

Bacterial Skin and Soft Tissue Infections

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Bacterial skin and soft tissue infections (SSTIs) are a common problem encountered in clinical practice, with approximately 14.2 million ambulatory care visits made for SSTIs in 2005.^{1,2} Bacterial SSTIs range from superficial epidermal infections to life-threatening necrotizing fasciitis. Although most SSTIs can be managed on an outpatient basis, physicians must remain alert for signs and symptoms indicative of a more serious infection requiring rapid evaluation and hospital admission. This article reviews the etiology, associated risk factors, and the general approach to diagnosis and treatment of SSTIs in immunocompetent outpatients, with a focus on SSTIs commonly seen in clinical practice.

ETIOLOGY OF SKIN AND SOFT TISSUE INFECTIONS

Most bacterial SSTIs are caused by gram-positive organisms, including *Staphylococcus aureus*, group A and B streptococci, *Streptococcus viridans*, and *Enterococcus faecalis*. Less common causes of infection include gram-negative organisms such as *Haemophilus influenzae*, *Pasteurella multocida*, *Campylobacter* species, *Vibrio* species, *Mycobacterium* species, *Pseudomonas* species, *Aeromonas* species, *Proteus* species, *Clostridium* species, and other anaerobes.³ As *Staphylococcus aureus* and streptococci species represent the most commonly identified causes of SSTIs,³ they are discussed in greater detail.

Staphylococcus aureus

Staphylococcus aureus is the most commonly identified infectious agent causing SSTIs in the United States. Most cases of staphylococcal SSTI are caused by community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA), with fewer cases attributed to healthcare-associated MRSA (HA-MRSA) and methicillin-sensitive *Staphylococcus aureus* (MSSA).^{4,5} In fact, up to three-quarters of SSTIs caused by *Staphylococcus aureus* can be attributed to CA-MRSA strains.⁶ In 1 study, 302 of 422 patients (76%) presenting to the emergency department with SSTIs were infected with *Staphylococcus aureus*. MRSA was isolated in 249 (59%) of these patients, MSSA in 71 (17%), and other bacteria in 64 (15%).⁶ Of 218 MRSA isolates sent to the Centers for Disease Control

TAKE HOME POINTS

- *Staphylococcus aureus* and *Streptococcus pyogenes* are the most commonly identified causes of skin and soft tissue infections (SSTIs).
- Many SSTIs are caused by methicillin-resistant *Staphylococcus aureus* (MRSA), and multidrug resistance is common with both community-associated (CA)-MRSA and healthcare associated (HA)-MRSA infections. However, HA-MRSA is susceptible to fewer antibiotic agents than CA-MRSA.
- Risk factors for developing SSTIs include breakdown of the epidermis (eg, ulceration trauma, pre-existing skin conditions), poor personal hygiene, crowding, comorbidities, close contact with a person with an SSTI, venous stasis, lymphedema, and surgical procedures.
- Most SSTIs can be managed on an outpatient basis, although patients with evidence of rapidly progressive infection, high fevers, or other signs of systemic inflammatory response should be monitored in the hospital setting.
- Superficial SSTIs typically do not require systemic antibiotic treatment and can be managed with topical antibiotic agents, heat packs, or incision and drainage.
- Systemic antibiotic agents that provide coverage for both *Staphylococcus aureus* and *Streptococcus pyogenes* are most commonly used as empiric therapy for both uncomplicated and complicated deeper infections.

and Prevention for analysis, 216 (99%) were consistent with CA-MRSA, with 212 identified as type USA 300 and 2 identified as type USA 400.⁶ Resistance to β -lactam

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antibiotic drugs in CA-MRSA strains has been attributed to the *mec IV* gene, which encodes the penicillin-binding protein 2a, an enzyme with decreased affinity for β -lactam antimicrobial drugs. Nosocomial MRSA strains generally contain either the *mec II* or *mec III* genes, which also confer resistance to methicillin.⁷

