Skin and Soft Tissue Infections: MRSA and Beyond

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Overview

- Update: 2011 IDSA MRSA Treatment Guidelines
  - Skin and soft tissue infections (SSTIs)
- Necrotizing fasciitis
- Animal bites
- Other skin and soft tissue infections

Case 1

32 y/o M with 3 days of an enlarging, painful lesion on his L thigh that he attributes to a "spider bite".

T 36.9 BP 118/70 P 82
What is the appropriate management of this patient?

A. Incision and drainage alone

B. Incision and drainage plus oral anti-MRSA antimicrobial agent

C. Oral anti-MRSA antimicrobial agent

Abscesses

- Incision and drainage is the primary treatment (AII).
  - For simple abscesses or boils, I&D alone likely adequate
- Do antibiotics provide additional benefit?
  - Multiple, observational studies: high cure rates with or without abx
  - 3 RCTs of uncomplicated skin abscesses; 2 large NIH trials pending

Is clinical cure the only important endpoint?

- Development of recurrent lesions

     % Development of recurrent lesions

     100% 90% 80% 70% 60% 50% 40% 30% 20% 10% 0%

     | Development of recurrent lesions |
     | ---------------------------------|
     |   | TMP-SMX | Placebo |
     | Rajendran '07 | Duong '09 | Schmitz '10 |
     | cephalaxin | p=.25 | *p<.04 | *p<.02 |
     | TMP-SMX | p=.52 | p=.58 | p=.02 |
     | TMP-SMX | p=.52 | p=.58 | p=.02 |

Antibiotic therapy is recommended for abscesses associated with:

- Severe, extensive disease, rapidly progressive with associated cellulitis or septic phlebitis
- Signs & sx of systemic illness
- Associated comorbidities, immunosuppressed
- Extremes of age
- Difficult to drain area (e.g. face, hand, genitalia)
- Failure of prior I&D *(AIII)*

**Microbiology of Purulent SSTIs**

![Microbiology of Purulent SSTIs](./images/microbiology.png)

- **MRSA** 59%
- **MSSA** 17%
- **β-hemolytic strep** 3%
- **Non β-hemolytic strep** 4%
- **Other** 8%
- **Unknown** 9%

*Moran NEJM 2006*

**Purulent Cellulitis**

- Cellulitis associated with purulent drainage or exudate without a drainable abscess
  - Empiric Rx for CA-MRSA is recommended *(AII)*.
  - Empiric Rx for β-hemolytic strep unlikely needed *(AII)*.
  - Duration of therapy: 5-10 days, individualize based on clinical response
Empiric oral antibiotic Rx for uncomplicated purulent SSTI

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMP/SMX DS</td>
<td>1-2 BID</td>
</tr>
<tr>
<td>Doxycycline, Minocycline</td>
<td>100 BID</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>300-450 TID</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600 BID</td>
</tr>
</tbody>
</table>

*Rifampin is NOT recommended for routine treatment of SSTIs

Case 2

28 year old woman with erythema of her left foot x 48 hours. No purulent drainage, exudate or abscess.

T 37.0 BP 132/70 P 78

What is the appropriate management of this patient?

A. Clindamycin 300 mg PO tid

B. Cephalexin 500 mg QID, monitor clinically with addition of TMP/SMX if no response

C. Cephalexin 500 mg QID and TMP/SMX 2 DS tab PO bid
Empiric Rx for β-hemolytic strep recommended (AII).

- Prospective study\(^1\), 248 hospitalized inpatients
  - 73% due to β-hemolytic strep; 27% with no identified cause.
  - Overall 99% response rate to β-lactam antibiotic.
- Retrospective study\(^2\)
  - ↑ treatment failures with TMP-SMX vs. β-lactam or clindamycin

The role of CA-MRSA is unknown.
- Recommend empiric Rx if fails to respond to β-lactam
- Consider in patients with systemic toxicity

\(^1\) Jeng et al Medicine 2010
\(^2\) Elliott et al Pediatrics 2009

Anti-β-hemolytic strep antibiotic (+/- anti-MSSA)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalexin</td>
<td>500 QID</td>
</tr>
<tr>
<td>Dicloxacillin</td>
<td>500 QID</td>
</tr>
<tr>
<td>Clindamycin*</td>
<td>300-450 TID</td>
</tr>
<tr>
<td>Linezolid*</td>
<td>600 BID</td>
</tr>
</tbody>
</table>

