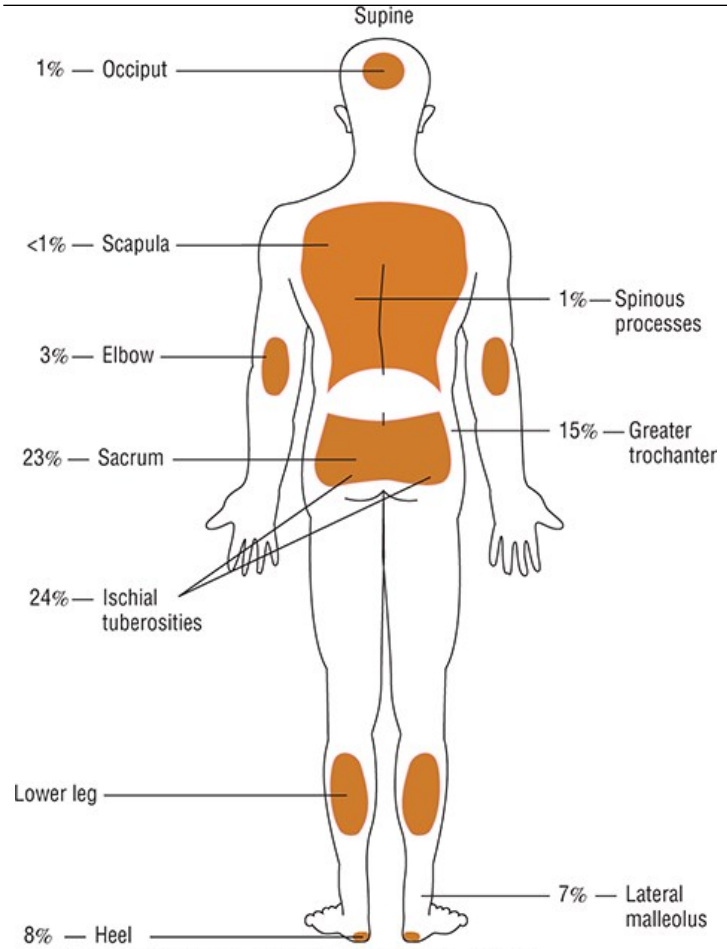
- Cultures should be collected from either a biopsy or fluid obtained by needle aspiration.

Other Diagnostic Tests

- Complete blood cell count often performed for assessment of potential infection.
- Consider magnetic resonance imaging if suspicious of underlying osteomyelitis.

Figure 133-5

Supine view of areas where pressure sore injuries tend to occur.



Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*

Treatment: Pressure Sores

Desired Outcomes

The primary goal for pressure injuries is prevention. Once pressure injury has developed, the goals of therapy are prevention of complications (ie, infections), preventing injuries from growing larger, and preventing the development of injuries in other locations.[58,59] Eradication of infection should include good wound care and topical therapies, and avoidance of broad-spectrum antimicrobials unless guided by results from appropriately collected cultures or in patients with bacteremia, sepsis, cellulitis, or osteomyelitis.

Drug and Nondrug Management

Prevention is the single most important aspect in the management of pressure injuries. Skin surveillance and frequent repositioning (ie, pressure reduction) are key in preventing pressure injuries.[29,58,59] Prevention is far easier and less costly than the intensive care necessary for the healing and eventual closure of pressure injuries. Of primary importance, then, is the ability to identify patients who are at high risk so that preventive measures may be instituted. Relief of pressure through proper positioning, and periodic repositioning, is probably the single most important factor in preventing pressure injury formation. Relief for a period of only 5 minutes once every 2 hours gives protection against pressure injury formation.[29,58,59,61] Repositioning seated patients every 15 to 60 minutes is also recommended.[29,58,59] Pressure relief devices such as mattresses or overlays filled with air, water, gel, or foam are helpful in preventing pressure injuries.[29] Cushions and ankle or heel protectors should also be encouraged.[29,59] Skin care and prevention of soilage are also important, with the intent being to keep the surface relatively free of moisture. Patients with problems of incontinence

should be cleaned frequently, and efforts should be made to keep the involved areas dry.[29,58,59]

