Skin and Soft Tissue Infections

Richard A. Jacobs, M.D., PhD.

- 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

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
Mycobacterial (M. fortuitum) furunculosis assoc. with footbaths at nail salon
M. chelonae cellulitis assoc with face lifts (methylene blue)
M. abscessus infections assoc with cosmetic surgery in the Dominican Republic
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

Other Interesting Syndromes

- Mycobacterial (M. fortuitum) furunculosis assoc. with footbaths at nail salon
- M. chelonae cellulitis assoc with face lifts (methylene blue)
- M. abscessus infections assoc with cosmetic surgery in the Dominican Republic
- 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
- "Tropical Diabetic Hand Syndrome" seen in tropical areas (usually Africa/India, but also US) and not assoc with vascular disease or peripheral neuropathy -- Staph and strep most common, but mixed infections occur

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

Role of Cultures

(Kuehlewein MA et al Arch Intern Med 1988;148:2451
Sachs MK Arch Intern Med 1990;150:1907)

- Diagnosis usually made clinically
- Culture of leading edge -- positive in 15–40%, especially those with underlying diseases (diabetes, malignancy)
- Indicated for:
  - Failure to respond
  - Immunocompromised
  - Suspect deep tissue infections (myositis, fasciitis)
- Blood Cultures

Role of Blood Cultures in S&ST Infections

(Perl B et al Clin Infect Dis 1999;29:1483)

- 757 pts with cellulitis; 553 with 710 BC’s
- Only 11(1.6%) positive -- most β-hemolytic strep; one with vibrio and one with Morganella
- Low yield, did not change therapy or outcome and expensive
Literature does not address:
- Immunocompromised patients
- Patients with multiple co-morbidities
- Unusual exposures
- Complicated soft tissue infections (myositis, fasciitis)

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

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.

What is the diagnosis?
What is the bacterial etiology?
What is appropriate therapy?
**Etiology of Cellulitis**

- **Outpatient** — Usually caused by Strep. pyogenes (Gp A strep); less commonly by S. aureus and rarely by 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.
- **Human Bites** — aerobic and anaerobic mouth flora as well as Eikenella corrodens.

**How common is S. aureus?**

- FNA or Bx of patients with cellulitis admitted to the hospital:
  - Of 8 (+) cultures, 7 were S. aureus.
  - (Arch Int Med 1989;149:293)
- FNA or Bx of cellulitis in Pediatric Acute Care Clinic:
  - Of 9 (+) cultures, 6 were S. aureus.
  - (Pediatr Infect Dis J 1987;6:685)

**The Way It Was**

- Gp A strep + MSSA = dicloxacillin or cephalaxin (Keflex®)

**The Way It Is**

- Gp A strep + ?? MRSA
TMP-SMX (95–100%); doxy/minocycline (90–95%); clindamycin (85–95%) 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

Outpatient
  - dicloxacillin or Keflex* if low prevalence of CA-MRSA
  - TMP-SMX or doxy/mino + β-lactam
  - Clindamycin
  - Duration of therapy
    - Standard 7–14 days
    - Recent data suggests 5 days as good as 10 days
  - Hospital-associated
    - Vancomycin +/- a third generation cephalosporin
  - *IDSA guidelines on Rx of S&ST infections--Summer of 2009

Purulent wounds and cellulitis with purulent drainage--50% caused by CA-MRSA

Treatment should include MRSA
  - Clindamycin
  - TMP-SMX/doxycycline + β-lactam

**PURE CELLULITIS** (without purulent drainage or abscess)
  - The role of CA-MRSA is unknown; in addition to coverage for β-hemolytic streptococci, empiric therapy for CA-MRSA may be considered

**CELLULITIS WITH PURULENT DRAINAGE**
  - Empiric therapy for CA-MRSA is recommended

A 10 year old boy is in the park with friends. As he goes after a ball, he passes close to a dog that was resting in the shade. The dog jumps up, chases the boy and bites him on the leg inflicting several puncture wounds on the calf. The father, who was supposed to be closely monitoring the boy, calls in a panic and wants to know what to do.

Is it a high risk bite that requires prophylactic antibiotics?

If so, which one and for how long?
A bite from which of the following is LEAST likely to become infected?

