Skin and Soft Tissue Infections

Management of the Hospitalized Patient
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Disclosures

- I have no disclosures.

Learning Objectives

At the end of this lecture, you will be able to:

1. Describe the new data on adjunctive antibiotic use after I+D of an uncomplicated abscess.

2. Name the most common organisms that cause purulent vs. nonpurulent SSTI and choose empiric antibiotics based on this.

1. Identify the key elements of diagnosis and management of necrotizing SSTIs.

2. List the indications for and drug of choice for prophylaxis of human and animal bites.

Roadmap

1. Uncomplicated abscess
2. Purulent cellulitis
3. Nonpurulent cellulitis
4. Necrotizing infections
5. Human and animal bites
Overview of Skin and Soft Tissue Infections

- SSTI
  - Nonpurulent SSTI
  - Purulent SSTI
  - Necrotizing SSTI
  - Nonpurulent cellulitis
  - Purulent cellulitis
  - Uncomplicated Abscess

Case #1

40 year old man with a history of injection drug use presents with a right hand abscess but is otherwise clinically stable.

He gets an I+D in the emergency room.

What is the Most Evidenced-Based Option?

1. No antibiotics needed
2. TMP/SMX
3. Doxycycline
4. Amoxicillin/clavulanate
2 Studies That Changed Practice

- 2 RCT's of 800-1200 patients
- Small abscesses (most <3cm) + surrounding erythema
- All got I+D plus (oral antibiotics vs placebo for 7-10 d)
- ~50% MRSA, 17% MSSA

Talan et al., NEJM 2016, 374:823. Daum et al., NEJM 2017;376:2545.

Antibiotics Are Better Than I+D Alone

- Clinical Cure (%)
  - Clindamycin: 83%
  - TMP-SMX: 73%
  - Placebo: 69%

Talan 2016
Daum 2017

Empiric Oral Antibiotics for Abscess/Purulent SSTI

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose (S-10 days)</th>
<th>Strep Activity</th>
<th>Side effects/Comments</th>
<th>Local S. aureus susceptibility (know yours!)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMP-SMX</td>
<td>1 DS bid</td>
<td>+/-</td>
<td>+Hyperkalemia, AKI, Hyper-sensitivity</td>
<td>&gt;95% sensitive</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100mg bid</td>
<td>+/-</td>
<td>+GI, photosensitivity</td>
<td>&gt;90% sensitive</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>300mg tid</td>
<td>++</td>
<td>+GI, risk C. difficile, Can have resistance</td>
<td>45-85% MSSA, 80-85% MRSA</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600mg bid</td>
<td>++</td>
<td>+$55, Marrow suppression, Serotonin Syn w/5HT</td>
<td>&gt;100% sensitive</td>
</tr>
</tbody>
</table>


Microbiology of Skin Abscesses (Purulent SSTI)

- MRSA: 55%
- MSSA: 17%
- Other: 21%
- Beta-hemolytic Strep: 3%
- GNRs: 4%

Preferred Oral A8x for Known MRSA or MSSA

**MRSA**
- TMP-SMX
- Doxycycline
- Clindamycin
- Linezolid

**MSSA**
- Cephalexin
- Dicloxaciniln
- Any MRSA options

*Stevens et al., Clin Infect Dis 2014, 59:e10.*

Case #1 Conclusion

- No abscess culture was done
- Given TMP-SMX 1 DS PO bid x 1 week

Overview of Skin and Soft Tissue Infections

- SSTI
  - Nonpurulent SSTI
  - Purulent SSTI
  - Necrotizing SSTI
  - Uncomplicated Abscess

Case #2

35 year old man with Behcet’s on high dose prednisone is admitted with fever, tachycardia, and the skin lesions shown, now s/p I+D in the ER. He is allergic to vancomycin.
Which Antibiotics Would You Start?

