

# Skin, Skin Structure, and Soft Tissue Infection Diagnosis and Treatment – Adult – Inpatient/Ambulatory Clinical Practice Guideline

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## Executive Summary

### Guideline Overview:

This clinical practice guideline is designed to lead prescribers through the evaluation, diagnosis, and treatment of skin, skin structure, and soft tissue infection (SSTI). It will focus on difficult diagnostic and treatment scenarios and is intended for use throughout the continuum of care, including outpatient clinics, emergency department, and inpatient wards.

### Key Practice Recommendations

1. Consider alternative diagnoses, such as DVT and venous stasis dermatitis in patients. In obese patients, consider venous insufficiency lymphedema. Avoid antibiotics in these non-SSTI diagnoses. (Class I, Level A)
2. *Staphylococcus* and *Streptococcus* species are the most common causes of SSTI. MRSA nasal AND pooled axilla/groin PCR should be obtained for patients with risk factors for MRSA or to reduce the probability that infection is caused by MRSA. (Class I, Level B)
3. Gram-negative bacteria, especially *Pseudomonas* species, are unlikely the cause of an SSTI. Anti-Pseudomonas treatment should be used conservatively in clinically stable patients. (Class IIb, Level C)
4. Non-pharmacologic treatments, including elevation and compression of lower extremities, should be used whenever possible. (Class I, Level C)
5. Erythematous area marked by pen may extend beyond margins during the first 48 hours. This should not be considered treatment failure if the patient is otherwise improving. (Class I, Level C)
6. Incision and drainage, if possible, should be performed for abscesses. (Class I, Level A)
7. Outpatient management of *Streptococcus* or MSSA can be achieved with cephalexin or dicloxacillin. (Class I, Level A)
  - a. If MRSA is suspected, antibiotic coverage with TMP/SMX or doxycycline/minocycline PLUS amoxicillin is recommended. (Class I, Level A)
8. Inpatient management of *Streptococcus* or MSSA can be achieved with cefazolin or oxacillin. (Class I, Level A)
  - a. If MRSA is suspected, additional antibiotic coverage with vancomycin is recommended and MRSA PCRs should be obtained. (Class I, Level A)
  - b. If Gram-negative organisms are suspected, the selection of ceftriaxone is reasonable. (Class IIa, Level B)

### Companion Documents

- [Renal Function-based Dose Adjustments – Adult – Inpatient – Clinical Practice Guideline](#)
- [Antibiotics for the Treatment of Gram-negative Infections – Adult – Inpatient Clinical Practice Guideline](#)
- [Intravenous Vancomycin Use – Adult – Inpatient Clinical Practice Guideline](#)
- [Treatment of Patients with Reported Allergies to Beta-Lactam Antibiotics – Adult – Inpatient Clinical Practice Guideline](#)
- [Medication Route Interchange – Adult – Inpatient – Clinical Practice Guideline](#)
- [UWHC Antibiograms](#)

## **Scope**

### **Disease/Condition:**

This clinical practice guideline is designed to lead prescribers through the evaluation, diagnosis, and treatment of skin, skin structure, and soft tissue infection (SSTI).

### **Clinical Specialty**

All medical specialties

### **Intended Users**

Physicians, Advanced Practice Providers, Nurses, and Pharmacists

### **Objective**

To optimize diagnosis, evaluation, treatment, and antibiotic utilization for the treatment of SSTI.

### **Target Population**

Patients with signs and symptoms of skin, skin structure, or soft tissue infections cared for in outpatient clinics, the emergency department, and inpatient wards.

### **Interventions and Practices Considered**

Diagnosis of skin, skin structure, or soft tissue infections; treatment of skin, skin structure, or soft tissue infections; and avoidance of antimicrobial use in patients without skin, skin structure, or soft tissue infections following evaluation.

### **Major Outcomes Considered**

1. Number of MRSA PCRs ordered for patients being managed for SSTI.
  - a. Discontinuation of anti-MRSA therapy with negative PCR results.
2. Successful management of skin, skin structure, or soft tissue infections measured by resolution of infection.
  - a. Avoidance of treatment failure as indicated by additional courses of antimicrobials.
3. Avoidance of antimicrobial use in patients without skin, skin structure, or soft tissue infections
4. Antibiotic utilization (by class) for SSTI treatment.

### **Methodology**

Electronic database searches (i.e., PUBMED) were conducted and workgroup members to collect evidence for review. Expert opinion, clinical experience, and regard for patient safety/experience were also considered during discussions of the evidence. A modified Grading of Recommendations Assessment, Development, and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology (Figure 1) has been used to assess the Quality and Strength of the Evidence in this Clinical Practice Guideline.<sup>1</sup>

Figure 1. Quality of Evidence and Strength of Recommendation Grading Matrix

|   |  | SIZE OF TREATMENT EFFECT →   |   |  |   |
|---|--|--|---|--|---|
|   |  | CLASS I<br><i>Benefit &gt;&gt;&gt; Risk</i><br>Procedure/Treatment <b>SHOULD</b> be performed/administered   | CLASS IIa<br><i>Benefit &gt;&gt; Risk</i><br>Additional studies with <i>focused objectives needed</i><br><b>IT IS REASONABLE</b> to perform procedure/administer treatment  | CLASS IIb<br><i>Benefit ≥ Risk</i><br>Additional studies with <i>broad objectives needed; additional registry data would be helpful</i><br>Procedure/Treatment <b>MAY BE CONSIDERED</b>                  | CLASS III<br><i>Risk ≥ Benefit</i><br>Procedure/Treatment should <b>NOT</b> be performed/administered <b>SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL</b>   |
| ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT | LEVEL A<br>Multiple populations evaluated*<br>Data derived from multiple randomized clinical trials or meta-analyses   | <ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Sufficient evidence from multiple randomized trials or meta-analyses</li> </ul> | <ul style="list-style-type: none"> <li>Recommendation in favor of treatment or procedure being useful/effective</li> <li>Some conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>      | <ul style="list-style-type: none"> <li>Recommendation's usefulness/efficacy less well established</li> <li>Greater conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>      | <ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>Sufficient evidence from multiple randomized trials or meta-analyses</li> </ul> |
|   | LEVEL B<br>Limited populations evaluated*<br>Data derived from a single randomized trial or nonrandomized studies      | <ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Evidence from single randomized trial or nonrandomized studies</li> </ul>       | <ul style="list-style-type: none"> <li>Recommendation in favor of treatment or procedure being useful/effective</li> <li>Some conflicting evidence from single randomized trial or nonrandomized studies</li> </ul> | <ul style="list-style-type: none"> <li>Recommendation's usefulness/efficacy less well established</li> <li>Greater conflicting evidence from single randomized trial or nonrandomized studies</li> </ul> | <ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>Evidence from single randomized trial or nonrandomized studies</li> </ul>       |
|   | LEVEL C<br>Very limited populations evaluated*<br>Only consensus opinion of experts, case studies, or standard of care | <ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Only expert opinion, case studies, or standard of care</li> </ul>               | <ul style="list-style-type: none"> <li>Recommendation in favor of treatment or procedure being useful/effective</li> <li>Only diverging expert opinion, case studies, or standard of care</li> </ul>                | <ul style="list-style-type: none"> <li>Recommendation's usefulness/efficacy less well established</li> <li>Only diverging expert opinion, case studies, or standard of care</li> </ul>                   | <ul style="list-style-type: none"> <li>Recommendation that procedure or treatment is not useful/effective and may be harmful</li> <li>Only expert opinion, case studies, or standard of care</li> </ul>               |
| Suggested phrases for writing recommendations*        |  | should<br>is recommended<br>is indicated<br>is useful/effective/beneficial   | is reasonable<br>can be useful/effective/beneficial<br>is probably recommended<br>or indicated  | may/might be considered<br>may/might be reasonable<br>usefulness/effectiveness is unknown/unclear/uncertain<br>or not well established   | is not recommended<br>is not indicated<br>should not<br>is not useful/effective/beneficial<br>may be harmful  |