*Have activity against MRSA
- If poor response, add anti-MRSA antibiotic

Complicated SSTI

- Surgical debridement & empiric Rx for MRSA pending cultures

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Adult</th>
<th>Evidence Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>15-20 mg/kg IV Q8-12</td>
<td>AI</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600 mg PO/IV BID</td>
<td>AI</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>4 mg/kg IV QD</td>
<td>AI</td>
</tr>
<tr>
<td>Telavancin</td>
<td>10 mg/kg IV QD</td>
<td>AI</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>600 mg PO/IV Q8</td>
<td>AIII</td>
</tr>
<tr>
<td>Ceftaroline</td>
<td>600 mg IV Q12</td>
<td>FDA approved after guidelines</td>
</tr>
</tbody>
</table>

*Tigecycline: associated with ↑ mortality; consider alternate agent for MRSA SSTI
- Treat for 7-14 days, individualize based on clinical response
Microbiology of Complicated SSTI

- 150 hospitalized pts with cSSTI & positive cultures
  - S. aureus or strep identified in 97% (sole pathogen in > 70%)
  - Use of agents with broad spectrum gram-negative and/or anaerobic activity in 60-80%
- Follow-up interventional study
  - Implemented algorithm to standardize Rx of inpatient SSTI
  - ↓ broad spectrum gram-negative (66% vs. 36%, p < .001)
  - ↓ duration of therapy (13 vs. 10 days, p < .001)
  - No difference in clinical outcomes

Summary: empiric management of SSTIs

<table>
<thead>
<tr>
<th></th>
<th>Purulent (MRSA)</th>
<th>Non-purulent (β-hemolytic strep)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outpatient</strong></td>
<td>• I&amp;D</td>
<td>• Cephalexin 500 QID</td>
</tr>
<tr>
<td></td>
<td>Consider addition of anti-MRSA antibiotic in select situations*a</td>
<td>• Dicloxacillin 500 QID</td>
</tr>
<tr>
<td></td>
<td>• I&amp;D plus vancomycin (or alternative) b</td>
<td>Consider addition of MRSA active agent if no response*a</td>
</tr>
<tr>
<td><strong>Inpatient</strong></td>
<td>• I&amp;D plus vancomycin (or alternative) b</td>
<td>• Vancomycin (or alternative) b or cefazolin</td>
</tr>
</tbody>
</table>

1. Systemic illness, purulent cellulitis/swound infection, comorbidities, extremes of age, abscess difficult to drain or face/head, septic phlebitis, lack of response of to I&D alone.
2. PO antibiotic: TMP-SMX x DS BID, Clindamycin 300 mg QD, Doxycycline 100 PO BID
3. Daptomycin, linezolid, telavancin, ceftaroline

Case 3

The patient in case 1 returns 4 weeks later with another abscess on his opposite thigh. He notes that after I & D of his first abscess, he didn’t keep his wound covered and occasionally touched the site to “make sure it was healing.”

The site of his old abscess is clean with a well-healed scar. He undergoes I&D and receives 1 week of TMP-SMX.
What is the appropriate management of this patient?

A. Emphasize personal hygiene measures
B. Decolonize with mupirocin and chlorhexidine showers
C. Decolonize with TMP-SMX and rifampin
D. A and B
E. A, B, and C

What is the Management of Recurrent Skin and Soft Tissue Infections?

- Cover draining wounds
- Hand hygiene
- Avoid sharing personal items if active infection
- Clean high-touch surfaces
- If above measures fail
- If ongoing household transmission
Intra-nasal mupirocin to prevent recurrent SSTI?

- RCT of 40 pts with recurrent MSSA SSTI
- Subjects: ≥ 3 SSTIs in 1 yr & S. aureus nasal carriers
- Nasal mupirocin BID vs. control 1 wk/mo x 1 yr
- SSTI free at 1 year: 47% vs. 6%; p < 0.02

Raz R. Arch Int Med. 1996

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Intra-nasal mupirocin to prevent CA-MRSA SSTI?