1. Clindamycin IV
2. TMP-SMX IV
3. Daptomycin
4. Daptomycin + pip/tazo

Empiric IV Antibiotics for Purulent SSTI

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MRSA SSTI</th>
<th>MRSA Bacteremia</th>
<th>MRSA Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Linezolid</td>
<td>✓</td>
<td>+/-</td>
<td>✓</td>
</tr>
</tbody>
</table>

- Other MRSA-active agents: telavancin, ceftaroline, dalbavancin, oritavancin, delafloxacin
- If MSSA confirmed ➔ use nafcillin or cefazolin
- Step down to oral antibiotics against MRSA/MSSA

Case #2 Conclusion

- Abscess cultures grew MSSA
- Blood cultures negative
- Daptomycin ➔ Cefazolin ➔ cephalexin (total 10 days)

Purulent SSTI: Take-Home Points

1. For uncomplicated abscesses, give oral antibiotics in addition to I+D (but weigh risks and benefits)
2. Empiric oral or IV antibiotics should include coverage for MRSA and MSSA (>70% of abscesses)
3. For oral agents, TMP-SMX, doxycycline, and clindamycin are all good empiric options but know your local susceptibility patterns
4. For IV agents, consider if you also need coverage for bacteremia or pneumonia
Case #3

A 45-year-old man with no significant PMH is admitted with fever to 38.2°C and a red painful leg. Other vitals stable. WBC is 12.

Should You Get Blood Cultures?

1. Yes
2. No
Nonpurulent SSTI: When to Get Blood Cultures?

- Yield of blood cultures in uncomplicated nonpurulent cellulitis is <5%
- Rarely changes management

When should you get blood cultures in cellulitis?
1. Severe infection (high fever, hypotension, > WBC)
2. Immunocompromise (including malignancy)
3. Risk for unusual organisms (immersion injury, bites)
4. Risk of *S. aureus* bacteremia (IDU, severe purulent cellulitis)


Nonpurulent SSTI: Skin Sampling for Culture

- Yield of needle aspiration: <5% - 40%
- Yield of skin biopsy: 20%

When should you consider a skin biopsy?
1. Failure of appropriate empiric Rx - especially if severe, immunocompromised or at risk for unusual organisms
2. Consider upfront in severe infections in immunocompromised
3. Concern for a cellulitis mimicker


Case #3: What Antibiotics Would You Start?

1. Vancomycin
2. Cefazolin
3. Vancomycin + pip/tazo
4. Cefazolin + clindamycin

Nonpurulent SSTI: Microbiology

- >95% response to beta-lactams
- So MRSA is not a major player

No MRSA Coverage Needed: How Are We Doing?

Regimens for nonpurulent cellulitis in ED visits that include MRSA coverage:

2007

56%

2010

68%

So Do You Need MRSA Coverage or Not?

Bottom Line: MRSA coverage is NOT needed in uncomplicated nonpurulent cellulitis

Empiric Abx for Nonpurulent SSTI

<table>
<thead>
<tr>
<th></th>
<th>Beta-hemolytic Strep</th>
<th>MSSA</th>
<th>MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV options</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PO options</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Dicloxacillin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

When to Expand Coverage?

When to Cover for MRSA?

• Severe infection
•• Severe immunocompromise
• Penetrating trauma (surgical site infection, IV drug use)
• Concurrent MRSA elsewhere
• Not getting better without it

When to Cover for GNRs?

• Severe infection
•• Severe immunocompromise
• Surgical site infections in abdomen or axilla
•• Orbital cellulitis
• Not getting better without it

IV: Vanco, Daptomycin, Linezolid PO: Clinda alone or beta-lactam + (doxycycline or TMP-SMX)

IV: pip/tazo, ceftepime, ertapenem
PO: Amoxicillin/clavulanate, fluoroquinolone

Case #3 Continued

He is started on cefazolin. By the next day, there is no change in his exam, vitals signs, or WBC count.

How many days would you wait for a clinical response before escalating therapy?

When Would You Escalate Abx For Cellulitis?

1. After 1 day
2. After 2 days
3. After 3 days
4. After 4 days

When Should Cellulitis Get Better?

- Cessation of spread, improved inflammation
- Defervesce and WBC ↓

Escalation of Abx within 2 days was common but not associated with 0 response → likely was premature

Bruijn et al., Clin Infect Dis 2016, 63:1034.

Case #3 Continued

- He was escalated to vancomycin and pip/tazo by the overnight provider.
- After another 36 hours he is doing much better and is ready for discharge. Now what regimen should he be discharged on?
What Antibiotics Should He Go Home On?

1. TMP-SMX
2. Cephalexin
3. Amoxicillin/clavulanate
4. Doxycycline + ciprofloxacin

What PO Option Do You Step Down To?

You have to make a decision on what is most likely (3 options):

- Escalation was not needed → cover Strep
- Cover for both MRSA and Streptococcus
- Cover for MRSA, Strep and GNRs

How Long Should You Treat?

