Skin and Soft Tissue Infections

Non-Purulent Infection

Definitions:
MILD: Typical cases of cellulitis in patients without systemic signs/symptoms of infection should include antimicrobial treatment targeting streptococci, particularly Group A streptococci; other streptococcal species may also be present.
MODERATE: For cellulitis in patients with systemic signs of infection (moderate); systemic antibiotics are indicated, targeting Group A streptococci.
SEVERE: cellulitis associated with penetrating trauma, MRSA infection elsewhere, IV drug use, SIRS, oral antibiotic failure, etc., antimicrobials targeting BOTH streptococci and MRSA are indicated.

TREATMENT
The following regimens include coverage for MSSA, community-acquired MRSA (CA-MRSA), and streptococci. Coverage for Gram negative organisms is unnecessary except in very specific patient populations (outlined below). **For mild non-purulent cellulitis, cephalexin monotherapy is likely sufficient.**

Oral Regimens
- Doxycycline 100 mg PO BID **PLUS** cephalexin 500 mg PO QID **OR** amoxicillin 500 mg PO TID*
  OR
- TMP/SMX 1-2 DS tab PO BID **PLUS** amoxicillin 500 mg PO TID*
  OR
- Clindamycin 300-400 mg PO TID

*TMP/SMX and doxycycline have poor activity against group A streptococci and should be combined with amoxicillin or cephalexin.

Parenteral Regimens
- Vancomycin (moderate to severe disease or nosocomial acquisition)
  OR
- Clindamycin 600 mg IV q8h (mild disease)

Duration: Recommended duration of treatment is 5 days but should be extended if infection has not completely resolved with this time frame. Step down to oral therapy recommended when patient is improving.

Type of Infection	**Suspected Organisms**	**Recommended Treatment**
Folliculitis	*S. aureus, P aeruginosa* (hot tub)	● Warm compresses ● No antibiotics
Furuncles, carbuncles, "boils"	*S. aureus,* including CA-MRSA	● -I&D ● If fever and/or surrounding cellulitis, see "oral regimens" above
Abscesses	*S. aureus*, including CA-MRSA	● I&D ● If surrounding cellulitis, systemic symptoms, and/or multiple lesions, see "oral regimens" above ● If gangrene, immunocompromised, extensive surrounding cellulitis, or severe systemic symptoms: ○ Consider surgical treatment ○ Vancomycin
Impetigo	*S. aureus*, including CA-MRSA, *S. pyogenes*	● Warm water soak ● Oral therapy (see regimens above)

Erysipelas (infection limited to the upper dermis including superficial lymphatics with a clear demarcation between involved and uninvolved tissue)	*S. pyogenes*, rarely *S. aureus*, or *S. agalactiae*	● Penicillin VK 250-500 mg PO QID ● Clindamycin 300 mg PO/600 mg IV TID ● If MRSA, add TMP/SMX DS BID
Cellulitis	*S. pyogenes, S. aureus*, including CA-MRSA, Diabetics: mixed aerobic (S. aureus), and anaerobic flora. Consider Gram-negative organisms in immunocompromised hosts or refractory patients. Consider anaerobes and fungi in IVDU	Mild: see “oral regimens” above. Moderate / severe: see “parenteral regimens” above Mild: [amoxicillin/clavulanate 875 mg PO BID **OR** ciprofloxacin 500 mg PO BID] **PLUS** clindamycin 300 mg PO TID Moderate-severe -Piperacillin/tazobactam (extended infusion) 3.375 g IV q8h **OR** meropenem 1 gm IV q8h. If concern for MRSA, add vancomycin Severe PCN allergy: ciprofloxacin + clindamycin **OR** aztreonam + clindamycin. If concern for MRSA, use vancomycin instead of clindamycin and add anaerobic coverage with metronidazole.