## Definitions<sup>2,3</sup>

1. Carbuncle: infection of several adjacent hair follicles producing a coalescent inflammatory mass with pus draining from multiple follicular orifices
2. Cellulitis: diffuse, spreading skin infection of the deeper dermis as well as subcutaneous fat that lacks distinctive anatomical features. It may be accompanied by lymphangitis and inflammation of the regional lymph nodes
3. Complicated infection: infection involving deeper soft tissues necessitating major abscesses, or an underlying disease state that complicates the response to treatment (e.g. diabetes mellitus)
4. Cutaneous abscess: collection of pus within the dermis and deeper skin tissues which is usually painful, tender, and has fluctuant red nodules often surmounted by a pustule and surrounded by a rim of erythematous swelling
5. Erysipelas: diffuse, spreading skin infection of the upper dermis including the superficial lymphatics. Lesions are fiery red, tender, painful plaques with well-demarcated edges that are raised above the level of the surrounding skin. It may be accompanied by lymphangitis and inflammation of the regional lymph nodes
6. Furuncle: infection of the hair follicle in which suppuration extends through the dermis into the subcutaneous tissue where a small abscess forms
7. Impetigo: skin infection consisting of discrete purulent lesions
8. Necrotizing fasciitis: subcutaneous infection that tracks along fascial planes and extends well beyond the superficial signs of infection, such as erythema or other skin changes
9. Skin and skin structure infection (SSSI): infection of skin and its supporting structures, but excluding deep tissues such as fascia and muscle and necrotizing infections (term utilized by Food and Drug Administration for therapeutic trials)
10. Skin and soft tissue infection (SSTI): infection involving the skin, subcutaneous connective tissue, fascia, or muscle
11. Systemic inflammatory response syndrome (SIRS):<sup>4</sup> a clinical response to a non-specific insult of either infectious or noninfectious origin. Two of the following variables:
  - a. Fever of more than 38°C (100.4°F) or less than 36°C (96.8°F)
  - b. Heart rate of more than 90 beats per minute
  - c. Respiratory rate of more than 20 breaths per minute or arterial carbon dioxide tension (PaCO<sub>2</sub>) of less than 32mm Hg or the requirement of invasive mechanical ventilation for an acute process
  - d. Abnormal white blood cell count (>12,000/μL or < 4,000/μL or >10% immature [band] forms)
12. Uncomplicated infection: simple abscess, such as impetiginous lesions, furuncles, and cellulitis

## Introduction

Skin, skin structure, and soft tissue infections are common in hospitalized patients; many opportunities for antimicrobial stewardship including cost-effective diagnosis and treatment exist.<sup>5,6,7</sup> Development of cellulitis algorithm has demonstrated reduction in institutional and medication costs, decreased length of stay without increasing length of stay.<sup>8</sup> Although staphylococci and streptococci are the causative organisms in the majority of cases of community-based skin, skin structure, and soft tissue infections, many patients receive broad-spectrum Gram-negative and anaerobic therapy and are treated longer than the recommended 7 to 14 days. Additionally, unnecessary low-yield laboratory testing (erythrocyte sedimentation rate) and radiographic imaging (plain film x-rays) are being ordered for patients despite limited utility for uncomplicated SSTI. The intent of this guideline is to guide treatment towards appropriate antibiotics, duration of treatment, and reduce excessive lab and radiographic testing.

## Recommendations

### 1. Presentation and diagnosis

- 1.1. 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.<sup>2,3,9,10</sup> (Class I, Level A)
  - 1.1.1. Diagnoses of deep venous thrombosis, venous stasis dermatitis, venous insufficiency, lymphedema, contact dermatitis, gout, herpes zoster, acute lipodermatosclerosis, septic arthritis, and osteomyelitis should be excluded.<sup>2,3,9,10</sup> (Class I, Level A)
- 1.2. In most cases of uncomplicated SSTI, erythrocyte sedimentation rate and radiographic imaging studies are of questionable diagnostic use and should not be obtained.<sup>9,11-14</sup> (Class III, Level B)
- 1.3. Obtaining laboratory studies should not delay empiric antimicrobial/surgical therapy. (Class I, Level A)
- 1.4. The majority of cellulitis cases do not lead to systemic infection. In the absence of systemic infection, the utility of blood/wound cultures, needle aspirations, skin biopsies, complete blood count with differential, creatinine, bicarbonate, creatine phosphokinase, and C-reactive protein levels is not well established and should not be obtained.<sup>2</sup> (Class III, Level B)
  - 1.4.1. Aspiration of the skin is not helpful in 75-80% of cases of cellulitis.<sup>15-23</sup>
  - 1.4.2. Results of blood cultures are positive in fewer than 5% of cases.<sup>24</sup>

### 2. Epidemiology

- 2.1. *Staphylococcus* spp.
  - 2.1.1. Furuncles, carbuncles, and abscesses are usually caused by *Staphylococcus aureus*.<sup>25-27</sup>
  - 2.1.2. Cellulitis or abscess that is fluctuant, has penetrating trauma, and/or with open ulcer with surrounding erythema is more likely caused by *Staphylococcus* species than *Streptococcus* species.<sup>25-28</sup>
    - 2.1.2.1. Risk factors for community-acquired MRSA (CA-MRSA) include:<sup>29</sup>
      - 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

- 2.1.2.2. Risk factors for hospital-acquired MRSA (HA-MRSA):<sup>30</sup>
  - 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
  - Hemodialysis
  - HIV infection/immunosuppression
- 2.1.3. MRSA nasal AND pooled axilla/groin PCR should be obtained for patients with risk factors for MRSA or to reduce the probability that infection is caused by MRSA.<sup>31-34</sup> (Class I, Level B)
  - 2.1.3.1. If MRSA PCRs are negative, deescalating to narrower spectrum antibiotics not covering MRSA is reasonable. (Class IIa, Level B)
- 2.2. *Streptococcus* spp.
  - 2.2.1. Impetigo, erysipelas, and cellulitis are commonly caused by Group A or other beta-hemolytic *Streptococcus* (but *Staphylococcus aureus* may also be present, see sections above describing MRSA risk factors).<sup>35,36</sup>
  - 2.2.2. Cellulitis that is diffuse or unassociated with a defined portal, erythematous, and non-purulent WITH lymphangitic spread is more commonly caused by *Streptococcus* species than *Staphylococcus* species.<sup>35</sup>
- 2.3. Gram-negative organisms
  - 2.3.1. The majority of skin, skin structure, and soft tissue infections (60-90%) are caused by Gram-positive organisms.<sup>25-28,35,37,38</sup>
    - 2.3.1.1. Complicating factors that increase suspicion of Gram-negative organisms:<sup>9</sup>
      - Infection caused while swimming
      - Infections near groin or rectum
      - Ulcers soaked in water
      - Diabetes mellitus
      - Vascular insufficiency
      - Periorbital cellulitis
      - Immunosuppression
      - Healthcare system contact within the past 90 days
- 2.4. *Pseudomonas* spp.
  - 2.4.1. Only 5% of chronic diabetic foot infections involve *Pseudomonas* spp.<sup>39</sup>
    - 2.4.1.1. Risk factors for infections caused by *Pseudomonas aeruginosa*:<sup>39</sup>
      - Nosocomial or healthcare-associated infection
      - Soaking of open wound in tap water
- 2.5. Anaerobes
  - 2.5.1. Risk factors for infections caused by anaerobic organisms.<sup>2,3,9,25-28,35,37,38</sup>
    - Diabetes mellitus
    - Vascular insufficiency
    - Necrotizing fasciitis
    - Surgical procedures involving the bowel or penetrating abdominal trauma
    - Decubitus ulcer
    - Perianal abscess
    - Site of injection in injection drug users
    - Spread from vulvovaginal infection
    - Human bite wound