The medical approach to the treatment of pressure injuries depends on the stage of the disease. Medical management is indicated for lesions that are of moderate size and relatively shallow depth (stage 1 or 2 lesions) and are not located over a bony prominence. Depending on their location and severity, from 30% to 80% of these injuries will heal without an operation. Surgical intervention is almost always necessary for ulcers that extend through superficial layers or into bone (stage 3, stage 4, and unstageable lesions).[24,56]

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 prepare the wound for an operative procedure. The main factors to be considered for successful topical therapy (local care) are (a) relief of pressure, (b) debridement of necrotic tissue as needed, (c) wound cleansing, (d) dressing selection, and (e) prevention, diagnosis, and treatment of infection.[29,58,59,61]

Relief of pressure is important once pressure injury has developed. The same repositioning methods and pressure-reducing devices used for preventive care also apply to treatment.[29,58,59,61]

The goals of debridement and cleansing measures are removal of devitalized tissue and reduction of bacterial contamination, which can slow granulation time and impede healing.[29,58,59,61] Debridement can be accomplished by surgical, mechanical, or chemical means.[24,58,59,61] Surgical debridement rapidly removes necrotic material from the wound and is recommended for urgent situations (eg, cellulitis and sepsis).[29,58,59,61] Mechanical debridement involves wet-to-dry dressing changes in which saline-soaked gauze is applied to the wound; after drying, the gauze is removed and with it any adherent necrotic tissue. Other effective mechanical therapies include hydrotherapy (use of the whirlpool [Hubbard tank] to remove necrotic tissue and debris), wound irrigation, and dextranomers (beads placed in the wound to absorb exudate and bacteria).[24,58,59] Chemical debridement includes enzymatic and autolytic agents. Enzymatic debridement involves application of topical debriding agents to remove devitalized tissue. This method is recommended for patients who cannot tolerate surgery or are in a long-term care or home setting.[29,58,59,61] Autolytic debridement involves the use of synthetic dressings that allow devitalized tissue to self-digest via enzymes present in wound fluids. Autolytic debridement is contraindicated in the treatment of infected pressure injuries.[29,58,59,61]

Pressure injury wounds should be cleaned with normal saline.[24,29,59,61] No cleansing solution or technique has demonstrated greater efficacy on healing.[63] Cleansing agents that are cytotoxic, such as povidone–iodine, iodophor, sodium hypochlorite solution, hydrogen peroxide, and acetic acid, should be avoided.[29,58,59,61] Many of these agents destroy granulation tissue and impair healing. Many different types of dressings are available for pressure injuries.[24] Wound dressing materials should keep the wound moist, allow free exchange of air, act as a physical barrier to bacteria, and prevent physical damage.[24,29,59] Controlled studies of the various types of wound dressings have shown no significant differences in healing outcomes.[58,63] Occlusive dressings (hydrocolloid, such as DuoDERM™ or Tegaderm™) and transparent dressings (eg, 3M Tegaderm™) are not recommended for infected wounds.[24,29,59] If occlusive dressings are used, any infection should be controlled or the dressing frequency increased.

Topical antibiotics (silver sulfadiazine, triple antibiotic) or medical grade honey may be considered for a clean ulcer that is not healing or is producing a moderate amount of exudate despite appropriate care.[29,58,59] When used, topical antibiotics should be limited to a 2-week trial or until additional definitive debridement can be performed, whichever comes first.[29,58,59] Systemic treatment of pressure-related ulcers is generally reserved for infections associated with bacteremia, sepsis, cellulitis, fasciitis, or osteomyelitis.[29,58,61] Empiric therapy for infected pressure sores or associated infectious complications should cover MRSA, anaerobes, enterococci, and more resistant gram-negative bacteria such as *Pseudomonas* (see Table 133-5).[58,59] Thereafter, antibiotics should be guided by results from appropriately collected cultures.

Other nonpharmacologic approaches to shorten the healing time have included the use of hyperbaric oxygenation, hydrotherapy, high-frequency/high-intensity sound waves, and electrotherapy.[29,61] Electrical stimulation is the only adjunctive therapy that is proven effective.[29,61] Various comorbid conditions (diabetes mellitus, smoking, peripheral vascular disease, malnutrition) may impair wound healing. Eliminating or optimizing these factors is recommended, although studies have not demonstrated benefit.[24,59]

Evaluation of Therapeutic Outcomes

With appropriate wound care and antimicrobial therapy, infected pressure injuries can heal. A reduction in erythema, warmth, pain, and other signs and symptoms should be seen in 48 to 72 hours.