- 1° prophylaxis (prospective, cluster RCT)
  - 134 soldiers with CA-MRSA nasal colonization
  - Mupirocin (5d) vs. placebo
  - SSTI: 10.6% mupirocin vs. 7.7% placebo; p = NS
- 2° prophylaxis (retrospective)
  - 38 HIV+ with CA-MRSA SSTI and nasal colonization
  - Recurrent SSTI: 32% mupirocin vs. 52% no Rx; p = NS

Ellis et al. AAC '07, Rahimian et al. ICHE '07

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Chlorhexidine for primary prevention of SSTI

- Cluster RCT of 1562 military recruits
- Chlorhexidine wipes vs. placebo 3 x/week
- Results: SSTI rate at 6 weeks
  - 9.4% (chlorhexidine) vs. 7.1% (placebo); p=0.13
- Results: S. aureus colonization (45% baseline)
  - 52.6% (chlorhexidine) vs. 67% (placebo)

Whitman TJ. Infect Control Hosp Epidemiol. 2010
Oral Antibiotics for Decolonization?

- Cochrane review:\(^1\): No benefit of oral abx in MRSA eradication among patients in healthcare settings
- Systematic review:\(^2\): Rifampin + anti-staph abx vs. anti-staph abx alone
  - Rifampin combo superior in ↓ S. aureus colonization
  - No studies evaluated impact on infection rates
- Watch out for drug interactions, side effects, development of resistance

\(^1\)Cochrane Review 2003; \(^2\)Falagas ME AJIC 2007; 35: 106-14

Recurrent MRSA SSTI:
Decolonization regimens to consider...

- Mupirocin twice daily x 5-10 days (CIII)
- Mupirocin twice daily x 5-10 days AND topical skin antiseptic (e.g. chlorhexidine or dilute bleach baths) x 5-14 days (CIII)
  - Bleach baths: ¼ cup per ¼ tub (13 gallons) of water for 15 min, 2x/week for 3 mths
- Oral antimicrobials not routinely recommended (AllI). Consider oral agent in combination with rifampin only if other measures fail (CIII):

Raz Arch Intern Med 1996; Ellis MIR JAC 2007; Whitman ICHE 2010; \(^3\)Bates NEJM 2010

Case 4

- 54 yo F with DM, pimple in R groin 5 days ago, erythema, worsening pain, swelling, and blistering x 24 hours
- T 38.5 P100 BP100/60 R18 98%RA

Dulek S, Marfone M, J Fam Pract. 2005 55(5) 398
### What would your empiric therapy be in this case?

A. Send home, Rx cephalexin and TMP/SMZ  
B. Admit, IV vancomycin and piperacillin-tazobactam  
C. Call surgery, IV vancomycin and clindamycin  
D. Call surgery, IV vancomycin, piperacillin-tazobactam, clindamycin

### Necrotizing skin and skin structure infections

- **Definition:** infections of any layer within the soft tissue compartment that are associated with necrotizing changes  
- **Monomicrobial** (Group A strep > S. aureus, Clostridia, gram neg rare)  
  - associated w/ minor injuries  
- **Polymicrobial** (gram +, gram -, anaerobes)  
  - associated w/ abdominal surgery, decub ulcers, IVDU, spread from GU tract

### Risk Factors for Necrotizing SSTI

- IVDU  
- Diabetes  
- Obesity  
- Chronic immunosuppression  
- Often no precipitating factor
Clinical Presentation

- Nonspecific complaints: pain, GI (N/V/D), influenza-like symptoms
- Physical exam difficult to distinguish from cellulitis, sometimes only mild local erythema – pain out of proportion

<table>
<thead>
<tr>
<th>Missed Dx of Necrotizing Fasciitis</th>
<th>Initial Diagnoses by PCP/ER</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal Pain</td>
<td>6 (40%)</td>
<td></td>
</tr>
<tr>
<td>Influenza</td>
<td>3 (20%)</td>
<td></td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>2 (13%)</td>
<td></td>
</tr>
<tr>
<td>Hemorrhoids</td>
<td>1 (6%)</td>
<td></td>
</tr>
<tr>
<td>Gout</td>
<td>1 (6%)</td>
<td></td>
</tr>
<tr>
<td>1° burn</td>
<td>1 (6%)</td>
<td></td>
</tr>
<tr>
<td>Necrotic</td>
<td>1 (6%)</td>
<td></td>
</tr>
</tbody>
</table>