### 3. General principles for treatment

- 3.1. Patients should elevate the affected area in order to quicken improvement by promoting gravity drainage of the edema and inflammatory substances. (Class I, Level C)
- 3.2. The erythematous area should be outlined with pen daily. (Class I, Level C)



- 3.2.1. **The erythema may extend beyond pen margins within the first 24 to 36 hours without representing treatment failure.**
- 3.3. If lower extremities are edematous, ACE wrap should be applied from toes to thighs every eight hours for lower extremity infections to assist in reduction of lymphedema. (*Class I, Level C*)
- 3.4. Blood culture results are positive in fewer than 5% of cases of outpatient cellulitis and should not routinely be obtained for patients being treated as outpatients.<sup>24</sup> (*Class I, Level B*)
  - 3.4.1. If a patient is hospitalized, blood cultures should usually be considered. (*Class I, Level C*)
- 3.5. Needle aspiration cultures and punch biopsy specimens provide variable results (5-30% yield) and should not routinely be obtained for outpatients.<sup>15-23</sup> (*Class I, Level B*)
  - 3.5.1. Needle aspiration may be considered for hospitalized patients and immunocompromised hosts where the diagnostic yield is higher.<sup>2</sup> (*Class I, Level B*)

#### 4. Specific disease state management

##### 4.1. Impetigo/erysipelas/cellulitis – superficial/subcutaneous cellulitis

- 4.1.1. Cellulitis that is diffuse or unassociated with a defined portal, erythematous, and non-purulent with lymphangitic spread is most commonly caused by *Streptococcus* species.<sup>35</sup>
- 4.1.2. Cellulitis or abscess that is fluctuant, has penetrating trauma, and/or with open ulcer with surrounding erythema is more likely caused by *Staphylococcus* than by *Streptococcus* species.<sup>28</sup>
  - 4.1.2.1. See *Epidemiology* section for MRSA risk factors.
- 4.1.3. Risk factors for developing impetigo, 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.<sup>40</sup>
- 4.1.4. An antistreptolysin O (ASO) titer is indicated as an adjunct for diagnosis of certain beta-hemolytic streptococcal infections.<sup>2</sup> (*Class I, Level B*)
- 4.1.5. MRSA nasal and pooled axilla/groin PCR should be obtained for patients with risk factors for MRSA or patients receiving anti-MRSA therapy.<sup>31-34</sup> (*Class I, Level B*)
  - 4.1.5.1. If MRSA PCRs are negative, deescalating to narrower spectrum antibiotics not covering MRSA is reasonable. (*Class IIa, Level B*)
- 4.1.6. For patients with erythematous, non-purulent cellulitis with extensive lymphangitic spread, the recommended antimicrobial treatments directed at *Streptococcus* species only are listed in *Table 1* (antibiotics are listed in order of preference).<sup>2,3,9,10</sup> (*Class I, Level A*)
- 4.1.7. For superficial or subcutaneous cellulitis or abscess that is fluctuant, has penetrating trauma, and/or with open ulcer with surrounding erythema, the recommended antimicrobial treatments directed to cover *Streptococcus* spp. and MSSA with a low risk for MRSA are listed in *Table 2* (antibiotics are listed in order of preference).<sup>2,3,9,10</sup> (*Class I, Level A*)
- 4.1.8. For cellulitis or abscess that is fluctuant, has penetrating trauma, and/or with open ulcer with surrounding erythema, the recommended antimicrobial treatment directed to cover *Streptococcus* spp. and *Staphylococcus* spp. are listed in *Table 3* (antibiotics are listed in order of preference).<sup>2,3,9,10</sup> (*Class I, Level A*)
  - 4.1.8.1. For patients requiring IV therapy or for MRSA infections, vancomycin IV with a goal trough concentration of 10-15 mcg/mL is reasonable.<sup>2,3,9,10</sup> (*Class IIa, Level B*)
    - 4.1.8.1.1. Refer to [Intravenous Vancomycin Use – Adult – Inpatient Clinical Practice Guideline](#)
  - 4.1.8.2. Ceftaroline, daptomycin, or linezolid can be effective alternative agents in specific patient types and if the skin infection is the rate limiting factor for hospital discharge.<sup>2,3,9,10,41-43</sup> (*Class IIa, Level B*)
  - 4.1.8.3. Long-acting lipoglycopeptide antibiotics, such as oritavancin or dalbavancin, are indicated to facilitate discharging patients or for outpatient management.<sup>44,45</sup> (*Class I, Level B*)
    - 4.1.8.3.1. Insurance coverage should be evaluated to ensure coverage of medications.
  - 4.1.8.4. Tedizolid is reasonable for outpatient management.<sup>46,47</sup> (*Class IIa, Level B*)



4.1.8.4.1. Tedizolid should not be used in neutropenic patients.<sup>48</sup> (Class III, Level B)

- 4.1.9. For cellulitis or abscess that is fluctuant, has penetrating trauma, and/or with open ulcer with surrounding erythema, the recommended antimicrobial treatment directed to cover *Streptococcus* spp, MSSA, MRSA, and Gram-negative organisms (except *Pseudomonas* spp.) are listed in Table 4 (antibiotics are listed in order of preference).<sup>2,3,9,10,41-43</sup> (Class IIa, Level B)
- 4.1.10. Refer to [Treatment of Patients with Reported Allergies to Beta-Lactam Antibiotics – Adult – Inpatient Clinical Practice Guideline](#) for more information in patients with reported allergies.
- 4.1.11. Clindamycin may exhibit inducible resistance to MRSA; caution should be used when prescribing this agent for CA-MRSA.<sup>2,3,9,10</sup> (See [UWHC Antibiograms](#)) (Class IIa, Level B)
- 4.1.12. Trimethoprim/sulfamethoxazole has activity against most MRSA strains; however, activity against *Streptococcus* spp. is variable. Alternative agents (including combination therapy) should be considered for the treatment of possible streptococcal infection. (Class I, Level C)
- 4.1.13. For outpatient management with oral treatment, five days of oral antibiotic therapy is usually as effective as a ten-day course. A duration of therapy of five days should be used depending on initial response.<sup>7</sup> (Class IIa, Level A)
- 4.1.14. For treatment of erysipelas/cellulitis initially requiring IV antimicrobial therapy or hospitalization, total antibiotic treatment duration of seven days is usually appropriate and total duration of antimicrobial therapy should generally be considered for this duration for most patients.<sup>2,9,10</sup> (Class IIb, Level C)

**Table 1. Antimicrobial agents directed at *Streptococcus* spp.** (erythematous, non-purulent SSTI with lymphangitic spreading)<sup>A,B</sup>

| PO   | IV  |
|--|---|
| <ul style="list-style-type: none"> <li>• Amoxicillin 500 mg PO TID<sup>C</sup></li> <li>• Cephalexin 500 mg PO QID<sup>C</sup></li> <li>• Clindamycin 300-450 mg PO TID-QID</li> </ul> | <ul style="list-style-type: none"> <li>• Penicillin G 4 million units IV Q4hr<sup>C</sup></li> <li>• Cefazolin 1-2 g IV Q8hr<sup>C</sup></li> <li>• Clindamycin 600-900 mg IV Q6-8hr</li> </ul> |

<sup>A</sup> Treatment for 5-7 days duration is usually sufficient depending on initial response

<sup>B</sup> The activity of TMP/SMX is not sufficient to recommend monotherapy treatment of *Streptococcus* spp. infection

