Appendix A. Diagnosis and Treatment of Gram Positive Bacterial Skin and Soft Tissue Infections – Top Ten Myths
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Myth 1: Skin that is red and swollen is definitely cellulitis

Truth 1: Local presentation of edema, erythema, heat, “orange peel” appearance, vesicles, bullae, petechiae, and pain should lead to a diagnosis of skin and skin structure infection,2,3,9,10 a. Diagnoses of deep venous thrombosis, venous stasis dermatitis, venous insufficiency, lymphedema, contact dermatitis, gout, herpes zoster, acute lipodermatosclerosis, non-infectious phlebitis and fixed drug reaction should be excluded.
b. All inflammatory responses include hyperemia, warmth, swelling, and usually pain
c. A simple physical exam skill that can help differentiate true cellulitis from other etiologies of erythema of the lower extremity is to have the patient lie horizontally on exam table/bed, manually elevate leg at 45 degree angle or higher, and hold it there for 1-2 minutes while observing whether the erythema abates. Cellulitis erythema will persist upon elevation whereas erythema due to other etiologies often disappears with elevation.

Myth 2: Bilateral leg swelling and redness always means bilateral leg cellulitis

Truth 2: Bilateral leg swelling is usually due to other disease states and does not mean that the patient has developed bilateral cellulitis.40,53 Statistical probability would also make this occurrence exceedingly rare.

a. Risk factors for developing erysipelas or cellulitis include obesity, previous cutaneous damage (from trauma, preexisting skin infections, ulceration, and other causes), and edema from venous insufficiency or lymphatic obstruction or disruption of lymphatic drainage, such as following lymph node dissection.
   1. Of 99 patients with bilateral leg swelling, 17 patients (17%) were found to have acute deep vein thrombosis by venous duplex ultrasound.2
b. Patients should elevate the affected area in order to hasten improvement by promoting gravity drainage of the edema and inflammatory substances.
c. If edematous, apply ACE wrap from toes to thighs every 8 hours for lower extremity infections to assist in reduction of lymphedema.

Myth 3: Patients with no risk factors for community acquired- methicillin-resistant Staphylococcus aureus (CA-MRSA) cannot get MRSA

Truth 3: Any patient may develop cellulitis caused by CA-MRSA. The likelihood is increased if the patient has risk factors for MRSA.

a. Between 2006 and 2009, a microbiologic study of skin and soft-tissue infections examined the etiology of skin and soft tissue infections (SSTI) in a general population. A culture was obtained in 23% (149,200/ 648,699) of SSTI episodes, and a pathogen was identified in 58% (87,839/149,200) of the cultures. Staphylococcus aureus was the pathogen in 80% of the positive cultures 70,026/87,839), with 50% (35,180/70,026) of the Staphylococcus aureus isolates being MRSA.54
b. Risk factors for community-acquired MRSA (CA-MRSA) include:29
   • History of MRSA infection or colonization in patient or close contact
   • High prevalence of CA-MRSA in local community or patient population
   • Recurrent skin disease
   • Crowded living conditions (e.g. homeless shelters, military barracks)
   • History of incarceration
   • Participation in contact sports
   • Skin or soft tissue infection with poor response to beta-lactam antibiotics
• Recent and/or frequent antibiotic use
• Injection drug use
• Member of Native American, Pacific Island, Alaskan Native populations
• Male with history of having sex with men
• Shaving of body hair

c. Risk factors for hospital-acquired MRSA (HA-MRSA) include:\(^{30}\)
   - Nasal colonization
   - Presence of indwelling devices such as catheters, tracheostomies, and nasogastric tubes
   - Hospital admission within past 90 days
   - Prolonged hospitalization
   - Residence in long-term care facility
   - Antibiotic therapy in past 90 days
   - Diabetes mellitus
   - Dialysis
   - HIV infection/immunosuppression

d. In the absence of cultured abscess samples, MRSA nasal AND pooled axilla/groin PCR or culture should be obtained for inpatients with risk factors for MRSA or to determine the likelihood that infection is caused by MRSA\(^{31-34,55}\)
   1. If MRSA PCRs or cultures are negative, medications covering for MRSA may potentially be de-escalated to beta-lactam antibiotics.\(^{55}\)

Myth 4: All cellulitis needs to be treated with antibiotics

Truth 4: Not all cellulitis needs to be treated with antibiotics.
   a. For simple abscesses and boils (less than 5 cm in diameter of erythema and abscess), incision and drainage alone is likely adequate as sole treatment and **no treatment with antibiotics are necessary**\(^{2,3,5,29}\)
   b. For patients with abscesses/erythema (combination diameter) greater than 5 cm, multiple lesions, cutaneous gangrene, signs of systemic infection, rapid progression of cellulitis, areas that are difficult to drain (face, hand, genitalia), and/or risk factors for reduced ability to heal, such as diabetes or immunosuppression; treatment with antibiotic therapy should be considered\(^{29}\)

Myth 5: All hospitalized patients need to be treated as though they have MRSA infection