Wong CH Crit Care Med 2004

Initial Diagnoses by PCP/ER

Musculoskeletal Pain 6 (40%)
Influenza 3 (20%)
Gastroenteritis 2 (13%)
Hemorrhoids 1 (6%)
Gout 1 (6%)
1° burn 1 (6%)
Necrotic 1 (6%)  

Bisno CID 2000

Necrotizing soft tissue infections: physical findings on admission

<table>
<thead>
<tr>
<th>Findings</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenderness</td>
<td>100%</td>
</tr>
<tr>
<td>Erythema</td>
<td>86%</td>
</tr>
<tr>
<td>Warmth</td>
<td>83%</td>
</tr>
<tr>
<td>Bullae</td>
<td>44%</td>
</tr>
<tr>
<td>Induration</td>
<td>42%</td>
</tr>
<tr>
<td>Fluctuance</td>
<td>34%</td>
</tr>
<tr>
<td>Crepitus</td>
<td>27%</td>
</tr>
<tr>
<td>Necrosis</td>
<td>19%</td>
</tr>
<tr>
<td>Sensory/motor</td>
<td>11%</td>
</tr>
<tr>
<td>Hypotension</td>
<td>11%</td>
</tr>
<tr>
<td>Fever</td>
<td>10%</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>10%</td>
</tr>
</tbody>
</table>

n=89; 14% dx with nec fasc on admit

Wong CH Jour of Bone and Joint Surg. 2003

Necrotizing soft tissue infections: radiographic techniques

- Plain films
  - Low sensitivity
  - Helpful if gas present
- CT and ultrasound
  - May identify other Dx (abscess)
- MRI
  - Enhanced sensitivity, low specificity

Mortality rate was 20%.

Consider for invasive group A strep infections.

- Decreases toxin synthesis
  - Limited clinical data: 1 retrospective, unblinded study of children with invasive group A strep infection:
    - Clindamycin vs. β-lactam + clindamycin
    - Outcome: lack of disease progression or improvement
      - Deep infection: 83% vs. 14%, p = .0006
      - Superficial infection: 83% vs. 48%, p = .07

What is the role of clindamycin?

- Early surgical consult/ intervention
- Empiric antimicrobial therapy
  - Piperacillin/tazobactam or carbapenem (group A strep, other gram pos, gram negs and anaerobes) plus
  - Clindamycin (group A strep – toxin inhibition) plus
  - Vancomycin (MRSA)

Summary: Management of necrotizing skin and soft tissue infections

*Consider IVIG in severe cases of streptococcal toxic shock syndrome
Case 5

- 21 yo M is tossing a ball in Golden Gate Park with a friend. As he goes after the ball, he passes close to a dog that was resting in the shade with his owner. The dog jumps up and bites him on the leg inflicting several deep puncture wounds on the calf.

In addition to wound care, what is the appropriate management of this patient?

A. Antibiotic prophylaxis with clindamycin
B. Antibiotic prophylaxis with amoxicillin/ clavulanate
C. Administer rabies immunoglobulin and rabies vaccine for post-exposure prophylaxis
D. A and C
E. B and C

Animal Bites

- 50% of Americans are bit by animals
- 20% require medical attention
- Animal bites account for 1% of ER visits
- Bites result in 10,000 inpt admits/year
Microbiology of Animal Bites: What’s in their mouth and on your skin

- Average 5 organisms (range 0-16) per wound

<table>
<thead>
<tr>
<th></th>
<th>Dogs</th>
<th>Cats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pasteurella sp.</td>
<td>50%</td>
<td>75%</td>
</tr>
<tr>
<td>Streptococcus sp.</td>
<td>40%</td>
<td>40%</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>20%</td>
<td>4%</td>
</tr>
<tr>
<td>Anaerobes mixed w/ aerobes</td>
<td>48%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Anaerobes alone</td>
<td>1%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Tzan NEJM 1998

Antibiotic Coverage for Pasteurella

- What you want to use but won’t work…
  - cephalxin
  - dicloxacillin
  - clindamycin

- What works…
  - penicillin/amoxicillin
  - doxycycline
  - fluoroquinolones

Animal bites

- Empiric treatment regimens
  - Amoxicillin/clavulanic acid +/- anti-MRSA
  - Pen allergy: cipro + clindamycin or moxifloxacin