USA 300 and USA 400 are clones of CA-MRSA that are infiltrating the hospital environment, making the distinction between HA-MRSA and CA-MRSA less clear.^{8–10} USA 300 has been associated with more invasive tissue disease, including abscess formation.^{6,11} Knowing the type of MRSA is important for selecting an appropriate empirical antimicrobial therapy, as HA-MRSA and CA-MRSA exhibit different antimicrobial susceptibility patterns.^{6,12–14} Differentiating between HA-MRSA and CA-MRSA based on clinical presentation is difficult as both present with erythema, edema, and fluctuance of the affected area.¹² However, CA-MRSA strains tend to affect younger patients, men who have sex with men, athletic teams, prisoners, intravenous drug users, and people living in lower socioeconomic areas, whereas HA-MRSA is more often associated with patients in hospitals and nursing facilities.^{12,15}

Staphylococcus aureus is capable of secreting several toxins, which vary depending on the strain. One toxin commonly implicated as the cause of increased virulence in CA-MRSA is the Pantone-Valentine leukocidin (PVL).¹² This cytotoxin causes destruction of leukocytes and tissue necrosis by inducing production of the potent chemotactic factors interleukin-8 and leukotriene B₄.^{19,20} The role PVL plays in the pathogenesis of CA-MRSA infections remains uncertain, as some studies do not show a clear linkage with increased virulence.¹⁶ The genes *lukF* and *lukS* encode PVL.^{17,18} *Staphylococcus aureus* also secretes enterotoxins, which are superantigens that bypass the usual immune system pathways and nonspecifically activate T cells, resulting in a massive release of cytokines. One study showed that up to half of isolates recovered from *Staphylococcus aureus* SSTIs produced enterotoxins.²¹

Streptococci

Streptococcus pyogenes (also called group A streptococcus) is the streptococcal species that most commonly causes SSTIs. However, non-group A β -hemolytic streptococci (eg, group C and G streptococci) have been implicated as causes of cellulitis, especially in patients with venous insufficiency.²² Multiple virulence factors play a role in *Streptococcus pyogenes* disease pathogenesis.²³ The M protein, the main antiphagocytic virulence factor, inhibits activation of the alternate complement pathway, thus permitting streptococci to avoid phago-

cytosis and causing destruction of polymorphonuclear leukocytes. The streptococcal pyogenic exotoxins (ie, SpeA, B, and C) act as superantigens that bind to major histocompatibility complex class 2 molecules and T-cell receptors. This binding promotes activation of T cells, which in turn secrete cytokines that may cause the characteristic hypotension and multiorgan failure associated with streptococcal toxic shock syndrome.²⁴ Other factors that enhance streptococcal pathogenesis include surface structures, such as the hyaluronic acid capsule and fibronectin proteins (which aid in adherence, colonization, and invasion under various environmental conditions), and the enzymes hyaluronidase, streptokinase, and 4 separate types of DNases (which contribute to the microorganism's ability to disseminate through tissue planes).²⁵

RISK FACTORS

Risk factors for the development of SSTIs include compromise of the epidermis as well as poor personal hygiene, crowding, comorbidities, and close contact with a person with an SSTI.^{3,24} Breakdown of the epidermis serves as the entry point for infectious organisms and may be caused by ulceration, trauma, peripheral vascular disease, or preexisting skin conditions that allow bacteria to gain access to deeper tissues. Skin conditions that can predispose to SSTIs include eczema and psoriasis (which cause small fissures on the skin) and superficial fungal infections typified by tinea pedis and onychomycosis (which can cause changes in the affected skin that may lead to superimposed infection with bacteria). Venous stasis and lymphedema also can predispose patients to SSTIs. Patients with lymphedema have defective mechanisms for filtering bacteria and therefore tend to have higher microbial counts.²⁵ Surgical procedures such as vein harvesting and mastectomy with lymph node removal are also risk factors.^{26,27} Specific risk factors will be discussed in relation to the associated infection in the following section.

CLINICAL PRESENTATION

Impetigo

Impetigo is a localized skin infection most commonly seen in preschool-aged children and in patients from economically disadvantaged areas. It is more prevalent in tropical regions²⁴ and occurs more frequently in the summertime in the northern hemisphere.²⁸ The spread of infection is due to person-to-person transmission as well as via fomites (eg, towels, gym equipment). Clinical infection becomes apparent approximately 10 days after colonization with the implicated bacteria.³

There are 2 forms of impetigo: bullous and nonbullous.