TREATMENT NOTES

Microbiology

- Streptococci (especially Group A) and *S. aureus* including MRSA
- Rare causes of cellulitis are discussed below

Management

- Always elevate the affected extremity. Treatment failure is commonly associated with failure to elevate versus failure of antimicrobials.
- Improvement of erythema can take days, especially in patients with venous stasis or lymphedema, due to inflammation caused by the presence of bacterial debris in the skin.
- The microbiology laboratory routinely assesses *S. aureus* isolates for inducible clindamycin resistance. If culture data to guide therapy is unavailable and there is high risk or suspicion of CA-MRSA or failure to improve on clindamycin, consider a change to an alternate antimicrobial such as TMP/SMX or doxycycline.
- *S. aureus* resistance to fluoroquinolones is common and develops quickly. The vast majority of MRSA isolates are resistant to fluoroquinolones and therapy with this antimicrobial class is not recommended.
- Rifampin should **NEVER** be used as monotherapy because resistance develops rapidly.

- There is **NO EVIDENCE** that linezolid or daptomycin are superior to TMP/SMX, doxycycline, or clindamycin for the management of skin and soft tissue infections. Linezolid or daptomycin should only be considered when the *S. aureus* isolate is resistant to other agents or the patient is intolerant of these agents.
- Elimination or prevention of interdigital tinea is important for cases of relapsing lower extremity cellulitis.
- Specialty referral should be considered in cases of lymphedema, refractory tinea pedis, chronic dermopathies, venous insufficiency, or post-surgical cellulitis.

Other causes of cellulitis in select patient populations

- *Vibrio vulnificus* should be considered in those patients, particularly those with chronic liver disease, reporting an exposure to seawater or raw oysters followed by the development of bullae, vesicles, and/or ulcers,. Although rare, this is a rapidly fatal if left untreated. Antimicrobial regimen of choice: ceftriaxone 1 g IV q24h **PLUS** doxycycline 100 mg PO BID.
- Neutropenic hosts, solid organ transplant recipients, and patients with chronic liver disease, may have cellulitis due to Gram-negative organisms. Consider expanding coverage in these cases. Gram-negative cellulitis is exceedingly rare in other patient populations and routine Gram-negative coverage is unnecessary. Streamline coverage in these patient populations once Gram-negative organisms are ruled-out or causative agent is identified.
- If an eschar is present, consider angioinvasive organisms (*Pseudomonas aeruginosa*, *Aspergillus* species, other molds). Infectious Diseases consult is advised.
- Animal and human bites: *Pasteurella multocida* should be covered for cat and dog bites. Treat with amoxicillin/clavulanate 875 mg PO BID **OR** ampicillin/sulbactam 1.5-3 g IV q6h. For penicillin-allergic patients:
  Ciprofloxacin 400 mg-IV q12h or Ciprofloxacin 500-750 mg PO BID **PLUS** clindamycin 600 mg-IV q8h or clindamycin 300 mg PO TID. Consider a tetanus booster and/or rabies vaccination as indicated.

Purulent Infection

- Incision and drainage (I&D) is the primary treatment for a cutaneous abscess.
- Lesions that appear superficial can often have associated abscess formation that is not clearly appreciated without debridement of the wound or, on occasion, additional imaging.
- At the time of I&D, a sample should be obtained for culture and sensitivity testing. Superficial wound swabs of the purulent drainage prior to I&D is of limited utility and **NOT** recommended.
- Antibiotics are an adjunct to I&D in the management of uncomplicated skin abscesses caused by CA-MRSA.
- Indications for antimicrobial therapy in patients with cutaneous abscesses:
  - Severe or rapidly progressive infections
  - The presence of extensive associated cellulitis
  - Signs and symptoms of systemic illness
  - Diabetes or other immune suppression (e.g., transplant recipient)
  - Advanced age
  - Location of the abscess in an area where complete drainage is difficult
  - Lack of response to I&D alone.
- Antibiotic therapy should be given **BEFORE I&D** in patients with prosthetic heart valves or other conditions placing them at high risk for endocarditis.

TREATMENT

If antibiotic treatment is indicated based upon one of the above indications, the regimens, above, for management of non-purulent infections can be used. If CA-MRSA is strongly suspected or confirmed, monotherapy with amoxicillin or cephalexin is inappropriate.

