Management of Skin and Soft Tissue Infections

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UCSF, Division of Infectious Diseases

Overview
• Purulent SSTI
• Non-purulent SSTI
• Impetigo
• Recurrent SSTIs
• Necrotizing soft tissue infection
• Animal bites
• Potpourri of cases

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

How would you manage this patient?
A. Incision and drainage alone
B. Incision and drainage plus cephalaxin
C. Incision and drainage plus TMP-SMX

Abscesses: Do antibiotics provide benefit over I&D alone?

Is treatment failure the only important endpoint? **Recurrent SSTI?**

- Duong: 10 days
  - 9% TMP-SMX vs 28% placebo, p = .02
- Schmitz: 30 days
  - 13% TMP-SMX vs 26% placebo, p=.04

**Microbiology of Purulent SSTIs**

- MSSA: 17%
- MRSA: 59%
- 3% β-hemolytic strep
- 4% other
- 3% unknown
- 9%

**Antibiotic therapy is recommended for abscesses associated with:**

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

**Empiric oral antibiotic Rx for uncomplicated purulent SSTI**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult Dose</th>
</tr>
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<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

**Inducible clindamycin resistance?**

- When to consider?
  - erythromycin – resistant and clindamycin –susceptible
- Frequency – 0-7%
- How to test - D-test
- What to do if D-test + but clindamycin being used?
  - Improving – continue
  - Failing or moderate/severe infection-change

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**Case 2**

28 y/o woman presents with erythema of her left foot over past 48 hrs

No purulent drainage, exudate, or fluctuance.

T 37.0 BP 132/70 P 78

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**How would you manage this patient?**

A. Clindamycin 300 mg TID

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

C. Cephalexin 500 mg QID + TMP/SMX 1 DS BID

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**Nonpurulent Cellulitis: pathogen?**

β-hemolytic strep vs. *S. aureus*?

- Prospective study, hospitalized patients (N=248)

**Methods**

- Acute and convalescent titers (ASO and anti-DNaseB)
- Rx with β-lactam antibiotics (cefazolin/oxacillin)

**Results**

- 73% due to β-hemolytic strep; 27% none identified
- 96% response rate to β-lactam antibiotic


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**Empiric treatment of uncomplicated nonpurulent cellulitis?**

- 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

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**Summary: empiric management of SSTIs**

<table>
<thead>
<tr>
<th></th>
<th>Purulent (MRSA)</th>
<th>Non-purulent (β-hemolytic strep)</th>
</tr>
</thead>
</table>
| **Uncomplicated**   | • I&D Cont. add of anti-MRSA antibiotic in select situations2 | • Cephalexin 500 QID
|                     |                 | • Dicloxacillin 500 QID Cont. add of MRSA active agent if no response1 |
| **Complicated**     | • I&D plus vancomycin (or alternative) 2 | • Vancomycin (or alternative) 2 |

1. Systemic illness, purulent cellulitis/wound infection, comorbidities, extremes of age, abscess difficult to drain or face/hand, septic phlebitis, lack of response to I&D alone.
2. PO antibiotics: TMP-SMX 1 DS BID, Cephalexin 300 mg TID, Doxycycline 100 PO BID.

Daptomycin, linezolid, tigecycline, telavancin, ceftaroline
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Impetigo

• Definition: superficial, intra-epidermal infection
• Epi: Common in children, highly communicable
• Pathogens: S. aureus, Group A strep
• Treatment:
  – Few lesions (topical = systemic)
    • Mupirocin or Retapamulin ointment
  – Multiple lesions (systemic >> topical)
    • Pick agent(s) active against CA-MRSA and Group A strep

Case 3

• Patient presents with 4th abscess in 4 months
• Prior abscesses have been treated with I&D and antibiotics with resolution
• He asks if there is anything he can do to prevent recurrences

How would you manage this patient?

A. Emphasize personal hygiene measures
B. Decolonize with mupirocin and chlorhexidine
C. Decolonize with TMP-SMX and rifampin
D. Give daily low dose clindamycin
How to Manage Recurrent Skin and Soft Tissue Infections?

Decolonization strategies
- Intranasal mupirocin: + data in MSSA SSTI w/ + nasal Cx
- Chlorhexidine washes alone: not effective
-Suppressive oral antibiotics: clindamycin some efficacy
- Bleach baths: no benefit in recent RCT
- Oral therapy with rifamycins: personal experience


Bleach baths alone?
- Population: Children with S. aureus SSTI or invasive infections
- Intervention: Randomized to routine hygiene measures (N=492) +/- “bleach baths” 2x/week for 3 months (N=495)
- Outcomes: Recurrent SSTI: 17% bleach baths vs. 21% control

Kaplan SK. Clin Infect Dis. 2013

Combination therapy?
Mupirocin vs. mupirocin + chlorhexidine vs. mupirocin + bleach bath

Fritz SA. Infect Control Hosp Epi. 2011

PCN for Prevention of Recurrent Cellulitis
- Multicenter, double-blind RCT 274 pts with recurrent cellulitis
  - Penicillin 250 mg BID vs. placebo x 12 months
- Patient characteristics:
  - Chronic edema (66%), venous stasis (25%), tinea pedis (36%)
- Outcomes:
  - Recurrent cellulitis: 22% (PCN) vs. 37% (placebo), p=.01
  - After treatment stopped, no difference

Thomas NEJM 2013; 368: 1695-703
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Case 4

- 34 y/o M comes in with arm pain, fever
- Temp 38.9, HR 105, SBP 100, RR 20
- Appears ill and in more pain than what you would expect for cellulitis

What would your empiric therapy be in this case?