Nonbullous impetigo is the most common form and is caused by *Streptococcus pyogenes* alone or as part of a mixed infection with *Staphylococcus aureus*. The characteristic lesions of impetigo are thin-walled vesicles that rupture, leaving residual yellow crusts on the face and extremities. Lymphadenopathy is a common feature.³ Streptococcal impetigo is usually caused by *Streptococcus pyogenes* strains different from those that cause tonsillitis.²⁴ However, these skin strains may eventually colonize the nasal-pharyngeal cavity, leading to upper respiratory infections.³ Bullous impetigo is always associated with *Staphylococcus aureus*. This presentation is often localized to the trunk, and the bullae tend to be larger and less prone to rupture.³

Folliculitis

Folliculitis has many etiologies, which include infectious, eosinophilic, and drug-related causes. The most common bacterial causes of folliculitis include *Staphylococcus aureus*, *Streptococcus pyogenes*, *Pseudomonas* species, and *Proteus* species. Infection typically follows follicle damage. The presentation of folliculitis depends on its severity, which ranges from superficial inflammation of an individual hair follicle to a deeper infection of the follicle (known as a furuncle) to clusters of coalescing abscesses found deeper in the subcutaneous tissues (carbuncles).²⁹ Folliculitis is generally diagnosed clinically. Signs and symptoms of the various types of folliculitis include pruritus, papules, and pustule formation surrounding the hair follicle. Systemic signs such as fever and malaise are sometimes present and may be indicative of bacteremia.²⁹

Hidradenitis Suppurativa

Hidradenitis suppurativa is caused by an obstruction in the draining ducts of the apocrine glands of the axillae and genitalia, resulting in a tender nodular dilatation of the glands. The pooled secretions often become secondarily infected with gram-positive and gram-negative bacteria (eg, staphylococci, various streptococci including *Staphylococcus anginosus*, *Bacteroides* species, *Escherichia coli*, *Pseudomonas* species).³⁰ Risks for developing hidradenitis suppurativa include hormonal factors and obesity. For a significant number of patients, this condition represents a chronic and difficult-to-treat problem that commonly requires multiple surgical drainages. The repeated bouts of infection may cause scarring and sinus tract formation of the affected area, which complicates the long-term management of the disease and causes significant frustration to the patient.³¹

Erysipelas

Streptococcus pyogenes is the most common cause of

erysipelas. This infection is characterized by acute onset of skin erythema associated with fever and lymphangitis. The classic skin lesion is raised with well-demarcated, erythematous borders and is caused by prominent lymphatic compromise of the affected area. Erysipelas most often develops on the lower extremities, contrary to past trends when facial involvement was the most common presentation.^{32,33} *Streptococcus pyogenes* colonization of the skin or recent oropharyngeal infection, dermatophyte infection between the toes or of the toenails (ie, tinea pedis), chronic venous stasis, and preexisting leg ulcers are all predisposing factors for developing erysipelas. Because of the superficial nature of the disease, lymphatic spread and subsequent bacteremia are rarely found, making blood culture collection unnecessary in suspected cases.³³

Cellulitis

Cellulitis is a spreading infection of the epidermis and subcutaneous tissues (**Figure 1**). Staphylococcal and streptococcal species are the most frequent isolates recovered^{3,34} and are also the most common organisms implicated in recurrent cellulitis.^{25,35} Common physical findings in cellulitis include erythema, edema, warmth, and tenderness of the affected area. Patients may also experience fever, tender lymphadenopathy, and abscess formation, especially if *Staphylococcus aureus* is implicated as the causative agent. Unlike erysipelas, the involved area is poorly demarcated.³⁶

In a study of US veterans, smoking, homelessness, obesity, venous stasis, and untreated tinea pedis were associated with an increased risk of developing recurrent infection.³⁷ McNamara et al²⁷ found that concomitant dermatitis, a history of cancer, and a first episode of cellulitis located over the tibial region were important risk factors for developing subsequent infections. Lymphedema has also been identified as a major risk factor for recurrent cellulitis.^{25,37,38} This abnormality is usually seen after surgical procedures that damage the local lymphatic drainage (**Figure 2**). These patients may have abnormal lymphatic elimination of bacteria and higher than normal bacterial counts on the surface of the skin.²⁵

Staphylococcal Scalded Skin Syndrome

Staphylococcal scalded skin syndrome (SSSS; **Figure 3**) is generally preceded by *Staphylococcus aureus* infection, and it occurs more commonly in newborns, infants, and immunocompromised adults.³⁹ SSSS is caused by 2 epidermolytic toxins (*ETA* and *ETB*) produced by certain strains of *Staphylococcus aureus*.⁴⁰ The toxins act exclusively on the stratum granulosum and



Figure 1. Cellulitis of the foot. (Photo courtesy of Bradford Legge, DPM, the Jesse Brown VA Center, Chicago, IL.)