<sup>C</sup> Requires renal dosing adjustment

**Table 2. Antimicrobial agents directed at *Streptococcus* spp. and MSSA** (abscess, fluctuance, penetrating trauma, and/or open ulcer with surrounding erythema)<sup>A</sup>

| PO   | IV   |
|--|--|
| <ul style="list-style-type: none"> <li>• Dicloxacillin 500 mg PO QID<sup>B</sup></li> <li>• Cephalexin 500 mg PO QID<sup>B</sup></li> <li>• Clindamycin 300-450 mg PO TID-QID</li> </ul> | <ul style="list-style-type: none"> <li>• Oxacillin 1-2 g IV Q4hr</li> <li>• Cefazolin 1-2 g IV Q8hr<sup>B</sup></li> <li>• Clindamycin 600-900 mg IV Q6-8hr</li> </ul> |

<sup>A</sup> Treatment for 5-7 days duration is usually sufficient depending on initial response

<sup>B</sup> Requires renal dosing adjustment

**Table 3. Antimicrobial agents directed at *Streptococcus* spp., MSSA, and MRSA** (abscess, fluctuance, penetrating trauma, and/or open ulcer with surrounding erythema and patient has risk factors for, history of, or confirmed MRSA)

| PO   | IV   |
|--|--|
| <ul style="list-style-type: none"> <li>Trimethoprim-sulfamethoxazole 160-800 mg to 320-1600 mg PO BID<sup>A</sup> <b>PLUS</b> consideration of an antimicrobial agent from <i>Table 1</i> for <i>Streptococcus</i> coverage</li> <li>Doxycycline/minocycline 100 mg PO BID <b>PLUS</b> consideration of an antimicrobial agent <i>Table 1</i> for <i>Streptococcus</i> coverage</li> <li>Clindamycin 300-450 mg PO TID-QID</li> <li>Linezolid 600 mg PO BID</li> </ul> | <ul style="list-style-type: none"> <li>Vancomycin IV<sup>A</sup> (goal trough concentration 10-15 mcg/mL)</li> <li>Clindamycin 600-900 mg IV Q6-8hr</li> <li>Ceftaroline 600 mg IV Q12hr<sup>A</sup></li> <li>Daptomycin 4 mg/kg IV Q24hr<sup>A</sup></li> <li>Linezolid 600 mg IV Q12hr</li> <li>Oritavancin 1200 mg IV once</li> </ul> |

<sup>A</sup> Requires renal dosing adjustment

**Table 4. Antimicrobial agents directed at *Streptococcus* spp., MSSA, MRSA, and Gram-negatives (excepting *P. aeruginosa*)** (abscess, fluctuance, penetrating trauma, and/or open ulcer with surrounding erythema and risk factors for gram-negatives)

| PO   |   |
|--|---|
| <i>Streptococcus</i> spp., MRSA, Gram-negative (excepting <i>P. aeruginosa</i> )   | <i>Streptococcus</i> spp., MSSA, Gram-negative (excepting <i>P. aeruginosa</i> ); MRSA low suspicion after testing  |
| <ul style="list-style-type: none"> <li>(Doxycycline/minocycline 100 mg PO BID OR Trimethoprim-sulfamethoxazole 160-800 to 320-1600 mg PO BID<sup>A</sup>) <b>PLUS</b> Moxifloxacin 400 mg PO daily</li> <li>Clindamycin 300-350 mg PO TID-QID <b>PLUS</b> (Cefpodoxime 400 mg PO BID<sup>A</sup> OR Cefuroxime 500 mg PO BID<sup>A</sup>)</li> <li>Linezolid 600 mg PO BID <b>PLUS</b> Moxifloxacin 400 mg PO daily</li> </ul> | <ul style="list-style-type: none"> <li>Cefuroxime 500 mg PO BID<sup>A</sup></li> <li>Cefpodoxime 400 mg PO BID<sup>A</sup></li> <li>Moxifloxacin 400 mg PO daily</li> </ul> |
| IV   |   |
| <i>Streptococcus</i> spp., MRSA, Gram-negative (excepting <i>P. aeruginosa</i> )   | <i>Streptococcus</i> spp., MSSA, Gram-negative (excepting <i>P. aeruginosa</i> ); MRSA low suspicion after testing  |
| <ul style="list-style-type: none"> <li>Vancomycin IV<sup>A</sup> (trough goal concentration 10-15 mcg/mL) <b>PLUS</b> (Ceftriaxone 1-2 g IV Q24hr OR Cefazolin 1-2 g IV Q8hr<sup>A</sup>)</li> <li>Ceftaroline 600 mg IV Q12hr<sup>A</sup></li> <li>Daptomycin 4 mg/kg IV Q24hr<sup>A</sup> <b>PLUS</b> (Ceftriaxone 1-2 g IV Q24hr OR Cefazolin 1-2 g IV Q8hr<sup>A</sup>)</li> </ul>   | <ul style="list-style-type: none"> <li>Ceftriaxone 1-2 g IV Q24hr</li> <li>Cefazolin 1-2 g IV Q8hr<sup>A</sup></li> <li>Moxifloxacin 400 mg IV Q24hr</li> </ul>             |

<sup>A</sup> Requires renal dosing adjustment

#### 4.2. Cutaneous abscess with or without cellulitis/furuncles/carbuncles

- 4.2.1. These infections are typically polymicrobial, including *Staphylococcus aureus*.<sup>25-27</sup>
- 4.2.2. Risk factors for developing cutaneous abscesses include diabetes mellitus, vascular insufficiency, or traumatic injury.<sup>25-27</sup>
- 4.2.3. Primary treatment should be incision and drainage.<sup>2,3,9</sup> (*Class I, Level A*)
  - 4.2.3.1. For simple abscesses and boils (fewer than 5 cm in diameter of erythema and abscess), incision and drainage alone is likely adequate as sole treatment and **no treatment with antibiotics may be reasonable**.<sup>29</sup> (*Class IIb, Level B*)
  - 4.2.3.2. 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 is probably recommended.<sup>29</sup> (Class IIa, Level B)
- 4.2.4. Patients should be assessed for risk factors for MRSA, Gram-negatives, *Pseudomonas* species, and anaerobes (see *Epidemiology* section). (Class I, Level C)
- 4.2.4.1. If the decision is made to treat with antimicrobials, MRSA nasal and pooled axilla/groin PCR should be obtained for patients with risk factors for MRSA.<sup>31-34</sup> (Class I, Level B)
- 4.2.4.1.1. If MRSA PCRs are negative, deescalation to narrower spectrum antimicrobials not covering MRSA is reasonable. (Class IIa, Level B)
- 4.2.5. If the decision is made to treat with antimicrobials, coverage should be directed at *Staphylococcus* species, the recommended treatment agents are listed in *Table 3* (antibiotics are listed in order of preference).<sup>2,3,9,10</sup> (Class IIa, Level B)
- 4.2.5.1. For patients requiring IV therapy or for HA-MRSA infections, vancomycin IV with trough goal concentration of 10-15 mcg/mL is reasonable.<sup>2,3,9,10</sup> (Class IIa, Level B)
- 4.2.5.1.1. Refer to [Intravenous Vancomycin Use – Adult – Inpatient Clinical Practice Guideline](#)
- 4.2.5.2. Ceftaroline, daptomycin, or linezolid or tedizolid can be effective alternative agents in specific patient types and if the skin infection is the rate limiting factor for hospital discharge.<sup>2,3,9,10,41-43</sup> (Class IIa, Level B)
- 4.2.5.3. Long-acting lipoglycopeptide antibiotics, such as oritavancin or dalbavancin, are indicated to facilitate discharging patients or for outpatient management.<sup>44,45</sup> (Class I, Level B)
- 4.2.5.3.1. Insurance coverage should be evaluated to ensure coverage of medications.
- 4.2.5.4. Tedizolid is reasonable for outpatient management.<sup>46,47</sup> (Class IIa, Level B)
- 4.2.5.4.1. Tedizolid should not be used in neutropenic patients.<sup>48</sup> (Class III, Level B)
- 4.2.6. If the patient has risk factors for Gram-negative organisms, the recommended antimicrobial treatment directed to cover *Streptococcus* spp, MSSA, MRSA, and Gram-negative organisms (excepting *Pseudomonas aeruginosa*) are listed in *Table 4* (antibiotics are listed in order of preference).<sup>2,3,9,10,41-43</sup> (Class IIa, Level B)
- 4.2.7. If the patient has risk factors for anaerobic organisms, treatment options directed to cover *Streptococcus* spp., MSSA, MRSA, Gram-negative organisms (excepting *Pseudomonas aeruginosa*), and anaerobes are listed in *Table 5* (treatment regimens are listed in order of preference).<sup>2,3,9,10,41-43</sup> (Class IIa, Level B)
- 4.2.8. If the patient has risk factors for *Pseudomonas aeruginosa*, treatment options directed to cover *Streptococcus* spp., MSSA, MRSA, and Gram-negatives (including *Pseudomonas aeruginosa*), and anaerobes are listed in *Table 6* (treatment regimens are listed in order of preference).<sup>2,3,9,10</sup> (Class IIa, Level B)
- 4.2.9. Refer to [Treatment of Patients with Reported Allergies to Beta-Lactam Antibiotics – Adult – Inpatient Clinical Practice Guideline](#) for more information in patients with reported allergies.
- 4.2.10. For treatment of cutaneous abscess/furuncles/carbuncles, if incision and drainage is not sufficient and antibiotic therapy is used, antibiotic duration not exceeding 14 days may be considered.<sup>2,3,7,9,37</sup> (Class IIb, Level B)