- Prophylaxis?
  - Moderate-severe bites or on face/hands
  - Immunocompromised (splenectomized)
  - Cat bites
**Rabies – what type of bites are high risk?**

<table>
<thead>
<tr>
<th>Animal Type</th>
<th>Evaluation and disposition of animal</th>
<th>Post-exposure prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog, cats, ferrets</td>
<td>Suspected/confirmed rabid Healthy Animal lost</td>
<td>Prophylaxis 10 days observation/test Contact DPH</td>
</tr>
<tr>
<td>Skunk, raccoons, foxes, bats</td>
<td>Regarded as rabid unless proven negative by lab test</td>
<td>Immediate prophylaxis</td>
</tr>
<tr>
<td>Livestock, small rodents, rabbits, large rodents</td>
<td>Consider individually</td>
<td>Almost never require prophylaxis</td>
</tr>
</tbody>
</table>

[Rabies - Post-exposure prophylaxis](http://www.cdc.gov/mmwr/pdf/rr/rr57e507.pdf)

- Wound cleansing: virucidal agent (iodine)
- Rabies Immune Globulin
  - 20 IU/kg body weight
  - Infiltrate full dose around the wound(s) and remaining volume IM at site distant from vaccine
- Vaccinate: Days 0, 3, 7, and 14

[53 yo M ER physician presents with 9 day history of progressive cellulitis of L forearm. Initially noted a pustule → self I&D. Despite keflex + clindamycin x 4 days, progressive erythema and drainage. Started IV vanco + ceftriaxone with no improvement after 3 days.](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5902.pdf)
Further history...

- History of chronic “benign” neutropenia
- 3 weeks ago, trip to Arizona where cleared brush in order to replace a water drip line and scraped his arm
- 2 weeks ago, worked in home (Merced) vegetable garden clearing eggplant and pepper brushes
- 7 days ago, cleaned his fish tank
- No animal or tick bites
- Only recent travel to Arizona

All of the following are possible causes of his infection EXCEPT:

A. Mycobacterium marinum
B. Coccidioides immitis
C. Nocardia brasiliensis
D. Brucella melitensis
E. Sporothrix schenckii

Gram stain from wound culture

Nocardia brasiliensis
Nocardia

- Soil inhabitant
- Worldwide distribution
- Incubation period: <1-6 weeks
- Often with mild systemic symptoms
- *Nocardia brasiliensis > asteroides* for cutaneous dz
- Diagnosis: biopsy and culture
  - Partially acid-fast, gram variable branching rods.
- Treatment: TMP-SMX x 4-6 months

26 yo M with 6 week history of R hand papule → ulcer

Multiple visits to ED and urgent care, Receives several courses of abx, no improvement

*Leishmania panamensis*
Nodular lymphangitis: management?

- Take a good history
- Obtain biopsy
  - Pathology: stain for fungi and mycobacteria
  - Cultures: bacterial, fungal, and mycobacterial
- Consider empiric therapy based on severity of disease and history prior to biopsy results

Nodular Lymphangitis: DDx

- Short incubation (days)
  - Francisella tularensis (rabbits, ticks)
- Medium incubation (2-4 weeks)
  - Nocardia (brasiliensis >> asteroides) (soil)
- Long incubation (weeks-months)
  - Mycobacterium marinum (fish tanks)
  - Sporothrix schenckii (vegetation)
  - Leishmania spp (sandfly)
**“Masqueraders” of Infectious Cellulitis**

- Superficial thrombophlebitis and deep venous thrombosis
- Contact dermatitis
- Insect stings/tick bites
- Drug reactions
- Gouty arthritis
- Sweet syndrome
- Foreign body reaction (e.g. surgical mesh, orthopedic implants)
- Lymphedema
- Malignancy (e.g. T-cell lymphoma)

**Summary**

- Drainage/debridement is the mainstay of therapy of all purulent skin and soft tissue infections.
- For purulent SSTI requiring antibiotic therapy, cover for CA-MRSA.
  For non-purulent cellulitis, cover for (β-hemolytic strep + CA-MRSA.
- Amoxicillin/clavulanate is drug of choice for prophylaxis following dog, cat, and human bites.
- If no response to standard antibiotic therapy for SSTI, consider alternative diagnoses (e.g. unusual infections, non-infectious etiologies).
  Biopsy for culture and pathology.