Figure 2. Lymphedema and cellulitis of the arm post mastectomy. (Photo courtesy of James Willig, MD, University of Alabama, Birmingham, AL.)



Figure 3. Bullae of staphylococcal scalded skin syndrome. (Photo courtesy of Suzanne J. Templer, DO, University of Illinois at Chicago, Chicago, IL.)



Figure 4. Necrotizing fasciitis of the neck area. (Photo courtesy of Garrett Lam, MD, University of Illinois at Chicago, Chicago, IL.)

do not involve the mucosa. In the localized form of SSSS, the toxin is found in the periphery of the wound; this is typically seen in people with previous immunity to staphylococcal infections. In the generalized form of SSSS, the toxin spreads through the bloodstream. The initial symptom is a diffuse rash that progresses to bullae formation, followed by exfoliation of the affected skin. Fever, lethargy, and a positive Nikolsky's sign (ie, separation of the epidermal layer upon gentle stroking) are common presenting signs. This syndrome shares many features with toxic epidermal necrolysis;

however, it can be differentiated by the lack of mucosal involvement in SSSS.⁴¹

Necrotizing Infections

Necrotizing fasciitis may be caused by a single organism (eg, *Streptococcus pyogenes*, *Staphylococcus aureus*) but is more commonly polymicrobial (mixed aerobic and anaerobic species). *Vibrio* species, which are associated with seawater exposure, can cause very severe infections, particularly in patients with chronic liver disease or diabetes.^{3,42} Other predisposing factors for necrotizing complications include varicella infection, injection drug use, penetrating injuries, burns, childbirth, recent surgery, and muscle strain.^{43,44} The most commonly affected sites are the extremities.⁴³ Extremes of age and intravenous drug use portend a poorer prognosis.⁴⁴

Necrotizing infections typically progress more rapidly (within 24–48 hr) than more superficial cellulitic processes and have more devastating consequences, namely the destruction of fat, fascia, and underlying muscle. A recent study noted exceptions to this rapid course, finding that symptoms could be present for an average of 6 days prior to admission.¹¹ Initial signs and symptoms are diffuse swelling of the affected area without well-demarcated borders and pain out of proportion to physical findings, followed by bullae and blisters due to tissue ischemia from locally thrombosed blood vessels. The skin turns violaceous or ecchymotic and becomes gangrenous if left untreated (**Figure 4**).³ The patient may develop anesthesia, as the superficial nerves in the affected area infarct. Necrosis and ischemia block antibiotic delivery to the affected area.⁴⁵ Necrotizing fasciitis also should be suspected in the patient who appears toxic, fails to respond to antibiotics, and presents with skin necrosis.³ A “finger test” can be performed in cases where necrotizing fasciitis is suspected. An incision is made on the skin down to the deep fascia and a finger is used to dissect through the tissue planes. If minimal resistance is encountered or if a murky, foul-smelling fluid emanates, the test is considered positive.^{45,46}

DIAGNOSIS

Most SSTIs are diagnosed clinically. The cardinal signs of an SSTI include erythema, edema, tenderness to palpation, and increased warmth. Signs such as fluctuance, crepitus, induration, blisters, or bullae may help the clinician determine the depth of infection or the presence of an abscess. Symptoms such as fever, chills, and hypotension may be present in deeper infections.⁴⁷ A careful travel and environmental exposure history should be elucidated, as certain pathogens are associated with specific geographic locales. Examples include