1. Dog
2. Cat
3. Human
4. Monkey
5. Pig

**INFECTION RATE BY BITING ANIMAL**

<table>
<thead>
<tr>
<th>ANIMAL</th>
<th>LITERATURE</th>
<th>UCSF</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAT</td>
<td>30-50%</td>
<td>50%</td>
</tr>
<tr>
<td>HUMAN</td>
<td>15-30%</td>
<td>16%</td>
</tr>
<tr>
<td>DOG</td>
<td>2-4%</td>
<td>4%</td>
</tr>
</tbody>
</table>

**INFECTION–PRONE WOUNDS**

- ANIMAL
- LOCATION OF WOUND
- TYPE OF WOUND
- INTERVAL BETWEEN BITE TO OBTAINING MEDICAL CARE

**INFECTION RISK FACTORS**

<table>
<thead>
<tr>
<th>HIGH RISK</th>
<th>LOW RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biting species</td>
<td>Cat Pig Human Primate Dog Rodent</td>
</tr>
<tr>
<td>Wound Location</td>
<td>Hand Over a joint Foot Through-and-through oral Face Scalp Mucosal</td>
</tr>
<tr>
<td>Wound Type</td>
<td>Puncture Dirty Crush Old Clean Recent Abrasion/Open</td>
</tr>
<tr>
<td>Patient</td>
<td>Elderly Asplenic Alcoholic Diabetic Steroids PVD</td>
</tr>
</tbody>
</table>

**BACTERIOLOGY OF DOG AND CAT BITES**

- POLYMICROBIAL
  - Median of 5 isolates per culture
  - 56% aerobic and anaerobic
  - 36% aerobic only
  - 1% anaerobic only
  - 7% now growth

- PASTURELLA MOST COMMON ISOLATE
  - 50% of dog bites and 75% of cat bites
- STREPTOCOCCI, STAPHYLOCOCCI, MORAXELLA AND NEISSERIA MOST COMMON AEROBES
- FUSOBACTERIUM, BACTEROIDES, PORPHYROMONAS AND PREVOTELLA MOST COMMON ANAEROBES
**Bacteriology of Dog and Cat Bites**

- **Pasteurella**
  - GNR
  - Susceptible to PCN and its derivatives, 2nd and 3rd generation cephalosporins, tetracyclines, quinolones and TMP-SMX
  - **NOT SENSITIVE TO DRUGS OFTEN USED TO TREAT CELLULITIS**—1st generation cephalosporins, penicillinase-resistant penicillins, clindamycin, erythromycin
- **Anaerobes**
  - Often produce β-lactamase

**Prophylaxis for Dog & Cat Bites**

- **NOT WELL STUDIED**—no consensus—tendency is to be liberal
  - High risk animal—cat, human, primate
  - High risk type—puncture, crush
  - High risk location—hand, foot, face
  - High risk individual—splenectomy, DM, immunocompromised, prednisone

**Prophylaxis**

- **Choice of Antibiotics**
  - For simplicity would favor Augmentin® in most cases, even though less expensive more narrow spectrum regimens might work
  - Duration 5 days

**Treatment of Dog and Cat Bites**

- **Combination β-Lactam + β-Lactamase Inhibitor**
  - Unasyn® (ampicillin + sulbactam)
  - Timentin® (ticarcillin + clavulanic acid)
  - Zosyn® (piperacillin + tazobactam)
  - Augmentin® (amoxicillin + clavulanic acid)
- **2nd Generation Cephalosporin with Anaerobic Activity**
  - Cefoxitin
- **Clindamycin + Fluoroquinolone**
  - Carbapenem—ERTAPENEM

**Human Bites—Classification**

(Talan et al Clin Infect Dis 2003;37:1481)

- **Three Types**
  - Clenched Fist Injury (CFI)—20–50% infx rate and often assoc with Tx, septic arthritis, osteo, tendon rupture
  - Occlusive bites (non–CFIs) — low risk of infection similar to that of lacerations (5%) if superficial; if deep, similar to CFI
  - Self-inflicted bites (oral and mucocutaneous)—oral low risk of infection; “through-and-through” or mucocutaneous injuries have about 30% infection rate

