Skin and Soft Tissue Infections

Cellulitis

Note: The most common etiology of cellulitis with purulent drainage is *S. aureus*, although Group A streptococci and other streptococcal species can also present in this manner.

TREATMENT
The following regimens include coverage for MSSA, community-acquired MRSA (CA-MRSA), and streptococci. Coverage for gram negative organisms is not needed except in very specific patient populations (outlined below).

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 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: 7-10 days. May step down to oral therapy 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 (characterized by lesions that are raised above the level of surrounding skin, with a clear demarcation between involved and uninvolved tissue)	*S. pyogenes*, rarely *S. aureus*, or *S. agalactiae*	- PCN VK 250-500 mg PO QID - Clindamycin 300 mg PO/600 mg IV TID - If MRSA, add TMP/SMX DS BID
Cellulitis	*S. aureus*, including CA-MRSA, *S. pyogenes* Diabetics: mixed anaerobic and aerobic flora. Consider gram-negative organisms in immunocompromised hosts or refractory patients. Consider anaerobes and fungi in IVDU	<u>Mild:</u> see “oral regimens” above <u>Moderate / severe:</u> see “parenteral regimens” above <u>Mild:</u> [Amoxicillin/clavulante 875 mg PO BID **OR** Ciprofloxacin 500 mg PO BID] **PLUS** Clindamycin 300 mg PO TID <u>Moderate-severe</u> -Piperacillin/tazobactam 3.375 g IV q6h **OR** Meropenem 500 mg 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

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

Management

- Always elevate the affected extremity. Treatment failure is more commonly due to failure to elevate than failure of antibiotics.
- Improvement of erythema can take days, especially in patients with venous stasis or lymphedema, because dead bacteria in the skin continue to induce inflammation.
- The microbiology laboratory routinely tests *S. aureus* isolates for inducible Clindamycin resistance and this testing is reflected in the reported susceptibility data. If no culture data to guide therapy and high risk or suspicion of CA-MRSA or failure to improve on clindamycin, change clindamycin to alternate active agent such as bactrim or doxycycline.
- Resistance to fluoroquinolones in *S. aureus* is common and develops quickly. The vast majority of MRSA isolates are resistant to fluoroquinolones. Therapy with fluoroquinolones for *S. aureus* infections 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

- With bullae, vesicles, and ulcers after exposure to seawater or raw oysters, consider *Vibrio vulnificus*, especially in patients with chronic liver disease. Rare, but rapidly fatal if untreated. Treat with ceftriaxone 1 g IV q24h **PLUS** doxycycline 100 mg PO BID.
- Neutropenic, solid organ transplant, and cirrhotic patients 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.

- If an eschar is present, consider angioinvasive organisms (*Pseudomonas*, aspergillosis, mold). 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. If PCN allergy: Ciprofloxacin 500 mg PO / 400 mg IV q24h **PLUS** Clindamycin 300 mg PO TID/600 mg IV q8h. Remember to consider tetanus booster and/or rabies vaccination.

Cutaneous Abscess

- 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. A superficial wound swab of purulent drainage prior to I&D is of limited utility.
- 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., solid organ transplant)
    - 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 thought to be necessary due to one of the above indications, regimens are the same as for cellulitis above. If CA-MRSA is strongly suspected or confirmed, consider NOT adding Amoxicillin or Cephalexin to TMP/SMX, Doxycycline, or Clindamycin.

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 to nares twice daily 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 should not be used in patients who are not documented to have MRSA nasal colonization.
    - Bathing or showering with chlorhexidine (Hibiclens) or dilute bleach baths ever other day for 1 week then twice weekly; patients should be instructed not to get these substances into ears or eyes.
    - 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.

References:
IDSA Guidelines for Skin and Soft Tissue Infections. CID 2005; 41:1373-406
TMP/SMX for MRSA: Ann Intern Med 1992;117:390-8.
Management of CA-MRSA: http://www.cdc.gov/ncidod/dhqp/ar_mrsa_ca.html.