- RCT of 5 vs 10 days levofloxacin in uncomplicated nonpurulent cellulitis
- No difference in clinical response
- Bottom line (and IDSA Guidelines): Treat for 5 days as long as there is clinical improvement

Duration of Therapy: How Are We Doing?

Duration of Therapy for Uncomplicated SSTI in Hospitalized Adults

- Only 20% had an “appropriate” duration
Case #3 Conclusion

- He was discharged on cephalixin to complete a 5 day course of therapy

Nonpurulent SSTI: Take Home Points

1. Blood cultures are usually not indicated
2. The majority of nonpurulent cellulitis is caused by beta-hemolytic Streptococcus
3. Antibiotics should target beta-hemolytic Strep; MRSA coverage is not indicated in most patients
4. Duration of therapy = 5 days as long as there is clinical improvement

Nonpurulent Cellulitis: Therapy Review

Empiric (Strep) Oral
- Penicillin
- Amoxicillin
- Cephalexin
- Dicloxacillin
- Clindamycin

Duration = 5 days

Cover MRSA and Strep if:
- Severe infection
- Severe immunocompromise
- Trauma (surgical site infection, IV drug use)
- Concurrent MRSA elsewhere
- Not getting better without it
- IV: Vanco, Daptomycin, Linezolid
- PO: Clinda gg, beta-lactam + (doxy or TMP-SMX)
Case #4

84 year old man with peripheral vascular disease and diabetes is admitted with fever and progressive right leg pain.

Temp 39.3, HR 110
BP 79/41 \(\rightarrow\) pressors
WBC 16
Lactate 3.2
Other labs normal

What is the Best Next Step?

1. Plain films
2. Surgical evaluation
3. Calculate the LRINEC score
4. MRI

Which Antibiotics Would You Start?

1. Vancomycin
2. Vancomycin + clindamycin
3. Vancomycin + pip/tazo
4. Vancomycin + pip/tazo + clindamycin

Necrotizing Soft Tissue Infection (NSTI): Definition

- Defined as necrotizing infection of the dermis, subcutaneous tissue, fascia, or muscle
- A more inclusive term than necrotizing fasciitis
- Rare: 500-1500 cases/year
- Severe: mortality \(~20\%\), amputation in \(~16\%\)

Göh et al, BJS 2014, 101:s139.
NSTI: Microbiology

Polymicrobial (type I)
- Gram positives
- GNRs
- Anaerobes

Monomicrobial
- Group A Strep
- S. aureus
- GNRs
- Clostridium
- Vibrio
- Fungal

Positive wound cultures in 75%
Positive blood cultures in 35%


NSTI: Clinical Findings on Admission

Misdiagnosis is common: most do not have an admission dx of NSTI

NSTI: Evolution of Physical Findings

Early
- Warmth, erythema
- Tenderness (out of proportion, past margins)
- Swelling

Intermediate
- Bullae (serous)
- Tenderness
- Fluctuance
- Induration

Late
- Bullae (hemorrhagic)
- Skin anesthesia
- Crepitus
- Skin necrosis


The LRINEC Score

What is it?
- Laboratory Risk Indicator for Necrotizing Fasciitis
- Score composed of:
  - CRP (often missing!)
  - WBC
  - Hemoglobin
  - Sodium
  - Creatinine
  - Glucose
- Intermediate-high risk if ≥6

How good is it?
- Initial study:
  - Sensitivity 90%
  - Specificity 95%
  - PPV 92%, NPV 96%
- Subsequent studies:
  - Sensitivity 36-77%
  - Specificity ~90%
  - PPV 38-85%, NPV 86-95%
- Should not replace clinical suspicion!

Necrotizing Soft Tissue Infection: Imaging

Plain films
Gas in <25% of cases

CT
Sensitivity and specificity ~80-95%

MRI
Sensitivity ~100% but specificity only 60-70%


NSTI: Early Surgery is Critical

Survival if OR at 24h = 93%
Survival if OR at 48h = 75%

Time From Admission to Operation

NSTI: Antibiotics

MRSA
Vancomycin
Linezolid

GNR Coverage
Piperacillin/tazobactam
Carbapenem
Ceftriaxone + metronidazole
Cefepime + metronidazole

Clindamycin

NSTI: Why Clindamycin for Group A Strep?