ANIMAL AND HUMAN BITE WOUNDS

Approximately half the population in the United States will be bitten by either an animal or another human sometime during their lifetimes.[64-66] Animal bites (typically from dogs or cats) are common causes of injury, particularly to children, and are associated with significant risk of infection without prompt attention and appropriate management. Likewise, human bite wounds are often deceptively severe and frequently require aggressive management to reduce the risk of infectious complications. If left untreated, severe soft-tissue infection and osteomyelitis may occur, possibly requiring extensive debridement or amputation.

Epidemiology

Dog bites account for approximately 75% to 90% of all animal bite wounds requiring medical attention.[65] The Centers for Disease Control and Prevention reports that approximately 330,000 individuals seek emergency room attention for dog bites annually; rates of dog bite–related injuries are highest in children aged 5 to 9 years.[66] Most dog bites are to the extremities,[65] but the majority of bites to children less than 5 years of age are to the face and neck.[66] Cat bites are the second most common cause of bite wounds in the United States, accounting for up to 20% of all animal bites.[64] Cat bites occur most commonly on the upper extremities and face, with most injuries reported in women and older adults.[64,67] Human bites are the third most frequent type of bites requiring medical attention.

Infection rates after dog and cat bites are estimated at 20% overall. However, infection may occur in up to 30% to 80% of serious cat bites, a rate more than double that seen with dog bites.[64,67] Also, bite wounds to the hands become infected in 30% to 40% of cases.[64] Patients at greatest risk of acquiring animal bite–related infection have had a puncture wound (usually to the hand), have not sought medical attention within 8 hours of the injury, and are older than 50 years of age.[64,65,67]

Infected human bites can occur as bites from the teeth or from blows to the mouth (clenched-fist injuries). Bites by others can occur to any part of the body, but most often involve the hands. Infectious complications occur in 10% to 50% of patients with human bites.[67]

Etiology

Infections in bite wounds are caused predominantly by mouth flora from the animal or human biter, and from the victim's own skin flora (Table 133-11).[64,65,67-71] Most infections are polymicrobial, with a median of three to nine bacterial isolates per culture.[67-71] *Pasteurella* is the most frequent isolate from both dog and cat bites. *Pasteurella multocida* is part of the normal oral flora of up to 90% of cats; dog bites more commonly involve *P. canis* (approximately 26% of infections).[64,65,67,69] Tularemia (*Pasteurella tularensis*) and cat scratch disease (*Bartonella henselae*) have also been transmitted by cat bites, while rabies is associated with dog bites, particularly in developing countries.[64,65,69,70,72] Human bite wounds are notable for potential involvement of *Eikenella corrodens* in approximately 30% of infections.

TABLE 133-11

Bacterial Isolates from Infections in Animal and Human Bite Wounds

Organisms	Percentage of Isolates	
	Dog and Cat	Human
Aerobes	74-90	44
Pasteurella spp.	50-75	—
Streptococcus spp.	46-50	52-84

S. anginosus	—	52
S. mitis	22	12
S. pyogenes	12	14
S. mutans	12	2
Staphylococcus spp.	35-46	54
S. aureus	20	30
S. epidermidis	18	22
Neisseria spp.	32-35	4
Moraxella spp.	10-35	2
Corynebacterium spp.	12-28	12
Enterococcus spp.	10-12	6
Bacillus spp.	8-11	—
Eikenella corrodens	2	30
Enterobacteriaceae	6-12	8-15
Anaerobes	50-70	40-90
Fusobacterium spp.	32-33	32-34
Porphyromonas spp.	28-30	2
Bacteroides spp.	18-28	4
Prevotella spp.	19-28	22-36
Propionibacterium spp.	18-20	4
Peptostreptococcus spp.	8-16	22
Veillonella spp.	2	24
Mixed aerobic and anaerobic	50-75	40-66

Data from References 67-70.