Pseudomonas aeruginosa acquired from hot tubs,⁴⁸ *Vibrio vulnificus*^{3,42} and *Mycobacterium marinum*⁴⁹ from water exposures, and *Pasteurella multocida* and *Capnocytophaga canimorsus* from animal bites.³ A careful history should also determine whether the patient has been recently hospitalized, as this may place the patient at risk for multidrug-resistant organisms (ie, HA-MRSA).¹² When examining a patient with a skin infection, it is important to consider necrotizing soft tissue complications. Rapid spread, induration and crepitus of the affected tissues, fever, hypotension, and pain out of proportion to physical findings suggest necrotizing fasciitis, which should prompt surgical evaluation.³ Laboratory findings that may be seen in patients with necrotizing infections include leukocytosis greater than 15,000 cells/ μ L, hemoglobin below 11 g/dL, elevated C-reactive protein, new-onset renal failure, and hyponatremia.⁴⁶

Obtaining antibody serology for suspected streptococcal infections is generally not helpful in diagnosing superficial SSTIs, as this is a localized process and systemic antibodies are not produced.²⁴ Cultures of secretions draining from abscesses and other skin lesions (eg, furuncles, carbuncles) may assist in determining the causative organism. Although culture of a bullae or purulent drainage may yield the offending organisms, empiric therapy is usually initiated before the culture results become available. Additionally, ordering cultures may not be cost effective. According to 1 study that included 757 patients with cellulitis, blood cultures were cost-effective only when necrosis was suspected.⁵⁰

Imaging studies should be ordered when deeper infections are suspected. Plain films may be helpful in confirming the presence of air in the tissues, and ultrasound may be used to exclude subcutaneous abscess formation and deeper infections.⁵¹ Computed tomography scans and magnetic resonance imaging (MRI) may show air in the tissues or enhancement with intravenous contrast, but these signs are not specific to necrotizing SSTIs.^{52,53} Early surgical evaluation is required when possible signs of necrotizing infections appear on imaging. This step allows the appropriate parties to become involved early in a patient's care. MRI can help determine the depth of infection by showing increased thickness and/or enhancement of the fascia; nonetheless, other medical conditions such as polymyositis also cause enhancement of the fascia and may be confused with infectious fasciitis. MRI has been noted, in some instances, to overestimate the depth of the infection.^{52,53}

TREATMENT

In general, most SSTIs can be managed on an outpatient basis, although patients with evidence of rapidly

progressive infection, high fevers, or other signs of systemic inflammatory response should be monitored in the hospital setting. Superficial infections typically do not require systemic treatment and usually respond to topical agents. Impetigo is topically managed with mupirocin^{3,24} and fusidic acid.⁵⁴ Mild folliculitis may be treated with heat packs. In the case of furuncles and carbuncles, incision and drainage of abscesses is required. These procedures followed by application of heat packs are often all that is needed to resolve the infection, especially those caused by CA-MRSA. In some cases, the infection improves even when the initial oral antibiotic choice is faulty, further demonstrating that some superficial infections may resolve on their own. The reasons for this are unclear but may involve the anti-inflammatory effect of the medications.⁵⁵ Oral antibiotic drugs, however, may be given to patients with folliculitis following incision and drainage of an abscess when fever or extensive cellulitis is present.³ Superimposed infection with fungal organisms such as dermatophytes or *Pityrosporum* species also can occur in folliculitis, requiring combination antimicrobial therapy. Culture and sensitivity testing of pustular lesions should be performed to help guide oral antibiotic therapy.³

Hidradenitis suppurativa is treated with a combination of surgery coupled with culture-guided antimicrobial therapy of the drained purulence.³⁰ As *Streptococcus pyogenes* usually causes erysipelas, treatment typically involves β -lactam antibiotic drugs (eg, penicillin G, amoxicillin, macrolides) as well as bed rest with leg elevation.³³ In rare cases where the infectious etiology is *Staphylococcus aureus*, a penicillinase-resistant synthetic penicillin or first-generation cephalosporin should be used instead.³ Concomitant infections such as tinea pedis also should be treated.³³ In some cases, recurrences of erysipelas may be lessened by daily antibiotic prophylaxis.⁵⁶ Treatment of cellulitis is similar to that of erysipelas but should include agents that cover both MRSA as well as *Streptococcus pyogenes*.³ Antibiotics and supportive treatment are the standard of care for SSSS.³⁹