**Table 5. Antimicrobial agents directed at *Streptococcus* spp., MSSA, MRSA, Gram-negatives (excepting *P. aeruginosa*), and anaerobes (abscess, fluctuance, penetrating trauma, and/or open ulcer with surrounding erythema and risk factors for anaerobes)**

| <b>PO</b>  |  |
|--|--|
| <b><i>Streptococcus</i> spp., MRSA, Gram-negative (excepting <i>P. aeruginosa</i>) and anaerobes</b>   | <b><i>Streptococcus</i> spp., MSSA, Gram-negative (excepting <i>P. aeruginosa</i>), anaerobes; MRSA low suspicion after testing</b>  |
| <ul style="list-style-type: none"> <li>• (Trimethoprim-sulfamethoxazole 160-800 to 320-1600 mg PO BID<sup>A</sup> OR Doxycycline 100 mg PO BID) <b>PLUS</b> (Augmentin XR<sup>A,B</sup> 2000-125 mg PO BID OR Moxifloxacin 400 mg PO daily)</li> <li>• (Trimethoprim-sulfamethoxazole 160-800 to 320-1600 mg PO BID<sup>A</sup> OR Doxycycline 100 mg PO BID) <b>PLUS</b> (Cefuroxime 500 mg PO BID<sup>A</sup> OR Cefpodoxime 400 mg PO BID<sup>A</sup>) <b>PLUS</b> Metronidazole 500 mg PO TID</li> <li>• Clindamycin 300-450 mg PO TID-QID <b>PLUS</b> (Cefpodoxime 400 mg PO BID<sup>A</sup> OR Cefuroxime 500 mg PO BID<sup>A</sup>)</li> <li>• Linezolid 600 mg PO BID PLUS Moxifloxacin 400 mg PO daily</li> </ul> | <ul style="list-style-type: none"> <li>• Augmentin XR<sup>A,B</sup> 2000-125 mg PO BID</li> <li>• Moxifloxacin 400 mg PO daily</li> </ul>  |
| <b>IV</b>  |  |
| <b><i>Streptococcus</i> spp., MRSA, Gram-negative (excepting <i>P. aeruginosa</i>) and anaerobes</b>   | <b><i>Streptococcus</i> spp., MSSA, Gram-negative (excepting <i>P. aeruginosa</i>), anaerobes; MRSA low suspicion after testing</b>  |
| <ul style="list-style-type: none"> <li>• Vancomycin IV<sup>A</sup> (goal trough concentration 10-15 mcg/mL) <b>PLUS</b> Ceftriaxone 1-2 g IV Q24hr <b>PLUS</b> Metronidazole 500 mg IV Q8hr</li> <li>• Ceftaroline 600 mg IV Q12hr<sup>A</sup> <b>PLUS</b> Metronidazole 500 mg IV Q8hr</li> <li>• Ertapenem 1 g IV Q24hr<sup>A</sup> <b>PLUS</b> Vancomycin IV<sup>A</sup> (goal trough concentration 10-15 mcg/mL)</li> <li>• Ertapenem 1 g IV Q24hr<sup>A</sup> <b>PLUS</b> Daptomycin 4 mg/kg IV Q24hr<sup>A</sup></li> <li>• Tigecycline 100 mg IV x 1, then 50 mg IV Q12hr</li> </ul>  | <ul style="list-style-type: none"> <li>• Ampicillin-sulbactam 1.5-3 g IV Q6hr<sup>A</sup></li> <li>• Ceftriaxone 1-2 g IV Q24hr <b>PLUS</b> Metronidazole 500 mg IV Q8hr</li> <li>• Cefoxitin 2 g IV Q6hr<sup>A</sup></li> <li>• Moxifloxacin 400 mg IV Q24hr</li> </ul> |

<sup>A</sup> Requires renal dosing adjustment

<sup>B</sup> Augmentin XR is the preferred agent, but based on ability to pay amoxicillin-clavulanate 500-125 mg PO BID with or without addition of amoxicillin 500-1000 mg PO QID may be considered as an alternative

**Table 6. Antimicrobial agents directed at *Streptococcus* spp., MSSA, MRSA, Gram-negatives (including *P. aeruginosa*), and anaerobes (abscess, fluctuance, penetrating trauma, and/or open ulcer with surrounding erythema and risk factors for *P. aeruginosa*)**

| <b>PO</b>  |  |
|--|--|
| <b><i>Streptococcus</i> spp., MRSA, Gram-negatives (including <i>P. aeruginosa</i>) and anaerobes</b>  | <b><i>Streptococcus</i> spp., MSSA, Gram-negatives (including <i>P. aeruginosa</i>) and anaerobes; MRSA low suspicion after testing</b>  |
| <ul style="list-style-type: none"> <li>• (Trimethoprim-sulfamethoxazole 160-800 to 320-1600 mg PO BID<sup>A</sup> OR Doxycycline 100 mg PO BID) <b>PLUS</b> Levofloxacin 500-750 mg PO daily<sup>A</sup> <b>PLUS</b> consider Metronidazole 500 mg PO TID</li> <li>• Clindamycin 300-450 mg PO TID-QID <b>PLUS</b> Ciprofloxacin 500 mg PO BID<sup>A</sup></li> <li>• Linezolid 600 mg PO BID <b>PLUS</b> Levofloxacin 500-750 mg PO daily<sup>A</sup> <b>PLUS</b> consider Metronidazole 500 mg PO TID</li> </ul> | <ul style="list-style-type: none"> <li>• Augmentin XR<sup>A,B</sup> 2000-125 mg PO BID <b>PLUS</b> Ciprofloxacin 500 mg PO BID<sup>A</sup></li> <li>• Levofloxacin 500-750 mg PO daily<sup>A</sup> <b>PLUS</b> Metronidazole 500 mg PO TID</li> <li>• Clindamycin 300-450 mg PO TID-QID <b>PLUS</b> Ciprofloxacin 500 mg PO BID<sup>A</sup></li> </ul> |
| <b>IV</b>  |  |
| <b><i>Streptococcus</i> spp., MRSA, Gram-negatives (including <i>P. aeruginosa</i>) and anaerobes</b>  | <b><i>Streptococcus</i> spp., MSSA, Gram-negatives (including <i>P. aeruginosa</i>) and anaerobes; MRSA low suspicion after testing</b>  |
| <ul style="list-style-type: none"> <li>• Piperacillin-tazobactam<sup>C</sup> <b>PLUS</b> Vancomycin IV (goal trough concentration 10-15 mcg/mL)</li> <li>• Cefepime<sup>C</sup> <b>PLUS</b> Vancomycin IV (goal trough concentration 10-15 mcg/mL) <b>PLUS</b> Metronidazole 500 mg IV Q8hr</li> <li>• Meropenem<sup>C</sup> <b>PLUS</b> Vancomycin IV (goal trough concentration 10-15 mcg/mL)</li> </ul>   | <ul style="list-style-type: none"> <li>• Piperacillin-tazobactam<sup>C</sup></li> <li>• Cefepime<sup>C</sup> PLUS Metronidazole 500 mg IV Q8hr</li> <li>• Meropenem<sup>C</sup></li> </ul>   |

