Current Approach to Skin and Soft Tissue Infections
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“CURRENT APPROACH”

2012 IDSA UPDATE TO THE 2005 PRACTICE GUIDELINES FOR THE DIAGNOSIS AND MANAGEMENT OF SKIN AND SOFT-TISSUE INFECTIONS

Outline

- General comments about approach to S&ST Infections
- Present Cases
- Incorporate proposed new guidelines

General Approach to S&ST Infections

- Location of infx may help define bacteriology
- Primary infx (breach of intact skin) usually monomicrobial; Secondary infx (pre-existing abnormality) often polymicrobial
- Impaired immunity – rapidly progressive (requiring early and aggressive Rx) and can be due to unusual organisms (procedures to define etiology more important)
- Environmental exposures
- Role of cultures
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- Role of cultures
Other Interesting Syndromes

- Nontuberculous mycobacteria (“Rapid Growers” M. fortuitum, chelonae-abscessus group) infections associated with nail salons and cosmetic surgery
  - Pseudomonas “Hot-Foot Syndrome” assoc. with wading pools with abrasive grit on floor
  - Aeromonas hydrophilia wound infections associated with mud football.
  - “Hot Tub Lung” due to Mycobacterium avium complex in otherwise healthy individuals

General Approach to S&ST Infections

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Role of Cultures

- Blood Cultures (Clin Infect Dis 1999;29:1483)
  - Low yield (1-2%), did not change therapy or outcome, expensive
- NEW RECOMMENDATIONS—BCs should be obtained & biopsy with culture considered:
  - Malignancy
  - Severe systemic Sxs (high fever/hypotension)
  - Unusual predisposing factors
    - Immersion injuries, animal bites, neutropenia and severe cell-mediated immunodeficiency

Masqueraders of Cellulitis

- Superficial and deep venous thrombosis
- Contact dermatitis
- Insect stings/tick bites
- Fixed drug eruptions
- Hydradenitis suppurativa
- Erythema nodosum
- Panniculitis
- Sweet syndrome
- Pyoderma Gangrenosum

Case

- 45 year old man with minor trauma to leg
- Subsequently developed an ulcer treated with oral cephalosporins, but lesion progressed.
- Eventually admitted to the hospital for IV antibiotics—cultures negative—continued enlargement of lesion
- Taken to surgery 3 times to resect to clean margins—cultures negative or S. epi—after each surgery lesion progressed
- Eventually transferred to UCSF
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Case Presentation

- A 66 year old woman with chronic LE edema secondary to CHF presents with the acute onset of a red, warm swollen and tender left foot. Erythema and tenderness extend to the mid-tibial area.
## Etiology of Cellulitis

- **Outpatient** – Usually caused by *Strep. pyogenes* (Gp A strep); *S. aureus* and other strep (gp B,C,G)
- **Hospital-associated** – May include *gram-neg organisms*, (E.coli, klebs, pseudomonas, enterobacter) as well as staph (including MRSA) and strep
- **Decubitus/Diabetic/Vascular Ulcers** – *polymicrobial* including staph, strep, enterococcus, enteric gram-negatives, pseudomonas, anaerobes
- **Animal Bites** – *Pasteurella multocida* (< 24 hours); staph, strep, “mouth” anaerobes later
  - Augmentin® (TMP-SMX, FQ, doxycycline)
  - NOT ACTIVE – Keflex®, dicloxacillin, clindamycin erythromycin
- **Human Bites** – aerobic and anaerobic mouth flora as well as *Eikenella corrodens*
  - Antibiotic considerations same as *Pasteurella multocida*