Necrotizing fasciitis therapy should initially consist of broad-spectrum coverage of gram-positive, gram-negative, and anaerobic organisms. A common regimen might include a broad-spectrum β -lactam and clindamycin. Therapy can be tailored once wound and blood culture results become available.^{3,44} Immediate surgical débridement is necessary to salvage as much viable tissue as possible, and repeated débridement may be needed.⁴⁵ Adjunctive therapies to surgical débridement and to antibiotic administration include intravenous immunoglobulin and hyperbaric oxygen. Intravenous immunoglobulin has been utilized in *Staphylococcus aureus*

multisystem disease, but there have been no studies of its use in SSTIs alone. The clinical benefit of this form of therapy is unproven.^{57,58} The use of hyperbaric oxygen is hampered by the paucity of data and the limited availability of this technology.⁴⁴

Systemic Antibiotic Therapy

In addition to procedures such as incision and drainage of abscesses, antibiotic therapy is often required to eradicate SSTIs. Systemic antibiotic agents that provide coverage for both *Staphylococcus aureus* and *Streptococcus pyogenes* are most commonly used as empiric therapy for both uncomplicated and complicated deeper infections. Antibiotic resistance is a concern, given that many SSTIs are caused by MRSA and multidrug resistance is common with both CA-MRSA and HA-MRSA infections. HA-MRSA is generally susceptible to vancomycin, linezolid, and trimethoprim-sulfamethoxazole.^{12,59} In contrast, CA-MRSA is usually sensitive to these antibiotics (trimethoprim-sulfamethoxazole susceptibility depending on the location) as well as a broader range of oral antimicrobial agents such as clindamycin, quinolones, and tetracycline drugs.^{6,12–14,60} Since substantial geographic variation in antibiotic sensitivities occurs throughout the country, practitioners should familiarize themselves with the local susceptibility patterns of commonly encountered organisms.^{61–63} The following provides an overview of the antimicrobial agents used to treat SSTIs.

β -Lactam antibiotic drugs. Prior to the emergence of CA-MRSA, β -lactam drugs were first-line therapy for community-acquired SSTIs.⁶⁴ Empiric therapy with a β -lactam drug may no longer be sufficient for treatment now that USA 300 and other MRSA clones are being identified more frequently as the causative agents for SSTIs. Although streptococci remain sensitive to penicillin, staphylococci are now almost universally resistant. MSSA, however, are usually sensitive to β -lactam drugs except penicillin. Physicians should be aware when treating patients who have an SSTI due to MRSA (eg, toxic shock syndrome) that cell-wall active agents such as nafcillin may cause cellular lysis with release of toxins into the bloodstream, which can upregulate the host's immune response and thereby cause a paradoxical worsening of symptoms.⁶⁵ Extended-spectrum penicillins (eg, nafcillin, dicloxacillin) or first-generation cephalosporins (eg, cephalexin, cefazolin), with or without the addition of an antibiotic that stops toxin production (eg, clindamycin), are examples of β -lactam drugs that are effective against MSSA and streptococci.⁶⁶

Clindamycin. Clindamycin is an important adjunct to therapy for SSTIs because of its ability to suppress

bacterial toxin production, including streptococcal pyrogenic exotoxin A, PVL, and staphylococcal enterotoxin B. However, MRSA may become resistant to clindamycin upon exposure to this drug via an inducible *erm* gene found in certain strains. The microbiology laboratory usually performs a disk diffusion test, known as a D-test, to determine if inducible resistance is present. The test is completed by placing a clindamycin antibiotic disk approximately 2 cm away from an erythromycin antibiotic disk on growth medium containing colonies of *Staphylococcus aureus*. If inducible resistance is present, there will be an abrupt flattening of the clindamycin zone of inhibition in the area between the 2 disks reflecting the growth of bacteria within the clindamycin diffusion zone. The area around the clindamycin disk resembles the letter D (hence, the name of the technique).⁶⁴