<sup>A</sup> Requires renal dosing adjustment

<sup>B</sup> Augmentin XR is the preferred agent, but based on ability to pay amoxicillin-clavulanate 500-125 mg PO BID with or without addition of amoxicillin 500-1000 mg PO QID may be considered as an alternative

<sup>C</sup> See [Antibiotics for the Treatment of Gram-negative Infections – Adult – Inpatient Clinical Practice Guideline](#) for dosing guidance

#### 4.3. Infection caused by animal (dog and cat) bites

4.3.1. Aerobic and anaerobic bacteria such as *Pasteurella*, *Staphylococcus aureus*, *Bacteroides tectum*, *Fusobacterium* species, *Capnocytophaga* species, and *Porphyromonas* species are the likely pathogens.<sup>2,3,9,10</sup>

4.3.2. **Not all bite wounds become infected or require treatment.** Risk factors for bite wounds that are at high risk of infection include a deep puncture, crushing injury, cat bites, or heavy contamination.<sup>2,3,9,10</sup> (Class I, Level C)

4.3.3. See Table 7 for antimicrobial agents that are reasonable for treatment.<sup>2,3,9,10</sup> (Class IIa, Level B)

4.3.4. Refer to [Treatment of Patients with Reported Allergies to Beta-Lactam Antibiotics – Adult – Inpatient Clinical Practice Guideline](#) for more information in patients with reported allergies.

4.3.5. Total antibiotic treatment duration of seven days may be reasonable and antimicrobial therapy limited to this duration may be considered for most patients.<sup>2,9,10</sup> (Class IIb, Level C)

4.3.6. The need for tetanus vaccine and rabies vaccine and/or immune globulin should be assessed. (Class I, Level C)

#### 4.4. Infection caused by human bites

4.4.1. Aerobic and anaerobic bacteria such as streptococci, *Staphylococcus aureus*, *Eikenella corrodens*, *Fusobacterium*, *Peptostreptococcus*, *Prevotella*, and *Porphyromonas* are the likely pathogens causing infection.<sup>2,3,9,10</sup>

- 4.4.2. **Not all bite wounds become infected or require treatment.** Risk factors for bite wounds that are at high risk of infection include a deep puncture, crushing injury, heavy contamination, or location on a hand.<sup>2,3,9,10</sup> (Class I, Level C)
- 4.4.2.1. Due to resistance of *Eikenella corrodens* to first-generation cephalosporins, macrolides, clindamycin, and aminoglycosides, treatment with these agents is not recommended.<sup>2,3,9,10</sup> (Class I, Level B)
- 4.4.3. See *Table 7* for antimicrobial agents that should be used for treatment (antibiotics are listed in order of preference).<sup>2,3,9,10</sup> (Class IIa, Level B)
- 4.4.4. Refer to [Treatment of Patients with Reported Allergies to Beta-Lactam Antibiotics – Adult – Inpatient Clinical Practice Guideline](#) for more information in patients with reported allergies.
- 4.4.5. Total antibiotic treatment duration of seven days may be reasonable and antimicrobial therapy limited to this duration for most patients may be considered.<sup>2,9,10</sup> (Class IIb, Level C)

**Table 7. Antimicrobial agents for skin infections caused by animal or human bites<sup>A,B</sup>**

| PO   | IV   |
|--|--|
| <ul style="list-style-type: none"> <li>Augmentin XR 2000-125 mg PO BID<sup>C,D</sup></li> <li>Moxifloxacin 400 mg PO daily</li> <li>(Cefuroxime 500 mg PO BID<sup>D</sup> OR Cefpodoxime 400 mg PO BID<sup>D</sup> OR Trimethoprim-sulfamethoxazole 160-800 mg to 320-1600 mg PO BID<sup>D</sup> OR Doxycycline 100 mg PO BID OR Ciprofloxacin 500 mg PO BID<sup>D</sup>)</li> <li><b>PLUS</b><br/>(Clindamycin 300-450 mg PO TID-QID OR Metronidazole 500 mg PO TID)</li> </ul> | <ul style="list-style-type: none"> <li>Ampicillin-sulbactam 1.5-3 g IV Q6hr<sup>D</sup></li> <li>Cefoxitin 2 g IV Q6hr<sup>D</sup></li> <li>(Ceftriaxone 1-2 g IV Q24hr OR Ciprofloxacin 400 mg IV Q12hr<sup>E</sup>) <b>PLUS</b><br/>(Metronidazole 500 mg IV Q8hr OR Clindamycin 600-900 mg IV Q6-8hr)</li> <li>Ertapenem 1 g IV Q24 hr</li> <li>Moxifloxacin 400 mg IV Q24hr</li> </ul> |

<sup>A</sup> Not all animal bites will cause infection

<sup>B</sup> Assess need for tetanus vaccine and rabies vaccine and/or immune globulin

<sup>C</sup> Augmentin XR is the preferred agent, but based on ability to pay amoxicillin-clavulanate 500-125 mg PO BID with or without addition of amoxicillin 500-1000 mg PO QID may be considered as an alternative

<sup>D</sup> Requires renal dosing adjustment

<sup>E</sup> See [Antibiotics for the Treatment of Gram-negative Infections – Adult – Inpatient Clinical Practice Guideline](#) for dosing guidance

#### 4.5. Necrotizing fasciitis

- 4.5.1. Findings of purple bullae, sloughing of skin, marked edema, and systemic toxicity prompt surgical intervention is recommended.<sup>2,3,9,10</sup> (Class I, Level A)
- 4.5.2. Recent surgery, peripheral vascular disease, diabetes mellitus, decubitus ulcers, and spontaneous mucosal tears of the gastrointestinal or genitourinary tract increase the likelihood of polymicrobial infection with mixed aerobic and anaerobic organisms.<sup>2,3,9,10</sup>
- 4.5.3. Surgical debridement should be the primary treatment.<sup>3</sup> (Class I, Level A)
- 4.5.4. The recommended agents to be used for treatment are listed in *Table 8*.<sup>3</sup> (Class IIa, Level B).
- 4.5.4.1. Clindamycin should only be continued beyond 72 hours if Group A *Streptococcus* is isolated and the patient remains hypotensive in order to block TSS protein synthesis.<sup>3</sup> (Class I, Level B)
- 4.5.4.2. Vancomycin may be considered for patients with risk factors for, history of, or confirmed MRSA, or until MRSA is excluded from cultures. (Class IIb, Level B)
- 4.5.5. Antibiotic duration determination by the extent of surgical incision and response to antibiotics post-operatively may be reasonable.<sup>3</sup> (Class IIb, Level B)