### Therapeutic Considerations

#### THE WAY IT WAS
- Gp A strep + MSSA = dicloxacillin or cephalaxin (Keflex®)

#### THE WAY IT IS
- Gp A strep + ?? MRSA

### Table 1. Etiology of cellulitis

<table>
<thead>
<tr>
<th>Source</th>
<th>Date ranges</th>
<th>Location</th>
<th>Adult (A) or pediatric (P)</th>
<th>Location of media aspiration/biopsy (L) or culture (C)</th>
<th>No. of patients cultured (n)</th>
<th>Positive culture (%)</th>
<th>Culture positive for group A streptococcus (%)</th>
<th>Culture positive for other pathogens (%)</th>
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<tbody>
<tr>
<td>Vassar et al.</td>
<td>1975-1978</td>
<td>NR</td>
<td>N</td>
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<td>O'Connell et al.</td>
<td>1980-1981</td>
<td>Boston, MA</td>
<td>A, P</td>
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<td>Goldberg et al.</td>
<td>1989-1991</td>
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<td>Lis et al.</td>
<td>1990-1993</td>
<td>Argentina</td>
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<td>5</td>
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<td>Edie &amp; Hill.</td>
<td>1990-1991</td>
<td>Kansas City, MO</td>
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<td>Books et al.</td>
<td>1989-1990</td>
<td>Norfolk, VA</td>
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<td>Egeredt et al.</td>
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<td>Stone et al.</td>
<td>1987-1988</td>
<td>Portmouth, VA</td>
<td>P</td>
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<td>6</td>
<td>6</td>
<td>5</td>
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<td>Everard et al.</td>
<td>1990-1991</td>
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<td>1</td>
<td>1</td>
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<tr>
<td>Newell &amp; Norma</td>
<td>1980-1981</td>
<td>Pittsburgh, PA</td>
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<td>Kibbe et al.</td>
<td>1984-1990</td>
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<td>Dowsett et al.</td>
<td>1986-1989</td>
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<td>4</td>
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<tr>
<td>Lebje et al.</td>
<td>1990-1994</td>
<td>France</td>
<td>NR</td>
<td>N, C</td>
<td>28</td>
<td>9</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

**Total 16% 50% 27%**
Therapeutic Considerations

- TMP-SMX (95-100%); doxy/minocycline (90-95%); clindamycin (85-90%) are active against CA-MRSA
- TMP-SMX and doxy/mino +/- against gp A strep
  - If use these must add β-lactam [PCN, Amox, 1st gen ceph (Keflex®)]
- Clinda active against gp A strep

GOAL

- Convince you that:
  - Majority of cases of nonculturable cellulitis (without abscess, ulcers, drainage) are due to BHS or MSSA
  - AND
  - 1st generation cephalosporin (Keflex® or Cefazolin) is reasonable empiric therapy

Study Design

- Prospective evaluation of all patients presenting with diffuse, nonculturable cellulitis requiring admission to the hospital
- Measured anti-streptolysin O (ASO) antibodies
  - Rise after infection with GAS, GCS and GGS
  - 98% of adults have titers < 170 IU/mL
- Anti-deoxyribonuclease-B (anti-DNase-B or ADB)
  - Rise after infection with GAS
  - 95% of adults have titers < 120 U/mL
Study Design

- Measure acute and convalescent (2-12 weeks) titers
- Exclusions:
  - Those with abscess, furuncle, ulcer
  - Those who received more than one dose of an antibiotic active against MRSA
- OUTCOME MEASURE:
  - Response to β-lactam antibiotics

Additional Evidence
Clin Infect Dis 2013;March 1

- Randomized, multi-centered double-blind placebo controlled study
- Patients with non-purulent cellulitis
- Cephalexin vs Cephalexin + TMP-SMX
- Outcome measure—cure at 14 days
  - Cephalexin + TMP-SMX = 85%
  - Cephalexin + Placebo = 82%

Approach to Patient with Cellulitis

Cellulitis

Culturable (eg abscess, furuncle wound)

- Direct therapy to GpA strep & MSSA (diclox/cephalexin)
- Worse after 2-3 D of RX
  - Add coverage for MRSA (TMP-SMX)\n
NO

YES

I&D and treat for MRSA & GpA strep (clindamycin, doxy + cephalexin, TMP-SMX + cephalexin)
IDSA Guidelines

- For "typical" cases of cellulitis (nonculturable) use an antibiotic active against streptococci
- Many would include coverage for MSSA as well
- Treat for MRSA if there is drainage or an open wound (culturable), penetrating trauma or systemically ill
- Recommended duration is 5 days as long as improvement has occurred
  - Extend to 10 days if not improved in 5 days
- Elevation; interdigital toe exam to correct possible portals of entry

Case Presentation

- A 56 year old diabetic presents with an ulcer on the metatarsal-phalangeal area of the plantar aspect of the foot. There is surrounding cellulitis with a necrotic base to the ulcer, but no purulent material can be expressed and bone is not showing. He has no F/C.