Recurrent MRSA Skin Infections

1. **Patient education regarding approaches to personal and hand hygiene**
    - Practice frequent hand hygiene with soap and water and/or alcohol-based hand gels, especially after touching infected skin or wound bandages.
    - Cover draining wounds with clean, dry bandages.
    - Do not share personal items (e.g. razors, used towels or clothing before washing).
    - Regular bathing.
    - Avoid shaving.
    - Launder clothing, sheets, towels in hot water.
    - Clean all personal sporting clothing/equipment.
2. **Decontamination of the environment**
    - Clean high-touch areas in the bathroom with a disinfectant active against *S. aureus* daily (e.g. Clorox bleach wipes)
3. **Topical decolonization (consider if a patient has ≥ 2 episodes per year or other household members develop infection)**
    - Mupirocin applied intranasally BID for 5 days may be considered in patients with documented evidence of MRSA nasal colonization; mupirocin therapy should be initiated after resolution of acute infection. Mupirocin is not recommended for patients without documented MRSA nasal colonization.
    - Bathing or showering with chlorhexidine (Hibiclens) or dilute bleach baths every other day for 1 week then twice weekly; patients should be instructed not to get these substances into ears, eyes, or other mucous membranes.
    - Systemic antibiotics are NOT recommended solely for decolonization.
4. **Evaluation of family members**
    - Intra-family transmission should be assessed and if present, all members should participate in hygiene and decolonization strategies above, starting at the same time and after the acute infection is controlled.

NOTE: Data on efficacy and durability of the decontamination and decolonization strategies described above are limited.

Diabetic Foot Infections

TREATMENT

Infection should be considered in any foot wound of a patient with diabetes. Evidence of infection generally includes ≥ 2 of the following: erythema, local warmth, local swelling or induration, local tenderness or pain and/or purulent discharge (thick, opaque to white) or sanguineous secretion. Treatment will depend on clinical severity.

Infection Severity	**Clinical Manifestations**
Uninfected	No signs or symptoms of infection
Mild	Local infection (described above) involving only the the skin and subcutaneous tissue (without involvement of deeper tissues and without systemic signs [described below]). Erythema: >0.5cm to ≤2cm
Moderate	Local infection (as above) with erythema >2 cm, or involving structures deeper than skin and subcutaneous tissues (e.g., abscess, osteomyelitis, septic arthritis, fasciitis), **AND** NO systemic inflammatory response signs (SIRS; described below).
Severe	Local infection (as above) with the signs of SIRS, as manifested by ≥ 2 of the following: ● Temperature >38C or <36C ● Heart rate >90 beats/min ● Respiratory rate > 20 beats/min or PaCO2 <32 mmHg ● White blood cell count >12,000 or <4000 or ≥ 10% immature (band) forms

MILD INFECTIONS

Oral Regimens

- Cephalexin 500 mg PO QID
  OR
- Clindamycin 300 mg PO TID (covers MRSA)
  OR
- Amoxicillin/clavulanate 875 mg PO BID

<u>MODERATE</u> INFECTION (may be treated with oral or initial parenteral agent[s]) or <u>SEVERE</u> INFECTION (usually treated with parenteral agent[s])

- Ampicillin-sulbactam 1.5-3 g-IV q6h
  OR
- Ertapenem 1g IV q24h
  OR
- Ciprofloxacin 500 mg PO BID / 400 mg IV q12h **PLUS EITHER** Clindamycin 600 mg IV q8h/300 mg PO TID **OR** Metronidazole 500 mg IV/PO TID
  OR
- Piperacillin/tazobactam (extended 4-hr infusion) 3.375 g IV q8h (if *P.aeruginosa* a concern)
  OR
- Piperacillin/tazobactam (extended 4-hr infusion) 3.375 g IV q8h **PLUS** Vancomycin 15 mg/kg/dose IV q8h (if MRSA is a concern)
  OR
- Ciprofloxacin 400 mg IV q12h **PLUS** Metronidazole 500 mg IV q8h **PLUS** Vancomycin 15 mg/kg//dose q8h

TREATMENT NOTES

Management

- A multidisciplinary approach to management should include wound care consultation, podiatry consult, assessment of vascular supply, vascular and/or general surgery consultation and infectious diseases consultation.
- Risk factors for MRSA
  - History of colonization or infection with MRSA
  - Recent (within 3 months) or current prolonged hospitalization > 2 weeks
  - Transfer from a nursing home or subacute facility
  - Injection drug use
- Consider necrotizing fasciitis in patients who are severely ill.
- Avoid fluoroquinolones in patients who received them as outpatient therapy.
- Antibiotic therapy should be narrowed based on culture results.