**Table 8. Recommended agents for necrotizing fasciitis**

| IV  |
|---|
| <ul style="list-style-type: none"> <li>• (Ampicillin-sulbactam 1.5-3 g IV Q4hr<sup>A</sup> OR Piperacillin-tazobactam<sup>B</sup>) <b>PLUS</b> Ciprofloxacin 400 mg IV Q12hr<sup>B</sup> <b>PLUS</b> Clindamycin<sup>C</sup> 600-900 mg IV Q6-8hr</li> <li>• Vancomycin IV (goal trough concentration 10-15 mcg/mL) <b>PLUS</b> Ciprofloxacin 400 mg IV q12hr<sup>A</sup> <b>PLUS</b> Clindamycin<sup>B</sup> 600-900 mg IV q6-8hr</li> </ul> |

<sup>A</sup> Requires renal dosing adjustment

<sup>B</sup> See [Antibiotics for the Treatment of Gram-negative Infections – Adult – Inpatient Clinical Practice Guideline](#) for dosing guidance

<sup>C</sup> Clindamycin should only be continued if Group A *Streptococcus* is isolated and should only be continued for 48-72 hours (If anaerobic coverage is still desired, consider substituting with metronidazole)

## 5. Prevention of recurrent infection

- 5.1. Causes of infection such as *Tinea pedis* should be treated to prevent recurrence.<sup>49</sup> (Class I, Level B)
- 5.2. Skin should be kept well hydrated with emollients to avoid dryness and cracking. (Class I, Level B)
- 5.3. Underlying edema should be reduced by elevating the infected extremity and by the use of compression stockings. (Class I, Level B)
- 5.4. Penicillin VK 500 mg orally twice daily or 1 g orally daily or similar antibiotics daily may be considered for patients with recurrent *Streptococcus* or *Staphylococcus* cellulitis, especially patients with recurrent lymphedema and lymphangitis.<sup>50-52</sup> (Class IIb, Level B)

## 6. Daily monitoring checklist

- 6.1. Daily monitoring for signs and symptoms of improvement should be done. (Class I, Level C)
  - 6.1.1. Cessation of lesion spread at 48 to 72 hours denotes improvement.
    - 6.1.1.1. **Lesions may spread within the first 24 to 36 hours without representing treatment failure.**
    - 6.1.1.2. The “quality” of erythema may also indicate improvement without regression of margins (e.g. fire engine red to pink may indicate improvement).
  - 6.1.2. Fever is not worsening 48 to 72 hours after initiation of therapy denotes improvement.
- 6.2. Monitoring culture results and MRSA test results is reasonable. (Class IIa, Level C)
  - 6.2.1. Ensure patient is receiving adequate coverage from antibiotics for isolated organisms.
  - 6.2.2. Antibiotics should be narrowed to target offending agent based on culture/laboratory results to narrowest effective treatment.
    - 6.2.2.1. If MRSA PCRs are negative, deescalation to narrower spectrum antimicrobials not covering MRSA is reasonable. (
- 6.3. Transition from intravenous to enteral antimicrobial therapy should be evaluated.
  - 6.3.1. See [Medication Route Interchange – Adult – Inpatient – Clinical Practice Guideline](#).

## UW Health Implementation

### Benefits/Harms of Implementation

- Implementation of this guideline will standardize the care of patients treated for urinary tract infections.
- Utilization of this guideline drives prescribing towards narrow spectrum agents. This reduces antimicrobial pressure on the bacterial biomass and reduces the emergence of bacterial resistance.

### Implementation Strategy

- This guideline will be disseminated to clinical staff and available electronically.
- This guideline will serve as a resource for clinical inservices.

### Implementation Tools/Plan

- This clinical practice guideline will be posted for reference in UConnect.
- Links to this clinical practice guideline will be available electronically at point of use sites.

### Disclaimer



CPGs are described to assist clinicians by providing a framework for the evaluation and treatment of patients. This Clinical Practice Guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

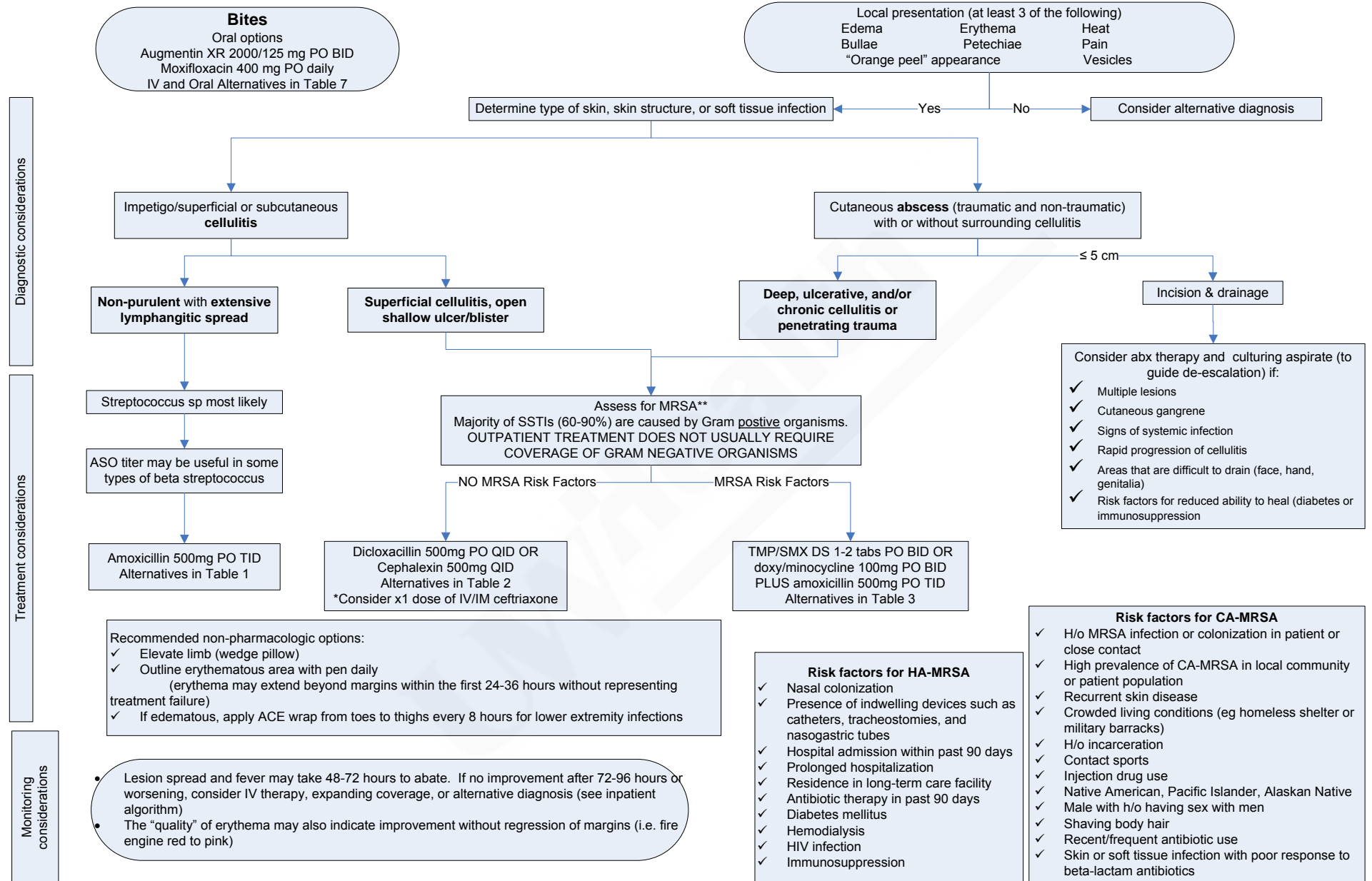
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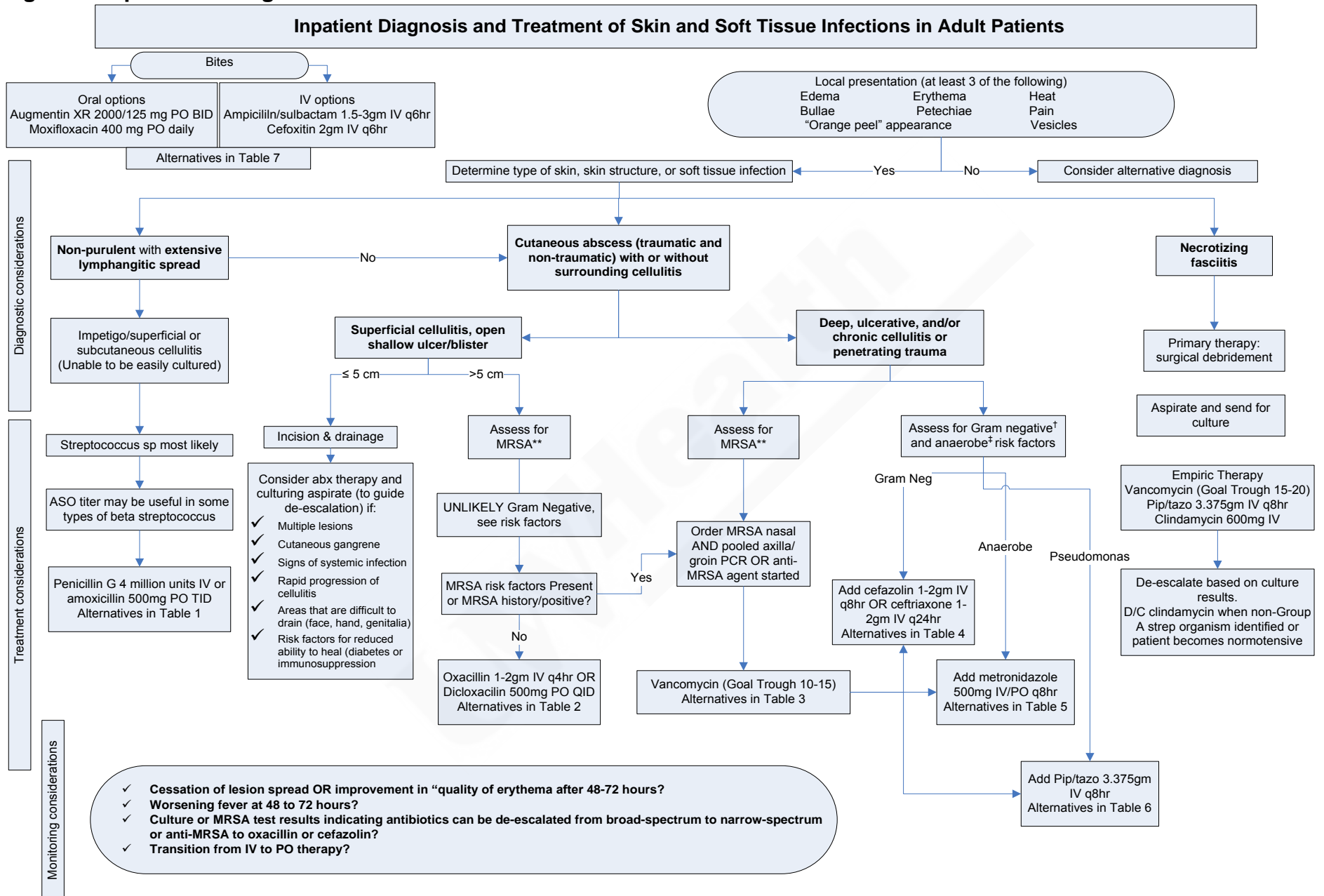
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**Figure 1. Outpatient Management of Skin and Soft Tissue Infections**