A. Cephalexin plus TMP-SMX, send home
B. Clindamycin, piperacillin-tazobactam, and vancomycin
C. Call surgery, vancomycin and ceftriaxone
D. Call surgery, clindamycin, piperacillin-tazobactam, and vancomycin

Necrotizing skin and skin structure infections

- Definition: infections of any layer within the soft tissue compartment that are associated with necrotizing changes
- Monomicrobial
  - associated w/ minor injuries
- Polymicrobial
  - associated w/ abdominal surgery, decub ulcers, IVDU, spread from GI tract

Necrotizing soft tissue infections: risk factors

- IVDU
- Diabetes
- Obesity
- Chronic immune suppression

Why is early diagnosis so important?

Wong CH. Jour of Bone and Joint Surg. 2003

Anaya DA. Clin Infect Dis. 2007
Necrotizing soft tissue infections: clinical clues

- Tenderness
- Erythema
- Warmth
- Blisters
- Induration
- Crepitus
- Necrosis
- Nerve/nerve deficits
- Hypotension
- Shock

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

Necrotizing Skin and Soft Tissue Infection: Pathogens

<table>
<thead>
<tr>
<th>Monomicrobial</th>
<th>Polymicrobial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A strep</td>
<td>Aerobic Gram +/-Gram -</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>PLUS</td>
</tr>
<tr>
<td>Clostridia sp</td>
<td>Anaerobes</td>
</tr>
<tr>
<td>Gram negatives</td>
<td></td>
</tr>
<tr>
<td>Vibrio vulnificus</td>
<td></td>
</tr>
</tbody>
</table>


Empiric treatment of necrotizing soft tissue infections

- Early surgical intervention! (be annoying)
- Antimicrobial therapy
  - Piperacillin/tazobactam or carbapenem
    (gram negatives and anaerobes)
  - Vancomycin
    (MRSA)
  - Clindamycin
    (group A strep)

Strep toxic shock syndrome

- Isolation of GAS from sterile site
- Clinical signs of severity
  - Hypotension
- Clinical and laboratory abnormalities
  - Renal impairment, coagulopathy, liver abnormalities, ARDS, extensive tissue necrosis
Is IVIG useful in strep toxic shock syndrome?

- **Observational Study – ’99**
  - Improved 7 day survival and 30 day survival
  - But...Cases > Controls
    - Clindamycin (95% vs. 55%, P=0.01)
    - Surgery (67% vs. 38%, P=0.04)

- **Double-Blinded RCT – ’03**
  - Ended early due to poor enrollment, 21 patients
    - No significant mortality benefit at 28 day
    - Reduction in organ failure score at 2 and 3 days


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### Case 5

37 y/o male presents to clinic 4 days after receiving a dog bite to his forearm. He complains of pain, some purulent drainage.

### Which antibiotic regimen would be most appropriate for this patient?

A. Ampicillin/sulbactam
B. Cefazolin
C. Clindamycin
D. Vancomycin and metronidazole
E. No antibiotics needed

### 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
Animal bites: bacteriology
*Their mouth and 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><em>Pasturella sp.</em></td>
<td>50%</td>
<td>75%</td>
</tr>
<tr>
<td><em>Streptococcus sp.</em></td>
<td>46%</td>
<td>46%</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>20%</td>
<td>4%</td>
</tr>
<tr>
<td>Anaerobes mixed w/ aerobes</td>
<td>48%</td>
<td>63%</td>
</tr>
<tr>
<td>Anaerobes alone</td>
<td>1%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Talan DA. NEJM. 1999

Antibiotic coverage for *Pasturella*

- What you want to use but won’t work...
  - 1st generation cephalosporin
  - anti-staphylococcal penicillins
  - clindamycin
- What works...
  - amoxicillin
  - doxycycline
  - fluoroquinolone

Animal bites

- Empiric treatment regimens
  - Amoxicillin/clavulanic acid +/- MRSA agent
  - Pen allergy: cipro + clindamycin or moxifloxacin
- Prophylaxis?
  - Moderate-severe bites or on face/hands
  - Immunocompromised (splenectomized)
  - Cat bites

Human bites

- Bacteriology
  - Mixed infection with streptococci, anaerobes and gram negatives (*Haemophilus* sp., *Elkinella* sp.)
  - High rates of infection
- Treatment
  - Same as animal bites
- Prophylaxis – everyone, Augmentin

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

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

http://www.cdc.gov/rabies/resources/contacts.html

http://www.cdc.gov/mmwr/preview/mmwrhtml/rr57e507a1.htm
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Which of the following reflect true infectious cellulitis?