Recurrent Cellulitis


- Low dose penicillin (250 mg BID) reduces the risk of recurrent cellulitis compared to placebo (22% v 37%; P = 0.01)
- Risk factors for failure:
  - BMI ≥ 33
  - ≥ 3 previous episodes of cellulitis
  - Edema
- Correct predisposing factors
  - Tinea pedis, ulcerations, edema, onychomycosis
### Bacteriology

*(J Clin Microbiol 2007;45:2819)*

- **S. AUREUS (including MRSA) + STOOL**
  - On average 5 isolates per wound
  - Aerobes—48%
    - S. aureus, streptococci, enterococci, enterobacteriaceae, pseudomonas
  - Aerobes + Anaerobes
    - Bacteroides fragilis group
    - Prevotella
    - Porphyromonas

### Therapy of Diabetic Foot Ulcers

- **Mild infections direct therapy against GPC**
  - Dicloxacillin, cephalaxin, clindamycin, Augmentin®
- **If concern about MRSA**
  - Add TMP-SMX or doxycycline
- **Duration of therapy—1-2 weeks**
- **If fail therapy obtain cultures and base therapy on results**
  - Tissue biopsy or curettage of the ulcer base

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**Outcomes of Therapy - Diabetic Foot Infections**

*(Arch Int Med 1990;150:750)*

<table>
<thead>
<tr>
<th></th>
<th>Clindamycin</th>
<th>Cephalexin</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healing</td>
<td>(n=25)</td>
<td>(n=27)</td>
<td>(n=52)</td>
</tr>
<tr>
<td>Healed</td>
<td>10(40%)</td>
<td>9(33%)</td>
<td>19(37%)</td>
</tr>
<tr>
<td>Improved</td>
<td>14(56%)</td>
<td>18(67%)</td>
<td>32(62%)</td>
</tr>
<tr>
<td>Unimproved</td>
<td>1(4%)</td>
<td>0(0%)</td>
<td>1(2%)</td>
</tr>
</tbody>
</table>

Lipsky et al CID 2012;54:132-173
Osteomyelitis

- Diagnosis
  - MRI—98% sensitivity and 89% specificity
  - Bone Biopsy—gold standard
    - Poor correlation between superficial cultures and bone biopsy
- Therapy
  - Based on culture
  - Duration—6 weeks—usually with surgery

Lipsky et al CID 2012:54;132-173

Adjunctive Therapy

- VAC (vacuum-assisted closure) therapy
  - Advanced wounds (Grade 3) and post-surgical patients promotes wound closure and shortens hospitalization
- Growth Factors
  - Becaplermin—Regranex® (a topically applied human recombinant platelet-derived growth factor)
    - FDA approved; increases complete wound closure
    - High cost; post-marketing reports of increased risk of cancer
- HBO (Hyperbaric Oxygen)
  - More data needed—some suggestion that it may be beneficial
  - HBO + Growth Factors currently under study
Impetigo

- Caused by gp A strep (rarely gp B, C and G) and S. aureus
- Disease of children (age 2-5) but can occur in adults
- Predisposing factors include warm climate, crowding, poor hygiene

Impetigo - Therapy & Complications

- Per IDSA Recommendations
  - Antibiotics active against streptococci and MSSA
    - 1st generation cephalosporin (Keflex®), dicloxacillin, Augmentin®, clindamycin for penicillin-allergic patient
  - If fail to respond, culture
    - On rare occasions MRSA may be cause
    - If confirmed clindamycin, doxycycline or TMP-SMX
  - Topical antibiotics (mupirocin) for localized disease
  - Non-suppurative complication—post-streptococcal GN
    - Antibiotics do not prevent GN
    - Rheumatic fever not reported

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**Erysipelas**

- Caused by *group A strep* (occasionally other gps)
- Bimodal distribution – infants/children and older adults
- Usually face and extremities; abdomen if assoc with surgery
- Painful, raised, erythematous, rapidly spreading lesion with well demarcated edges
- Systemic symptoms common
- Therapy same as non-culturable cellulitis

**Cutaneous Staphylococcal Infections**

- Folliculitis
- Furunculosis (boils)
- Carbuncles (coalescent boils)
- Skin abscesses
- Recurrent skin abscess

**Cutaneous Staphylococcal Infections**

- Folliculitis
- Furuncle (Boil)
- Carbuncle

**Infections of hair follicles**

<table>
<thead>
<tr>
<th>Epidermis</th>
<th>Dermis</th>
</tr>
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<tbody>
<tr>
<td><strong>Folliculitis</strong></td>
<td><strong>Furuncle (Boil)</strong></td>
</tr>
<tr>
<td><strong>Carbuncle</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1mm peri-follicular red papule or pustule</th>
<th>About 1 cm tender red papule or fluctuant nodule</th>
<th>Several cm diam red plaque</th>
</tr>
</thead>
<tbody>
<tr>
<td>Areas of sweat &amp; abrasion</td>
<td>Areas of sweat &amp; abrasion</td>
<td>Nape of neck</td>
</tr>
</tbody>
</table>
Folliculitis