Linezolid. Much like clindamycin, linezolid suppresses bacterial toxin production and has a long post-antibiotic effect.⁶⁷ It is approved for the treatment of uncomplicated and complicated SSTI caused by *Staphylococcus aureus* and streptococci based on data from clinical trials comparing it to the β -lactam antibiotic drugs.^{68,69} This antimicrobial agent is bacteriostatic to *Staphylococcus aureus* and enterococcus strains, with some bactericidal activity against streptococci.⁶⁹ Linezolid may be used as an alternative agent for the treatment of SSTI in patients with a confirmed penicillin allergy.³

Fluoroquinolones. In general, *Streptococcus pyogenes* infection is susceptible to fluoroquinolones. However, there is geographic variability in susceptibilities, with up to 80% of CA-MRSA isolates showing resistance at some institutions.^{6,13} With the increased use of this class of antibiotics, resistance to fluoroquinolones also has been increasing.⁷⁰ Care must be exercised when prescribing fluoroquinolones (eg, ciprofloxacin, levofloxacin) without the appropriate culture data.

Other agents. Vancomycin is an intravenous agent that can be administered to patients with SSTIs who have allergies against β -lactam agents;³ it is effective against both CA-MRSA and HA-MRSA strains.¹² Retrospective studies and case reports indicate that sulfa and tetracycline drugs may be efficacious in treating SSTIs due to MRSA.⁷¹ Sensitivities to sulfa and tetracycline drugs vary from region to region, and patients previously exposed to certain classes of medications (eg, sulfa prophylaxis for prevention of *Pneumocystis jirovecii* pneumonia) may show increased rates of treatment failures.^{6,12-14,60} However, more head-to-head studies of the older antimicrobial agents are needed to better delineate their roles in treatment regimens. Newer antimicrobial agents, such as daptomycin and tigecycline, are

also approved for the treatment of SSTIs. Daptomycin is a lipopeptide that is only active against gram-positive organisms such as staphylococci (including MRSA strains) and streptococci.⁷² Tigecycline is structurally related to tetracycline. It is thought to have a broad-spectrum activity with bacteriostatic in vitro activity against many gram-positive and gram-negative organisms, including MRSA and vancomycin-resistant enterococci; it is not effective against *Pseudomonas aeruginosa*.⁷³

Treatment duration. Short-course therapy for an uncomplicated SSTI is the standard of care. Treatment duration depends largely on patient response and extent of infection. In 1 study that compared a 5-day course of fluoroquinolone therapy with a 10-day course of levofloxacin for the treatment of uncomplicated cellulitis, the outcomes were similar in both groups, with 98% of patients in each treatment arm achieving clinical resolution.⁷⁴ In a separate study of 492 patients who had various SSTIs due to CA-MRSA, antibiotic treatment with a median duration of 10 days resulted in the best outcomes, although patients received between 7 and 14 days of medication.^{75,76}

Prevention of Recurrent SSTIs

Prophylactic antibiotic therapy is an option for patients with recurrent SSTIs, although whether this addition has a significant impact on future infections or contributes to microbial resistance in patients with erysipelas and cellulitis remains unclear.^{77,78} Long-term therapy is reserved for patients without a clear and treatable predisposing condition.⁷⁸ Treating concomitant fungal infections, reducing edema by compressive stockings, leg elevation, or diuretic therapy and keeping the skin moist to avoid fissures are all options to help prevent recurrent SSTIs.²⁷ Nasal colonization with *Staphylococcus aureus* has been identified as a risk factor for repeated SSTIs. A placebo-controlled trial designed to determine if eliminating MRSA carriage from the anterior nares would prevent recurrent skin infections showed no overall reduction in the number of cases.⁷⁹ Other studies for patients with recurrent erysipelas and furuncles have shown similar results, calling into question the practice of MRSA decolonization.^{80,81} More evidence on this subject needs to be gathered before firm recommendations can be made.

SUMMARY

Ranging from superficial cellulitis to life-threatening necrotizing fasciitis, SSTIs are common in clinical practice. Treating underlying skin conditions such as onychomycosis and psoriasis may help reduce the frequency of SSTIs. Empiric therapy with β -lactam drugs may no

longer be adequate for treatment now that MRSA strains are being identified more frequently as the causative agents for SSTIs. It is important for physicians to have a working knowledge of the local antimicrobial susceptibilities to avoid treatment failures and to prevent inappropriate antibiotic usage.

HP

Test your knowledge and comprehension of this article with the Clinical Review Quiz on page 48.

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