Microbiology

- Cellulitis without open wound or infected ulcer, antibiotic naive: beta-hemolytic streptococci, *S. aureus*
- Infected ulcer, chronic or previously treated with antibiotics: *S. aureus*, beta-hemolytic streptococci, Enterobacteriaceae
- Exposure to soaking, whirlpool, hot tub: usually polymicrobial, can involve *Pseudomonas*
- Chronic wounds with prolonged exposure to antibiotics: aerobic gram positive cocci, diptheroids, Enterobacteriaceae, other gram negative rods including *Pseudomonas*
- Necrosis or gangrene: mixed aerobic gram positive cocci and gram negative rods, anaerobes

Diagnosis

- Cleanse and debride wound(s) before obtaining specimens for culture.
- Obtain a tissue specimen for culture/biopsy by scraping from the ulcer base with a sterile scalpel or dermal curette. <u>Avoid swabbing non-debrided ulcers or wound drainage.</u>
- Ulcer floor should be probed carefully. If bone can be touched with a metal probe then the patient should be treated for presumed osteomyelitis with antibiotics in addition to possible surgical debridement.
- A deep foot-space infection can be present. Consider imaging to look for deep infections.
- Putrid discharge is diagnostic for the presence of anaerobes.

- MRI is more sensitive and specific than other modalities for detection of soft-tissue lesions and osteomyelitis.

Duration

- Duration of treatment will depend on rapidity of response, presence of adequate blood supply, need for surgical debridement and/or diagnosis of osteomyelitis.
- Duration of treatment can likely be shortened with adequate surgical intervention (7-10 days post-op); a longer with be needed for osteomyelitis (6-8 weeks).
- Change to an oral regimen when patient is stable.

Surgical Site Infections (SSI)

TREATMENT

Infections following clean procedures (e.g. orthopedic joint replacements, open reduction of closed fractures, vascular procedures, median sternotomy, craniotomy, breast and hernia procedures).

- Cefazolin 1 g IV q8h
  OR
- Penicillin allergic: Clindamycin 600 mg IV q8h
  OR
- Involvement of hardware: Vancomycin 15 mg/kg/dose IV q8h

Infections following contaminated procedures (GI/GU procedures, oropharyngeal procedures, OB/GYN procedures)

Patients not on broad-spectrum antibiotics at time of surgery and not severely ill

- Ceftriaxone 1 gm IV q24h **PLUS** metronidazole 500 mg PO/IV q8h
  OR
- Ertapenem 1 g IV q24h
  OR
- Severe penicillin allergy: ciprofloxacin 500 mg PO BID/400 mg IV q12h) **PLUS** Metronidazole 500 mg PO/IV q8h

Patients on broad-spectrum antibiotics at time of surgery or severely ill

- Piperacillin/tazobactam (extended 4-hr infusion) 3.375 g IV q8h **PLUS** Vancomycin 15 mg/kg/dose q8h (see dosing section), if hardware present or MRSA suspected
  OR
- Penicillin allergy: vancomycin 15 mg/kg/dose IV q8h (and see dosing section) **PLUS** ciprofloxacin 500 mg PO BID/400 mg IV q12h) **PLUS** metronidazole 500 mg PO/IV q8h

Deep fascia involvement

- Treat as necrotizing fasciitis (see dedicated section)

TREATMENT NOTES

Microbiology

- Following clean procedures (no entry of GI/GU tracts)
  - *Staphylococcus aureus* (including MRSA)
  - Streptococci, group A (esp with early onset, < 72 hours)
  - Coagulase-negative staphylococci
- Following clean-contaminated and contaminated procedures (entry of GI/GU tracts with or without gross contamination)
  - Organisms above
  - Gram-negative rods
  - Anaerobes (consider *Clostridia* spp in early-onset infections, 1-2 days)
- Generally, empiric use of Vancomycin is NOT indicated because the percentage of SSIs caused by MRSA at UCLA is low.