Folliculitis

Furuncle or boil

Carbuncle
Cutaneous Staphylococcal Infections/Therapy per Guidelines

- Enhanced hygiene
- Warm compresses
- I&D
- ABXs if systemic Sxs

Skin Abscesses

- Involves dermis and deeper skin tissues
- Treatment: (per new guidelines)
  - I&D (Aspiration inferior)
  - Systemic antibiotics ONLY IF:
    - Impaired host defenses
    - Systemic symptoms
    - Difficult to drain areas (face, hand, genitalia)
    - Failure to improve with drainage alone

Recurrent Skin Abscesses

- Increasing frequency
- Most commonly due to MRSA—still see some MSSA
- Pathogenesis:
  - Nasopharyngeal colonization
  - Skin colonization (axilla, groin, perirectal)
  - Auto-inoculation
- Treatment—eradicate colonization
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IDSA Recommendations for Treatment of Recurrent Abscesses

- Drain the abscess and culture
- Consider 5-10 days of treatment with an antibiotic**
- Consider a decolonization regimen of intranasal mupirocin and chlorhexidine washes and daily decontamination of personal items such as towels, sheets, and clothes**
- **weak recommendation with low quality of evidence

IDSA Guidelines for Therapy of MRSA Infections
CID 2011:52 (1 February) Liu et al.

- Emphasize personal hygiene
- Decolonization may be considered if continued infections despite good hygiene**
  - Nasal mupirocin twice daily for 5-10 days
  - Topical body decolonization with chlorhexidine or bleach baths for 5-14 days
- Oral antimicrobial regimens may be considered if the above measures fail
- **Poor evidence to support recommendation; based on opinions of experts

Regimen for Eradication of S. aureus Carriage

- My personal approach
  - TMP-SMX DS BID + Rifampin 300mg BID X 5 days—repeat every 6 weeks for 8 courses
  - Chlorhexidine 2-3 X per week
  - Personal Hygiene
    - Clothes daily
    - Towels Q 3 days
    - Sheets Q week
  - Vitamin C (1 gram/day)
Case Presentation

- A 25 y.o. previously healthy farm worker sustained trauma to his penis 2 days prior to admission. He presented to a local ED where he was found to have a small necrotic area on his penis that progressed while he was in the ED. He was given a dose of ceftriaxone and transferred to UCSF.

Questions

- What is the diagnosis?
- What is the bacteriology?
- What is appropriate therapy?

BACTERIOLOGY OF NECROTIZING FASCIITIS

- Type I
  - Anaerobes (peptostreptococcus, bacteroides, anaerobic/microaerophilic streptococci)
  - Enteric gram-negative bacilli (E. coli, klebsiella, proteus, serratia, etc)
- Type II (hemolytic streptococcal gangrene)
  - Group A streptococcus ± S. aureus
DEEP TISSUE INFECTIONS

- Consider polymicrobial
- Broad spectrum antibiotics
  - Vancomycin or linezolid
  - Piperacillin-tazobactam or a carbapenem
- Surgery
- If Group A strep is the cause
  - Penicillin + clindamycin

WHEN TO SUSPECT DEEP TISSUE INFECTION

- High risk patient – diabetes, trauma, surgery
- Wound necrosis
- Gas
- Exudate (foul smelling)
- Systemic symptoms out of proportion to local findings
- Anesthesia of involved area

Take Home Points

- Bacteriology can often be predicted by location of infection
  - Superficial infections usually GpA strep and S aureus
  - Deep infections polymicrobial
- History/Epidemiology can offer important clues to the diagnosis
- Mimickers of cellulitis
  - If not responding as expected think about biopsy

Take Home Points

- The etiology of cellulitis depends on the clinical scenario
- Outpatient cellulitis
  - Nonculturable/nonpurulent–Gp A strep & MSSA
  - Abscess/open wound–MRSA
- Diabetic foot ulcers are polymicrobial but only have to direct therapy to Gp A strep & MRSA
Take Home Points

- Recurrent skin abscesses (in my opinion) is best treated with an intermittent rifampin-based regimen
- Deep tissue infections are uncommon, but think of them if there is pain out of proportion to clinical findings
  - “A spider bite is NF until proven otherwise”