Truth 5: Hospitalized patients should be treated with antibiotics to cover organisms based on individual characteristics of the infection and risk factors for organisms.
   a. Of 322 hospitalized patients with SSTIs, 47% (150/322) had a positive culture result and of those with result, 43% (64/150) grew MRSA.\(^{5}\)
   b. Impetigo, erysipelas, and cellulitis that is diffuse or unassociated with a defined portal, erythematous, non-purulent with extensive lymphangitic spread is more commonly caused by Group A or other beta-hemolytic Streptococcus than Staphylococcal species (but Staphylococcus aureus may also be present)\(^{35,36}\)
   c. For cellulitis with abscess that is fluctuant, has penetrating trauma, shallow ulcer or blister with surrounding erythema, Streptococcus spp. and Staphylococcus spp. should be targeted with antimicrobial therapy (including MRSA).\(^{2,3,9,10}\)
      1. Abscess material should be obtained for culture whenever possible.
      2. MRSA nasal and pooled axilla/groin PCR or culture should be obtained in the absence of culture material for patients with risk factors for MRSA or patients receiving anti-MRSA therapy\(^{31-34}\)
      3. If MRSA PCR or culture are negative, medications covering for MRSA may potentially be de-escalated to more narrow-spectrum antibiotics
d. Severity of illness and co-morbidities, as well as risk factors for MRSA plays a large role in determining whether or not to empirically treat for MRSA.

Myth 6: If the redness extends beyond the drawn wound margin in a patient with cellulitis, the patient is getting worse

Truth 6: Because of the sub-acute spread of redness, edema, and/or induration in some patients at the time of presentation with SSTI, the lesion may continue to spread during a short period of time after administration of the first doses of antibacterial drug therapy.56

a. The erythema may extend beyond pen margins within the first 24 to 36 hours without representing treatment failure. The intensity of the erythema is often a more important variable, with improving cases resulting in less intensely red inflammation.
b. If erythema and fever continue beyond 48 to 72 hours, this is usually considered treatment failure and antimicrobial therapy should be reassessed. Exceptions may include beta hemolytic streptococcal infections where lymphangitis and lymphadenopathy may continue to evolve over multiple days.

Myth 7: All patients with tick bites and surrounding redness have cellulitis

Truth 7: Local tick bite reactions are predictable and do not indicate that a patient has cellulitis.57 These are usually no more than a few cm in size.

a. Erythema surrounding a tick bite can be differentiated from streptococcal and staphylococcal cellulitis based the characteristics of erythema. Erythema due to tick bites usually remains localized with limited spread to the site of the bite, while bacterial cellulitis and erythema migrans from Borellia will continue to extend several cm beyond the bite site.

Myth 8: Patients should never have another infection if they are taking antibiotic prophylaxis for recurrent infections,

Truth 8: Antibiotic prophylaxis may suppress infection, but recurrence may occur despite adherence to therapy. Treatment of causes of infection and optimization of treatment of other disease states may decrease the risk of recurrence.50-52

a. Of 398 patients, 40% (158/398) of patients reported cellulitis recurrence despite prophylactic treatment of benzathine penicillin58
b. Causes of infection such as tinea pedis should be treated to prevent recurrence49,59
c. The management of other disease states, such as diabetes mellitus and especially lymphedema, should be optimized in order to decrease the risk of recurrence.58
d. Skin should be kept well hydrated with emollients to avoid dryness and cracking

Myth 9: Since one cannot tell whether cellulitis is caused by Streptococcus, Staphylococcus, or CA-MRSA, each patient need two types of anti-infectives

Truth 9: Antimicrobial therapy should be selected based on characteristics of the infection and patient-specific risk factors for different organisms, and the severity of the patients illness. Most uncomplicated cellulitis will not need combination therapy with a beta- lactam and anti- MRSA anti-infective5,61

a. Cellulitis that is diffuse or unassociated with a defined portal, eryhematosus, and non-purulent with extensive lymphangitic spread is most commonly caused by Streptococcal species35
b. Cellulitis with abscess that is fluctuant, has penetrating trauma, and/or open ulcer with surrounding erythema is more likely caused by Staphylococcus than by Streptococcus species28
c. Dicloxacillin and cephalexin exhibit antimicrobial activity against MSSA and Streptococcus2,3,9,10
d. For patients with risk factors for MRSA, trimethoprim-sulfamethoxazole has activity against most MRSA strains; however, activity against Streptococcal spp. is variable. One recent study found it very active for beta-hemolytic strep. Alternative agents (including combination therapy) should be considered for the treatment of possible Streptococcal infection. Doxycycline is not active for beta-hemolytic streptococci.

e. Clindamycin has activity against Streptococcus, MSSA, and some strains of MRSA, although the sensitivity to MRSA is declining (see myth 10).

**Myth 10: Clindamycin is the most effective empiric antibiotic for CA-MRSA**

Truth 10: Clindamycin may exhibit inducible resistance to MRSA, and caution should be used when prescribing this agent for CA-MRSA. Microbiology labs are now routinely testing for this inducibility, and will report clindamycin as resistant. Resistance rates to clindamycin of greater than 35% have been reported for CA-MRSA, and 100% of H-MRSA are resistant. Trimethoprim-sulfamethoxazole and doxycycline resistance rates remain at less than 10% in most communities. Clindamycin also has the highest odds ratio for the development of Clostridium difficile.

**References for Appendix A**


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Skin, Skin Structure, and Soft Tissue Infection – Adult - Inpatient/Ambulatory Clinical Practice Guideline

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