Diabetic Foot Infections

TREATMENT

Treatment depends on clinical severity

Infection Severity	**Clinical Manifestations**
Uninfected	No purulence or inflammation
Mild	Presence of purulence and ≥ 1 signs of inflammation* and cellulitis (if present) ≤ 2 cm around ulcer limited to skin or superficial subcutaneous tissue
Moderate	Same as mild **PLUS** ≥ 1 of the following: > 2 cm of cellulitis, lymphangitic streaking, spread beneath the superficial fascia, deep tissue abscess, gangrene, involvement of muscle, tendon, joint, or bone.
Severe	Any of the above **PLUS** systemic

	toxicity or metabolic instability

*Erythema, pain, tenderness, warmth, induration

MILD INFECTIONS

Oral Regimens

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

Parenteral Regimens

- Clindamycin 600 mg IV q8h (covers CA-MRSA if no inducible Clindamycin resistance)
  OR
- Cefazolin 1 g IV q8h

MODERATE INFECTIONS

- 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
- Avoid fluoroquinolones in patients who were on them as outpatients.
- If patient at risk for MRSA, add Vancomycin to regimens that do not include Clindamycin (see dosing section)

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

SEVERE INFECTIONS

- Pipercillin/tazobactam 4.5 g IV q6h
  OR
- Ciprofloxacin 400 mg IV q12h **PLUS** Clindamycin 600 mg IV q8h
- BUT avoid fluoroquinolones in patients who were on them as outpatients.

If patient at risk for CA-MRSA (see above)

- Pipercillin/tazobactam 4.5 g IV q6h **PLUS** Vancomycin (see dosing section)
  OR
- Ciprofloxacin 400 mg IV q12h **PLUS** Metronidazole 500 mg IV q8h **PLUS** Vancomycin (see dosing section)
- BUT avoid fluoroquinolones in patients who were on them as outpatients.

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.
- Consider necrotizing fasciitis in patients who are severely ill.

- 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

- Cultures of the ulcer base after debridement can help guide therapy. Avoid swabbing non-debrided ulcers or wound drainage.
- Ulcer floor should be probed carefully. If bone can be touched with a metal probe then the patient should be treated for 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 rmodalities for detection of soft-tissue lesions and osteomyelitis.

Duration

- Duration of treatment will depend on rapidity of response and presence of adequate blood supply or osteomyelitis.
- Likely need shorter treatment with adequate surgical intervention (7-10 days post-op) and longer for osteomyelitis.
- Change to an oral regimen when patient is stable.

Reference:
IDSA Guidelines: Clin Infect Dis 2004;39:885-910.

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
- PCN allergy: Clindamycin 600 mg IV q8h
  OR
- Involvement of hardware: Vancomycin (see dosing section)

Exception: Saphenous vein graft harvest site infections should be treated with ertapenem 1 g IV q24h.

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

- Ertapenem 1 g IV q24h
  OR

- Severe PCN allergy: Ciprofloxacin 500 mg PO BID/400 mg IV q12h) **PLUS** Clindamycin 600 mg IV q8h

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

- Piperacillin/tazobactam 3.375 g IV q6h **PLUS** Vancomycin (see dosing section), if hardware present or MRSA suspected
  OR
- PCN allergy: Vancomycin (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 ADJUNT TO PROMPT SURGICAL DEBRIDEMENT.

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

TREATMENT (adjunct to surgery)

- Vancomycin (see dosing section) **PLUS** [Piperacillin/tazobactam 3.375 g IV q6h **OR** Cefepime 1 g IV q8h] **PLUS** Clindamycin 600-900 mg IV q8h
  OR

- PCN allergy: Vancomycin (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
  OR
- PCN allergy: Vancomycin (see dosing section) **PLUS** Clindamycin 600-900 mg IV q8h

TREATMENT NOTES

Conventional nomenclature and microbiology

Pyomyositis (purulent infection of skeletal muscle, usually with abscess formation)

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

Fasciitis (infection of the subcutaneous tissue that results in progressive destruction of fascia and fat, but may spare the skin)

- Type 1 - Polymicrobial infections with anaerobes, streptococci and gram-negative rods (Fournier's gangrene is a type 1 necrotizing fasciitis of the perineum)
- Type 2 - Group A streptococci
- Cases of fasciitis caused by community-acquired MRSA have been reported
- Case-cohort studies and case reports have suggested some benefit to treatment with intraveous 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, <u>surgical exploration is the preferred diagnostic test</u>. 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.