**Human Bites—Bacteriology**

- **Polymicrobial**
  - 4 isolates/wound—3 aerobes and 1 anaerobe
  - 54% aerobic + anaerobic
  - 44% aerobic
  - 2% anaerobic
**HUMAN BITES—BACTERIOLOGY**
(Talan et al Clin Infect Dis 2003;37:1481)

- Streptococci (84%), staphylococci (54%) and Eikenella corrodens (30%)—most common
  - Eikenella part of normal oral flora
  - Sensitive to PCN, 2nd and 3rd generation cephalosporins, quinolones, TMP-SMX
- Others—Haemophilus, corynebacterium, neisseria, gamella
  - Prevotella, fusobacterium, veillonella, peptostreptococcus—often produce β-lactamase

**NOT WELL STUDIED**

- High Risk Bites
  - Bites to the hand
  - Through-and-through mucosal bites
- Augmentin® reasonable choice for 5 days

**PROPHYLAXIS OF HUMAN BITES**

**TREATMENT OF HUMAN BITES**

- **COMBINATION β-LACTAM + β-LACTAMASE INHIBITOR**
  - Unasyn® (ampicillin + sulbactam)
  - Timentin® (ticarcillin + clavulanic acid)
  - Zosyn® (piperacillin + tazobactam)
  - Augmentin® (amoxicillin + clavulanic acid)
- **2nd GENERATION CEPHALOSPORIN WITH ANAEROBIC ACTIVITY**
  - Cefoxitin
- **CLINDAMYCIN + FLUOROQUINOLONE CARBAPENEM—ERTAPENEM**
**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—- inoculation of organism from colonized skin into abrasions, insect bites, etc

**Impetigo -- Clinical Manifestations**

- Papule —> evanescent vesicle —> pustule that enlarges —> breaks down over 4–6 days —> seropurulent discharge that dries to form typical thick golden-yellow crust
- Superinfection (S. aureus) can occur
- Heals slowly with depigmentation
- Dx by appearance; if any doubt can culture

**Impetigo -- Therapy & Complications**

- 1st generation cephalosporin (Keflex®), penicillinase-resistant penicillin (dicloxacillin) or amoxicillin–clavulanic acid (Augmentin®)
- Clindamycin for penicillin allergic patient
- Topical antibiotics (mupirocin) less effective — fail to eradicate skin colonization or prevent new lesion formation
- Non-suppurative complication — post-streptococcal GN
- Antibiotics do NOT prevent GN
- Rheumatic fever not reported

**Erysipelas**

- Caused by gp 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
Infection of the submandibular space, usually associated with dental extraction. Caused by “oral flora” -- aerobic and anaerobic strep, fusobacterium, bacteroides spp. Acute onset with brawny, painful edema (“bull-neck appearance”), fever, elevation of tongue with drooling and dysphagia.

Ludwig's Angina

○ Infection of the submandibular space, usually associated with dental extraction
○ Caused by “oral flora” -- aerobic and anaerobic strep, fusobacterium, bacteroides spp
○ Acute onset with brawny, painful edema (“bull-neck appearance”), fever, elevation of tongue with drooling and dysphagia

Ludwig's Angina -- Therapy

○ Maintain airway
○ Antibiotics -- PCN + flagyl or clindamycin
○ Surgery if abscess forms or fails to respond in several days

Cutaneous Staphylococcal Infections

○ Folliculitis
○ Furunculosis (boils)
○ Carbuncles (coalescent boils)
○ Recurrent furunculosis
Recurrent S. aureus Furunculosis

- Increasing frequency
- Most commonly due to MRSA
- Pathogenesis:
  - Nasopharyngeal colonization
  - Skin colonization (axilla, groin, perirectal)
    - 25% continuously colonized
    - 50% intermittently colonized
    - 25% never colonized
- Treatment—eradicate colonization

Draft Recommendations of IDSA

- "Lack of evidence-based data"
- "The role of decolonization in preventing recurrent infection is unclear and more data is needed to establish efficacy and identify optimal regimens"
- Emphasize personal hygiene
- Decolonization can be considered in selected cases—recurrent infections despite good hygiene
  - Recommend nasal Mupirocin and body decolonization with chlorhexidine baths
  - ORAL ANTIBIOTICS ARE NOT ROUTINELY RECOMMENDED