Pathophysiology

Animal bites have great potential for infection owing to the pressure that can be exerted during the bite and the vast number of potential pathogens that make up the normal oral flora.[64,65,67-70] Cats' teeth are slender and extremely sharp. Their teeth easily penetrate into bones and joints, resulting in a higher incidence of septic arthritis and osteomyelitis.[67-70] Although a dog's teeth may not be as sharp, they can exert a pressure of 200 to 450 lb/in.^{2} (~1,400-3,100 kPa) and therefore result in a serious crush injury with much devitalized tissue.[64,65,67-70] In addition, the polymicrobic (aerobic and anaerobic) nature of animal bites provides a synergistic relationship, thus making an infection harder to eradicate.[68]

Human bites are more serious and more prone to infection than animal bites, particularly clenched-fist injuries.[68] While the force of a punch may break a bone or sever a tendon or nerve, it most often causes a breach in the capsule of the metacarpophalangeal joint, leading to direct inoculation of bacteria into the joint or bone.[68,70] When the hand is relaxed, the tendons carry bacteria into deeper spaces of the hand, resulting in more extensive infection.[68,70]

CLINICAL PRESENTATION: Bite Wounds

General

Animal bites:

- Only general wound care is required for most patients with dog bites who present early (<12 hours) after injury; infection is more likely in patients presenting late (≥12 hours) after injury.

Human bites:

- Most patients with clenched-fist injuries present for medical care after infection is already established.

Symptoms

- Patients often seek medical care for infection-related complaints (ie, pain, purulent discharge, swelling) at the site of the injury.
- Wounds often have a purulent discharge, and decreased range of motion may be present.

Signs

- Erythema, swelling, and clear or purulent discharge at site of infected wound.

Animal bites:

- If *P. multocida* is present, a rapidly progressing cellulitis is observed within 24 to 48 hours of initial injury.
- Fever is often absent.
- Adenopathy or lymphangitis is uncommon.

Human bites:

- Lymphadenopathy is common.
- In clenched-fist injuries, edema may limit the ability of tendons to glide in their sheaths, thereby limiting a joint's range of motion.

Laboratory Tests

- Samples for bacterial cultures (aerobic and anaerobic) should be obtained from infected wounds.
- Wounds seen <8 hours or more than 24 hours after injury that show no signs of infection may not need to be cultured.
- White blood cell counts should be monitored for resolution of infection if initially elevated.

Other Diagnostic Tests

- Radiographic evaluation should be performed if damage to a bone or joint is suspected.

Treatment: Bite Wounds

Desired Outcomes

The goals of therapy of bite wounds, whether caused by animals or humans, are twofold: to provide effective prophylaxis against infection, when appropriate, and to achieve rapid eradication of established infection and prevent further complications. Effective treatment of bite wounds includes avoidance of unnecessary antimicrobials that contribute to increased resistance, and minimizing toxicities and cost of therapy.

Management of Bite Wounds

9 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.[64,65,67,70] Surgical debridement and immobilization of the affected area are often required in dog and human bites associated with more extensive tissue injury. Clinical failures due to edema have occurred despite appropriate antibiotic therapy.[64] Therefore, it is important to stress to patients that the affected area should be elevated for several days or until edema has resolved. In the case of animal bites, an immunization history of the animal should be obtained. It is also important for the patient's tetanus immune status to be determined. Because transmission of viruses (HIV, herpes, hepatitis B and C) is a possibility with human bites, information about the biter is important. Although the possibility of acquiring HIV through saliva alone is believed to be unlikely, the presence of virus-containing blood in the saliva makes disease transmission possible.[73] Bite victims exposed to blood-tainted saliva may be offered antiretroviral chemoprophylaxis, but each case should be individually assessed based on the potential for significant exposure and potential risks and benefits of antiretroviral therapy.[73]

Patients with clenched-fist injuries should be seen by a specialist in hand care to evaluate for penetration into the synovium, joint capsule, and bone.[15,68] Primary closure for human bites generally is not recommended. Tetanus toxoid and antitoxin may be indicated.