A

B

C

D
Which of the following reflect true infectious cellulitis?

- Acute true cellulitis
- Acute stasis dermatitis
- Acute on chronic stasis dermatitis
- Contact dermatitis

Case 6

- 66-year-old female underwent full-face fractional laser treatment with a 2790nm device. Five days later she developed multiple erythematous papules, some with central pustules, in the treatment areas.
- She had no lymphadenopathy and denied fevers or chills.

Case continued

- Empiric treatment:
  - minocycline, acyclovir, trimethoprim-sulfamethoxazole, and fluconazole
  - topical clindamycin, dapsone, and benzoyl peroxide
- Biopsy: suppurative and granulomatous dermatitis with focally dense infiltrates of histiocytes and neutrophils, stains for fungi and bacteria were negative

Culture results

- Day 6:
  - Bacterial culture: Numerous acid-fast bacilli

Incidence of cutaneous non-tuberculous mycobacteria infection (NTM) 1980–2009

Graph showing the incidence of NTM infection per 100,000 person-years for both males and females, with a notable increase in incidence from 1980–1999 to 2000–2009.

Clinical presentation of patients with NTM cutaneous infection

Rapid growing mycobacteria

<table>
<thead>
<tr>
<th></th>
<th>M. fortuitum</th>
<th>M. abscessus</th>
<th>M. chelone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>80</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>100</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>TMP-SMX</td>
<td>100</td>
<td>0</td>
<td>60</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>50</td>
<td>0</td>
<td>25</td>
</tr>
<tr>
<td>Linezolid</td>
<td>96</td>
<td>48</td>
<td>94</td>
</tr>
<tr>
<td>IV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amikacin</td>
<td>100</td>
<td>90</td>
<td>80</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>80</td>
<td>70</td>
<td>0</td>
</tr>
<tr>
<td>Imipenem</td>
<td>100</td>
<td>50</td>
<td>60</td>
</tr>
</tbody>
</table>

Treatment recommendations

- 2 active antibiotics for at least 3-4 months
  - Macrolide, doxycycline, fluoroquinolone, TMP-SMX based on susceptibilities
- In cases of severe disease consider IV therapy
  - Cefoxitin, imipenem, amikacin
- Surgical debridement is often key for cure and may be used alone in select cases

Case continued

- **M. chelone**
  - Susceptible: Clarithromycin, TMP-SMX
  - Resistant: Cipro, doxycycline
- Treatment: azithromycin + TMP-SMX × 4 mo

45 y/o man presents with several weeks of progressive painful “bumps” spreading up his left forearm. Had a fall while mountain biking 1 month ago and had road rash on hands

Which treatment is recommend for this patient?

A. Amoxicillin
B. Clarithromycin plus linezolid
C. Fluconazole
D. Itraconazole
E. TMP-SMX
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* (ulcer/systemic illness)
- Medium incubation (2-4 weeks)
  - Nocardia
- Long incubation (weeks-months)
  - NTM: *Mycobacterium marinum*
  - *Sporothrix schenckii*
  - Leishmania (ulcer)

Case 8

- 15 y/o boy was hit with a fish carcass causing a small cut on his left leg
- Several hours later he developed severe pain, erythema
- The image is his leg on presentation to the ED the next day

Which of these antibiotics would be active against this pathogen?

A. Penicillin  
B. Vancomycin  
C. Doxycycline  
D. Cefazolin  
E. Clindamycin

Vibrio vulnificus

- Gram-negative, motile, curved, rod
- Found in brackish water
- Clinical syndromes
  - Primary septicemia
  - Necrotizing soft tissue infections
  - Gastroenteritis
- Rx: 3rd gen cephalosporins, tetracyclines, FQs
Case 9.
35 y/o Filipino M presents w/ subacute onset of headache, diffuse bilateral pulmonary lesions and crusted papules and plaques of the face.

What is the best treatment for this man?
A. Vancomycin
B. Ceftriaxone
C. Fluconazole
D. Clindamycin

Diagnosis: Coccidioidomycosis
• Histology from tissue biopsy revealed a non-budding yeast form w/ spherules

Another cutaneous cocci case

Cutaneous manifestations of coccidioidomycosis
• Reactive
  – Syndromes w/in 48h of onset of illness
    • Acute exanthem
    • Erythema multiforme
    • Sweet’s Syndrome
  – Syndromes 1-3 wks post-onset of illness
    • Erythema nodosum
• Infectious
  – Primary cutaneous
    – Disseminated
      • Papules
      • Nodules
      • Verucous plaques
      • Abscesses
      • Pustules
      • Sinus tracts

Case 10.
27 year-old Tibetan student, studying in San Francisco presents with 2 years of draining abscesses on chest, neck, and armpits. He has no other symptoms, denies constitutional symptoms.
Cutaneous tuberculosis – many different manifestations

- Direct spread of infection from deep source
  - Scrofuloderma – direct spread from lymph nodes
- Disseminated infection
- Tuberculid (immune mediated)
- Pauci-bacillary infection (Lupus Vulgaris)