Regimens 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
  - Hibiclens 2x per week
  - Personal Hygiene
    - Clothes daily
    - Towels Q 3 days
    - Sheets Q week
    - Vitamin C

Vitamin C for Recurrent Furunculosis

(Levy R et al) Infect Dis 1996;173:1502)

- Patients with recurrent furunculosis
  - Negative nasopharyngeal cultures
  - Neutrophil dysfunction (chemotaxis, phagocytosis, superoxide generation)
  - Rx = Vitamin C 1 gram/day X 4–6 weeks
  - Result = clinical improvement and improvement in neutrophil function
  - Conclusion: "Lazy Leukocytes" --- transient neutrophil dysfunction improved by vitamin C, perhaps through its antioxidant effect

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.

Figure 2.—Actual skin necrosis and breakdown in a patient who developed several days after the initiation of infection.
Questions

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

FLESH EATING BACTERIA

BACTERIOLOGY OF NECROTIZING FASCIITIS

- Type I
  - Anaerobes (peptostreptococcus, bacteroides, anaerobic/microaerophilic streptococci)
  - Enteric gram-negative bacilli (E. coli, klebsiella, proteus, serrata, etc)

- Type II (hemolytic streptococcal gangrene)
  - Group A streptococcus + S. aureus
LUMPER vs. SPLITTER

DEEP TISSUE INFECTIONS

- Consider polymicrobial
- Broad spectrum antibiotics
  - Vancomycin + flagyl + tobramycin
  - Flagyl + 3rd generation cephalosporin
  - ß-lactam + ß-lactamase inhibitor +
    tobramycin
  - Carbapenem
- Surgery

Differential Diagnosis of Deep Tissue Infections

- Progressive Bacterial Synergistic Gangrene
- Synergistic Necrotizing Cellulitis
- Gas Gangrene
- Necrotizing Cutaneous Mucormycosis
- Anaerobic Cellulitis
- Fournier’s Gangrene

- Incubation Period
- Onset (gradual/acute)
- Pain/Swelling
- Exudate (Thin/Thick/Dark/SS/Purulent/Seropurulent/Dishwater)
- Gas
- Odor (Sour/Sweet)

WHEN TO SUSPECT DEEP TISSUE INFECTION

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

CASE PRESENTATION

- A 50 y/o faculty member
  - 4 months prior
    - Cactus fell on hand
    - ED for removal of spines
    - Rx = Augmentin X 7 days
  - 3 months prior – pain in index finger
  - 3 weeks prior – pustule with drainage and nodular lymphangitis
  - No systemic symptoms and not immunocompromised

- Onset (gradual/acute)
- Pain/Swelling
- Exudate
  - Thin/Thick/Dark/SS/Purulent/Seropurulent/Dishwater
  - Gas
- Odor (Sour/Sweet)
CAUSES OF ACUTE LYMPHANGITIS

<table>
<thead>
<tr>
<th>ORGANISM</th>
<th>FREQUENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gp A streptoccoccus</td>
<td>Common</td>
</tr>
<tr>
<td>S. aureus</td>
<td>Occasional</td>
</tr>
<tr>
<td>Pasteurella multocida</td>
<td>Occasional</td>
</tr>
<tr>
<td>Spirillium minor</td>
<td>Rare</td>
</tr>
<tr>
<td>Filariasis</td>
<td>Rare</td>
</tr>
</tbody>
</table>

QUESTION

» What is the diagnosis?

NODULAR LYMPHANGITIS

» Common causes
  - Sporothrix schenckii
  - Nocardia (brasiliensis > asteroides)
  - Mycobacterium marinum
  - Francisella tularensis
  - Leishmania species

» Less common causes
  - Fungi – cocci, crypto, histo, blasto
  - Mycobacteria – chelonae, kansasii, avium–intracellulare, tuberculosis
  - Bacteria – S. aureus, gp A strep, Pseudomonas pseudomallei, Bacillus anthracis
Selected References

- Baddour LM. Recent considerations in recurrent cellulitis. Current Infect Dis Reports 2001:3:46