10 All patients with human bite injuries should receive prophylactic antibiotic therapy ("early preemptive therapy") for 3 to 5 days due to high infection risk (Table 133-4).[70,71] Prophylactic antimicrobial agents should be given as soon as possible to all patients, regardless of the appearance of the wound, unless it can be documented that the wound does not involve hands, feet, or joints and penetrates no deeper than the epidermis.[15,70]

The role of prophylactic antimicrobial therapy for early, noninfected animal bite wounds remains controversial.[15,64,65,67,68,70] Recommendations from the IDSA suggest that prophylactic or early preemptive therapy seems to provide only marginal benefit for most patients in the absence of specific factors that increase the risk of infection.[15] The decision to administer prophylactic antibiotics is therefore based on an assessment of wound severity and host immune competence. Specifically, prophylaxis is more strongly 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; deep puncture wounds that cannot be adequately irrigated; or bite injuries that have penetrated the periosteum or joint capsule.[15,65] A 3- to 5-day course of prophylactic antibiotics is recommended when such therapy is considered to be appropriate.[15,65,67,68,70]

Empiric antibiotics for the treatment of established infection of bite wounds should be directed at a variety of aerobic and anaerobic flora (Table 133-4). Amoxicillin–clavulanic acid is most commonly recommended for oral outpatient therapy due to excellent activity against all likely pathogens, including *Pasteurella* and *Eikenella*.[15,64,65,67,68,70] Alternative oral agents include moxifloxacin or 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.[15,64,65,67,68,70] Although the combination of penicillin VK plus dicloxacillin has been recommended traditionally for the treatment of bite wounds, its use has become less common in favor of other alternatives. Failure to provide adequate initial treatment of bite wounds results in treatment failures and increased need for hospitalization for parenteral antibiotics.[15,64,65,67,68-70]

Hospitalization for minor wounds is unnecessary if surgical repair of vital structures is not needed. Patients with clenched-fist or other serious bite injuries and severe resultant infection may be considered for 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.[15,70] The combination of doxycycline or fluoroquinolone with metronidazole or clindamycin may be used in patients with severe β-lactam allergies. The length of antimicrobial therapy depends on the severity of the injury/infection. However, therapy should generally be continued for 7 to 14 days.[15,64,74]

Tetanus does not occur commonly after dog bites; however, it is possible. If the immunization history of a patient with anything other than a clean, minor wound is unknown, or if the last known vaccination was longer than 10 years ago, tetanus–diphtheria (TD) toxoids should be administered.[74] Both TD toxoids and tetanus immune globulin should be administered to patients who have never been immunized.[70,75]

Because the rabies virus can be transmitted via saliva, rabies may be a potential complication of a bite. When the symptoms of rabies develop after a bite, the prognosis for survival is poor. Roughly 3% of rabies cases documented in animals were in dogs (the most frequent vectors are skunks, raccoons, and bats).[72,76] In the United States, recommendations for postexposure prophylaxis after a dog bite depend on the health of the dog. If the animal is healthy and able to be observed for a 10-day period, active prophylaxis is only required if the dog develops signs of rabies.[67,72] If the dog is known or suspected to be rabid, postexposure procedures should be initiated; current treatment guidelines should be consulted for appropriate management recommendations.[72,76] Outside of the United States, locally applicable guidelines such as those from the World Health Organization should be consulted.[77]

Evaluation of Therapeutic Outcomes

Evaluation of treatment for either animal or human bites should follow the same general guidelines. Bite victims treated on an outpatient basis with oral antimicrobials should be followed up within 24 hours by either phone or office visit.[15] Hospitalization or change to IV therapy should be considered if the infection has progressed. For hospitalized patients with no improvement in signs and symptoms following 24 hours of appropriate therapy, surgical debridement may be needed. Physical therapy may be needed to improve complications such as residual joint stiffness and loss of function, particularly after human bites involving clenched-fist injuries.

ABBREVIATIONS

ABSSSI	acute bacterial skin and skin structure infection
AMS	altered mental status
CA-MRSA	community-associated methicillin-resistant *S. aureus*
DFI	diabetic foot infection
HA-MRSA	healthcare-associated methicillin-resistant *Staphylococcus aureus*
HIV	human immunodeficiency virus
IDSA	Infectious Diseases Society of America
MRSA	methicillin-resistant *Staphylococcus aureus*
MSSA	methicillin-susceptible *Staphylococcus aureus*
NPUAP	National Pressure Ulcer Advisory Panel
PVL	Panton-Valentine leukocidin
SCC*mec*	staphylococcal chromosomal cassette *mec*
SSTI	skin and soft-tissue infection
TD	tetanus–diphtheria