Risk factors for MRSA

- History of colonization or infection with MRSA
- Recent (within 3 months) or current prolonged hospitalization >2 weeks
- Transfer from a nursing home or subacute facility
- Injection drug use

Other management issues

- Many advocate that ALL infected wounds be explored both to debride and to assess the depth of involvement.
- Superficial infections may be adequately treated with debridement alone.
- Deeper infections (cellulitis, panniculitis) need adjunctive antibiotics.
- Patients with hypotension should have their wounds explored even they are unremarkable on physical exam.

Necrotizing Fasciitis (Serious, Deep-Tissue Infections)

THESE ARE SURGICAL EMERGENCIES. ANTIBIOTICS ARE ONLY AN ADJUNCT TO PROMPT SURGICAL DEBRIDEMENT.

Infectious Diseases should be consulted for all cases of necrotizing fasciitis.

TREATMENT (adjunct to surgery)

- Vancomycin 15 mg/kg/dose Q8H (see dosing section)
  PLUS
  Clindamycin 600-900 mg IV q8h
  PLUS
  Piperacillin/tazobactam (extended 4-hr infusion) 3.375 g IV q8h **OR** Cefepime 1 g IV q8h)
- Penicillin allergic patients: vancomycin 15mg/kg/dose IV q8h (and see dosing section) **PLUS** ciprofloxacin 400 mg IV q12h **PLUS** clindamycin 600-900 mg IV q8h

If confirmed beta-hemolytic streptococci:

- Penicillin G 24 Million Units as continuous infusion **PLUS** clindamycin 600-900 mg IV q8h
- Penicillin-allergic patients: vancomycin 15 mg/kg/dose IV q8h (and see dosing section) **PLUS** Clindamycin 600-900 mg IV q8h

TREATMENT NOTES

Conventional nomenclature and microbiology

Pyomyositis (purulent infection within individual skeletal muscle groups usually involving abscess formation). MRI is the recommended imaging modality for establishing the diagnosis of pyomyositis; CT and ultrasound may also be of utility. Culture of blood and abscess material should be obtained. In the case of abscess presence, drainage is critical for optimal therapy.

- *S. aureus* most commonly
- Clostridial myonecrosis - *Clostridia* spp (esp *C. perfringens)*
- Group A streptococcal myonecrosis

Fasciitis (a progressively destructive infection of the subcutaneous tissue tracking along the superficial fascia with involvement of all tissue between the skin and underlying muscle; skin may be spared)

- Fournier gangrene: a variant of necrotizing soft tissue infection that involves the scrotum and penis or vulva. Infections are commonly polymicrobial involving both aerobic and anaerobic flora.
- Cases of fasciitis caused by community-acquired MRSA have been reported
- Case-cohort studies and case reports have suggested some benefit to treatment with intravenous immunoglobulin (IVIG) in specific circumstances (e.g., streptococcal toxic shock). However, due to the lack of randomized controlled trials, IVIG should probably be reserved for select patients. Infectious Diseases consult is advised.

Diagnosis

- Can be difficult - gas production is not universal and is generally absent in streptococcal disease.
- Can follow minor or major trauma, especially when risk factors are present.

- Maintain high index of suspicion when:
    - Patients are very ill from cellulitis (hypotension, toxic)
    - Pain out of proportion to exam findings.
    - Anesthesia over affected area
    - Risk factors such as diabetes, recent surgery, or obesity
    - Findings such as skin necrosis or bullae
    - Putrid discharge with thin, “dishwater” pus
- CT scan can help with diagnosis but if suspicion is moderate to high, surgical exploration is the preferred diagnostic test. DO NOT delay surgical intervention to obtain CT.
- Initial histopathologic findings may be of prognostic importance. A poor neutrophil response with numerous organisms seen on routine stains implies a poor prognosis.

REFERENCES

Stevens D, et al. Practice IDSA guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America (IDSA). Clin Infect Dis. 2014;59(2):e10-e52.
http://cid.oxfordjournals.org/content/59/2/e10.full.pdf+html

Management of CA-MRSA: http://www.cdc.gov/mrsa/

Lipsky B, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis 2012;54(12):e132-e173.
http://cid.oxfordjournals.org/content/54/12/e132.full.pdf+html