**Figure 2: Inpatient Management of Skin and Soft Tissue Infections**



\*\* Risk Factors for Community-Acquired MRSA<sup>29</sup>

- H/o 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 shelter or military barracks)
- H/o incarceration
- Contact sports
- Injection drug use
- Native American, Pacific Islander, Alaskan Native
- Male with h/o having sex with men
- Shaving body hair
- Recent/frequent antibiotic use
- Skin or soft tissue infection with poor response to beta-lactam antibiotics

\*\* Risk Factors for Hospital-Acquired MRSA<sup>30</sup> (most likely clindamycin-resistant)

- 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
- Hemodialysis
- HIV infection
- Immunosuppression

† Risk factors for Gram-negative organisms<sup>9</sup>

- Infection caused while swimming
- Infections near groin or rectum
- Ulcers soaked in water (at risk for *Pseudomonas*)
- Diabetes mellitus with ulceration
- Vascular insufficiency with ulceration
- Periorbital cellulitis
- Immunosuppression
- Healthcare system contact within the past 90 days (at risk for *Pseudomonas*)

‡ Risk factors for anaerobes<sup>2,3,9,25-28,35,37,38</sup>

- Diabetes mellitus with ulceration
- Vascular insufficiency with ulceration
- Necrotizing fasciitis
- Surgical procedures involving the bowel or penetrating abdominal trauma
- Decubitus ulcer
- Perianal abscess
- Site of injection of IV drug users
- Spread from vulvovaginal infection

## **Appendix A. Diagnosis and Treatment of Gram Positive Bacterial Skin and Soft Tissue Infections – Top Ten Myths**

Authors: Lucas Schulz, PharmD; Robert Hoffman, MD; Jeffrey Pothof, MD; Barry Fox, MD

### **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.<sup>2,3,9,10</sup>

- 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.<sup>40,53</sup> 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.<sup>2</sup>
- 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/ 648699) 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.<sup>54</sup>
- b. Risk factors for community-acquired MRSA (CA-MRSA) include:<sup>29</sup>
  - 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:<sup>30</sup>
- 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
  - Hemodialysis
  - 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<sup>31-34,55</sup>
1. If MRSA PCRs or cultures are negative, medications covering for MRSA may potentially be de-escalated to beta-lactam antibiotics.<sup>55</sup>

**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**<sup>2,3,9,29</sup>
- 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<sup>29</sup>

**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.<sup>5</sup>
- 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)<sup>35,36</sup>
- 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).<sup>2,3,9,10</sup>
  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<sup>31-34</sup>
  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.<sup>56</sup>

- 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.<sup>57</sup> 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.<sup>50-52</sup>

- a. Of 398 patients, 40% (158/398) of patients reported cellulitis recurrence despite prophylactic treatment of benzathine penicillin<sup>58</sup>
- b. Causes of infection such as tinea pedis should be treated to prevent recurrence<sup>49,59</sup>
- 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.<sup>58</sup>
- d. Skin should be kept well hydrated with emollients to avoid dryness and cracking
- e. Underlying edema should be reduced by elevating the infected extremity and by the use of compression stockings<sup>59</sup>
- f. Reconfirmation of the diagnosis of cellulitis, appropriateness of antibiotic, dosing, timing, and adherence should also be assessed<sup>60</sup>

**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-infective<sup>5,61</sup>

- a. Cellulitis that is diffuse or unassociated with a defined portal, erythematous, and non-purulent with extensive lymphangitic spread is most commonly caused by Streptococcal species<sup>35</sup>
- 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 species<sup>28</sup>
- c. Dicloxacillin and cephalexin exhibit antimicrobial activity against MSSA and Streptococcus<sup>2,3,9,10</sup>

- 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.<sup>62</sup> Alternative agents (including combination therapy) should be considered for the treatment of possible Streptococcal infection.<sup>2,3,9,10</sup> 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).<sup>2,3,9,10</sup>

### 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.<sup>2,3,9,10,63,64</sup> Clindamycin also has the highest odds ratio for the development of Clostridium difficile.

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