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SELF-ASSESSMENT QUESTIONS

1. A 26-year-old male presents to the outpatient clinic complaining of a sore area on his upper back. He said it started as just one sore that was red and tender. On physical examination, several discrete nodules are present that are fluctuant, painful, and surrounded by areas of erythema and edema 1 to 2 cm in diameter. The man states that he is allergic to penicillin, although he does not know the type of reaction that he had previously. His temperature is 101.3°F (38.5°C); other vital signs are within normal limits. His white blood cell count is elevated at 14,300 cells/μL (14.3×10^9/L). The most appropriate initial therapy for this patient would be:

   A. Incision and drainage only

   B. Incision and drainage, followed by oral linezolid

   C. Incision and drainage, followed by oral doxycycline

   D. Incision and drainage, followed by intravenous vancomycin

2. A 76-year-old man presents to the emergency department with complaints of a burning pain on his lower leg. Physical examination reveals an erythematous, edematous lesion with a raised border that is sharply demarcated from uninfected skin. The man stated that he felt like he had the flu (fever, tired) before the pain began. His vital signs showed a temperature of 101°F (38.3°C) and a CBC revealed a white blood cell count of 15,100 cells/μL (15.1×10^9/L). The man states that he is allergic to erythromycin (it made him sick to his stomach). The most appropriate therapy for this patient would be:

   A. Oral dicloxacillin

   B. Oral clarithromycin

   C. Oral trimethoprim–sulfamethoxazole

   D. Oral penicillin VK

3. A 3-year-old girl is brought to the clinic with complaints of itchy blisters on her face. Her face has three small areas (approximately 15 cm^2 total) of erythema with a mixture of small vesicles filled with clear serous fluid and some larger pustules. Thin golden-yellow crusts of previously ruptured vesicles also cover her face. The child is afebrile, has a normal complete blood count and no known drug allergies. The most appropriate therapy

for this patient would be:

A. Oral dicloxacillin

B. Incision and drainage alone with no antibiotics

C. Topical retapamulin ointment

D. Oral penicillin VK

4. A 15-year-old male is brought to the emergency department by his parents with complaints of fever, chills, and headache. The young man stated that several days ago he had developed a blister on his right hand from pitching baseballs during practice. On physical examination, a bright red, narrow streak extends from the blister to his armpit. Regional lymph nodes are enlarged and tender. A complete blood count was performed which showed his white blood cell count to be elevated. The most appropriate therapy for this patient would be:

A. Oral ciprofloxacin

B. Topical mupirocin ointment

C. Intravenous penicillin G

D. Intravenous vancomycin

5. A 32-year-old female presents to her family physician complaining that her lower leg feels hot and painful. Physical examination shows the lower leg to have erythema, edema, and it is very warm to the touch. The erythematous area is nonelevated and has poorly defined margins. There is no drainage or exudates and no evidence of abscesses. She has no recollection of any trauma or injury to the area. The woman has normal vital signs and her complete blood count is normal. She has no known allergies. The most appropriate empiric therapy for this patient would be:

A. Oral dicloxacillin

B. Oral trimethoprim–sulfamethoxazole

C. Oral penicillin VK + clindamycin

D. Oral levofloxacin

6. A 24-year-old female presents to her family clinician complaining of a sore she thought might be from a spider bite. Physical examination reveals a purulent lesion on her lower left leg, surrounded by a 1 cm diameter area of redness and swelling. The patient is afebrile and has a normal white blood cell count. She has no known allergies. The most appropriate therapy for this patient would be:

A. Incision and drainage of the lesion with no antibiotics required

B. Incision and drainage of the lesion, followed by penicillin VK

C. Incision and drainage of the lesion, followed by oral ciprofloxacin

D. Incision and drainage of the lesion, followed by oral trimethoprim–sulfamethoxazole

7. A 54-year-old obese male presents to the emergency department complaining of severe pain in his left lower leg. His leg is hot, swollen and erythematous without any sharp margins; most of the calf from ankle to knee is affected. The lesion is remarkable for a deep cut 4 cm in length which is draining a yellowish, purulent-looking fluid. The patients states that he injured himself at home when he was cleaning out his garage and was cut by a piece of sheet metal. Vital signs reveal a high temperature (104°F [40.0 °C]) and a complete blood count revealed an elevated white blood count (22,000 cells/mm^3 [22×10^9/L]). He has no known allergies. Along with proper wound care, the most appropriate therapy for this patient would be:

A. Oral cephalexin

B. Oral trimethoprim–sulfamethoxazole

C. Oral amoxicillin–clavulanate

D. Oral levofloxacin

8. A 68-year-old female presents to the diabetes clinic for a routine visit. Her past medical history is significant for Type 2 diabetes mellitus, hyperlipidemia, hypertension, and chronic renal insufficiency. Vital signs showed an elevated blood pressure; an elevated glucose was noted on a chemistry panel. Physical examination reveals a small ulcer on the sole of her right foot. The lesion is erythematous, with the presence of pus and a foul-smelling odor. The patient has allergies to penicillin, ceftriaxone (difficulty breathing with both), and sulfa (rash). She has received multiple courses of antibiotic therapy previously, but the wound has never completely healed. The clinician counsels the patient on the importance of glucose and blood pressure control, as well as self-examination and care of her feet. He also initiates antimicrobial therapy for the infection on her foot, which he judges to be mild in severity. The most appropriate therapy for this patient would be:

A. Oral amoxicillin–clavulanic acid

B. Oral cephalexin

C. Oral moxifloxacin

D. Oral trimethoprim–sulfamethoxazole

9. One week later, the patient in the preceding question returns with no improvement in her ulcer. She states that she has been complianting in taking her therapy as prescribed. The clinician obtains a small aspirated sample for culture and sensitivity. The Gram stain shows many white blood cells and many gram-positive cocci in clusters. The culture grew methicillin-resistant *Staphylococcus aureus* (MRSA), which was resistant to penicillin, cephalexin, and erythromycin, but sensitive to clindamycin, doxycycline, levofloxacin, gentamicin, trimethoprim–sulfamethoxazole, and vancomycin. Anaerobic cultures were still pending. Appropriate management of this patient at this time would be:

A. Switch therapy to oral doxycycline

B. Switch therapy to intravenous gentamicin

C. Switch therapy to oral trimethoprim–sulfamethoxazole

D. Switch therapy to intravenous vancomycin

10. A 55-year-old male with a history of poorly controlled Type 1 diabetes mellitus is admitted to the hospital with suspected necrotizing fasciitis involving the perineum and lower abdomen. The affected area is extremely erythematous, swollen and taut, hot to the touch, and exquisitely painful. The patient has a temperature of 103.6°F (39.8°C) and a white blood cell count of 22,000 cells/μL (22×10^9/L). He has no known drug allergies. The most appropriate initiation therapy of this patient's infection would be:

A. Intravenous piperacillin-tazobactam

B. Intravenous ceftriaxone plus linezolid

C. Intravenous penicillin G plus clindamycin

D. Intravenous meropenem plus vancomycin

11. The most important aspect in the prevention of pressure injuries is:

A. Eliminating friction

B. Eliminating moisture

C. Eliminating pressure

D. Eliminating stress

12. An 8-year-old female is brought to the emergency department immediately after being bitten on the right side of her face by a neighbor's dog. The bite wound involves multiple deep puncture wounds and some significant tearing of the surrounding tissues. The most appropriate management of this patient's wound would be:

A. Proper wound care alone, no antibiotics needed

B. Oral antibiotic prophylaxis for 3 to 5 days

C. Oral antibiotic prophylaxis for 7 to 10 days

D. Tetanus–diphtheria toxoids and rabies prophylaxis, no antibiotics needed

13. The most appropriate therapy for an infected dog or cat bite would be:

A. Oral amoxicillin–clavulanic acid

B. Oral cephalexin

C. Oral penicillin VK + clindamycin

D. Intravenous vancomycin

14. A 16-year-old male is brought to the emergency department with a human bite wound to his arm suffered three hours ago during a fight at school. The wound shows no signs of infection at this time. The most appropriate therapy for this patient would be:

A. Oral amoxicillin–clavulanic acid for 3 to 5 days

B. Oral cephalexin for 5 to 10 days

C. Oral clindamycin for 7 to 10 days

D. No antimicrobial therapy at this time

15. Antimicrobial therapy for infections resulting from human clenched-fist injuries should include agents with antimicrobial activity against the following organism(s):

A. CA-MRSA

B. *Eikenella corrodens*, *Staphylococcus aureus*, and anaerobes

C. *Eikenella corrodens*, *Pasteurella multocida*, and *Staphylococcus aureus*

D. *Pasteurella multocida*, *Staphylococcus aureus*, and *Streptococcus pyogenes*

SELF-ASSESSMENT QUESTION-ANSWERS

1. **C.** The presence of multiple furuncles accompanied by fever and leukocytosis should be managed with incision and drainage plus with oral antibiotics such as doxycycline that provide coverage against *Staphylococcus aureus*. See the Folliculitis, Furuncles, and Carbuncles (Treatment) section for more information.