Toxin production
Clindamycin
Eagle effect (PCN less effective at high inoculum)

What’s the clinical data?
- Multiple observational studies show a mortality benefit with addition of clindamycin (by 2-8 fold)


Stevens et al., Clin Infect Dis 2014; 59:e10.
Case #4 Conclusion

- Started on vanc+ pip/tazo + clinda
- Multiple debridements → amputation (AKA)
- Blood and tissue cultures grew E. coli
- Narrowed to ceftriaxone for 14 days → Did well

Necrotizing Soft Tissue Infection: Take Home Points

1. Pain (usually out of proportion to exam) is the most common early finding for NSTI
2. LRINEC score should not replace clinical suspicion
3. Subcutaneous gas on plain films is uncommon
4. Early surgery is critical
5. Use broad spectrum antibiotics plus clindamycin

Necrotizing SSTI: Therapy Review

- Evaluate early for surgical intervention
- Broad spectrum coverage:
  - Vancomycin or linezolid
  - Pip/tazo, carbapenem, ceftriaxone + metronidazole, or cefepime + metronidazole
  - Clindamycin

Human and Animal Bites

- 35% Necrotizing SSTI
- 50% Nonpurulent cellulitis
- 15% Uncomplicated Abscess
- 35% Purulent cellulitis
- 50% Nonpurulent SSTI
- 15% Purulent SSTI

Bites
Case #5

35 year old woman gets a deep bite by her cat. 24 hours later she develops swelling and pain of her right index finger.

Should She Have Received Prophylaxis?

1. Yes
2. No
3. Not sure

What is the Most Likely Organism?

- *S. aureus*
- Streptococci
- *Pasteurella*
- *Capnocytophaga*

Bite Wounds: Microbiology

- **Dog Bites**: *Pasteurella* 50%, Strep 45%, S. aureus 20%, Anaerobes 50%, Capnocytophaga 2%
- **Cat Bites**: *Pasteurella* 75%, Strep 45%, S. aureus 5%, Anaerobes 60%
- **Human Bites**: Strep 40%, S. aureus 40%, Eikenella 20%, Anaerobes 50%

- Think “what’s in their mouth and what’s on your skin”
- The majority of infections are **polymicrobial**

Bite Wounds: Antibiotic Prophylaxis

**Indications**
- Immunocompromise
- Advanced liver disease
- Edema of the affected area
- Moderate to severe injuries, especially face or hand
- Deep penetrating injuries (cat bites)

**Antibiotic Choice**
- First line: amoxicillin/clavulanate x 3-5 days
- Alternatives: moxifloxacin > doxycycline
- Make sure tetanus is up to date


Bite Wounds: Management of Established Infection

1. **Empiric Coverage**
   - **IV**
     - Amoxicillin/sulbactam
     - Piperacillin/sulbactam
     - Moxifloxacin
     - Ceftriaxone + metronidazole
     - Add MRSA coverage for purulent infection
   - **PO**
     - Amoxicillin/clavulanate
     - Moxifloxacin
     - Doxycycline

2. Evaluate for deep infection
   - Arthritis, osteomyelitis
   - Especially in cat bites

3. Ensure tetanus is up-to-date


Case #5 Conclusion

- She had an I+D with culture that was positive for *Pasteurella*
- MRI of the hand was negative for osteomyelitis
- She received ampicillin/sulbactam for 4 days and then amoxicillin/clavulanate to complete a 7 day course

Bite Wounds: Take-Home Points

1. Bite wound infections are usually polymicrobial with Staph, Strep, anaerobes, and GNRs (*Pasteurella* for cat/dog and *Eikenella* for human)
2. Amoxicillin/clavulanate is first line for prophylaxis and treatment of bite wound infections
3. Prophylaxis is only indicated in specific situations (mod-severe bites, immunocompromise, deep cat bites)
Human and Animal Bites: Therapy Review

- SSTI
- Nonpurulent SSTI
- Necrotizing SSTI
- Nonpurulent cellulitis
- Purulent cellulitis
- Uncomplicated Abscess

Empiric Abx
- Oral
  - Amox/clav
  - Moxifloxacin
  - Doxycycline
- IV
  - Amp/sulbactam
  - Pip/tazo
  - Moxifloxacin
  - Ceftriaxone + metronidazole

- If purulent, also cover MRSA

Thank You!
Questions?
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