2. **D.** The intense pain, erythematous lesion with sharply demarcated, raised border and systemic findings are consistent with erysipelas. Appropriate treatment of erysipelas includes antibiotics such as oral penicillin VK that are targeted against streptococci. See the Erysipelas (Clinical Presentation and Treatment) sections for more information.

3. **A.** This infection is consistent with impetigo. Although a relatively small surface area is affected, lesions involving the face should be treated with systemic antistaphylococcal agents such as dicloxacillin. See the Impetigo (Treatment) section for more information.

4. **C.** Initial treatment of lymphangitis should consist of intravenous penicillin G for 48 to 72 hours, followed by oral penicillin VK. See the Lymphangitis (Treatment) section for more information.

5. **A.** This patient has mild nonpurulent cellulitis and should be treated with antibiotics that provide coverage against Group A streptococci and methicillin-susceptible *Staphylococcus aureus*. See the Cellulitis (Treatment) section for more information.

6. **A.** Incision and drainage alone, without antibiotic treatment, should be sufficient for initial management of this mild purulent cellulitis without evidence of more severe infection such as fever or leukocytosis. See the Cellulitis (Treatment) section for more information.

7. **B.** This patient has a more severe purulent cellulitis with evidence of systemic involvement including high fever and significant leukocytosis. Initial management should include treatment with antibiotics that provide coverage against streptococci and staphylococci including CA-MRSA. See the Cellulitis (Treatment) section of the chapter for more information.

8. **C.** This patient has previously received multiple courses of antibiotics, so antibiotics for this mild diabetic foot infection should include coverage for gram-negative bacilli as well as gram-positive cocci. Moxifloxacin would be the most appropriate choice in this case given the patient's previous history of apparent drug allergies. See the Diabetic Foot Infection (Treatment) section for more information.

9. **A.** The culture is positive for methicillin-resistant *S. aureus*, therefore patient should be switched to oral therapy that provides coverage against this pathogen. Doxycycline would be the most appropriate choice. See the Diabetic Foot Infection (Treatment) section for more information.

10. **D.** Appropriate initial antibiotic therapy of necrotizing fasciitis includes broad-spectrum coverage of gram-positive cocci, gram-negative bacilli, and anaerobes. The combination of meropenem and vancomycin provides the most appropriate spectrum of activity in this situation. See the Necrotizing Soft-Tissue Infection (Treatment) section for more information.

11. **C.** Although friction and moisture also play roles, elimination of pressure is the most important strategy to reduce development of pressure injuries. See the Pressure Injuries (Pathophysiology and Treatment) sections for more information.

12. **B.** Although controversial, moderate-to-severe bite wound injuries to the face are considered an appropriate indication for a 3- to 5-day course of prophylactic antibiotics. See the Animal and Human Bite Wounds (Treatment) section for more information.

13. **A.** Amoxicillin–clavulanic acid is most commonly recommended for oral outpatient therapy of infected dog and cat bites due to excellent activity against all likely pathogens, including *Pasteurella* and *Eikenella*. See the Animal and Human Bite Wounds (Treatment) section for more information.

14. **A.** Antibiotic prophylaxis should be considered for all patients with significant human bite wounds due to the high risk of subsequent infection. Amoxicillin–clavulanate is a commonly recommended agent and the usual duration of prophylaxis is 3 to 5 days. See the Animal and Human Bite Wounds (Treatment) section for more information.

15. **B.** *Eikenella corrodens*, *Staphylococcus aureus*, and anaerobes are pathogens commonly associated with human bite wounds. *Pasteurella* species are more commonly associated with animal bites, and CA-MRSA does not need to be routinely covered in human bite wounds.

    See the Animal and Human Bite Wounds (Treatment) section for more information.