Skin and Soft Tissue Infections & Osteomyelitis

David T. Bearden, Pharm.D.
Clinical Associate Professor
Department of Pharmacy Practice
Objectives

• Empiric regimen – cellulitis
• Bite wounds
• Cellulitis abx vs. diabetic foot abx
• Community-associated MRSA
• Therapy for osteomyelitis
Skin Defenses

- Dry
- Skin shedding = bacterial shedding
- Sebaceous secretions
  - Inhibit bacteria
  - Inhibit fungi
Skin and Soft Tissue Infections

- Predisposing factors:
  - High concentration of bacteria
  - Excessive moisture
  - Occlusion of the blood supply
  - Presence of bacterial nutrients
  - Disruption of the corneal layer
Types of infections

- Primary
  - Healthy skin
- Secondary
  - Damaged skin

- Cellulitis
- Erysipelas
- Impetigo
- Lymphangitis
- Diabetic foot
- Bite wounds
Cellulitis

• Spreading infection that affects the epidermis and dermis

• Common pathogens
  • GABHS, S. aureus
  • Group B Strept (NB), S. epidermidis
  • Gram negative – enteric GNR
Presentation

- Erythema and edema
  - Warm, red, demarcated
- Often lymphadenopathy
- Malaise, fever, chills, ↑WBC
- Hx minor abrasion, trauma
Cellulitis of lower leg
S. aureus cellulitis of the nose
Diagnosis

- Clinical presentation
- Saline needle aspiration (rare)
- Cx injury site

*Pathogen not usually isolated
Special Populations

- Diabetics
  - Mixed aerobes and anaerobes
  - Often vascular insufficiency
- Children 1-5 years
  - H. influenzae
  - ↓Vaccine
Treatment

• Non-pharmacologic – elevate, saline
• Empiric treatment
  • Cover *staphylococci* and *streptococci*
    • Mild – dicloxacillin, erythromycin, clindamycin, cephalexin (?)
    • Mod/Severe – IV nafcillin/oxacillin, clindamycin plus fluoroquinolone
  • Consider MRSA (pus, pt. populations)
Special Circumstances

- MRSA – vancomycin, or TMP/SMX
- Suspect gram negatives (anaerobes?)
  - DM
  - Foot, leg, axilla
  - $\beta$-lactam/ $\beta$L inhibitor
- Duration
  - 7 to 10 days
Erysipelas

** Streptococcus pyogenes – GAβHS

- Infants, children, nephrotic syndrome, lymphatic destruction
- Superficial w/ lymph involvement
- Sharp, demarcated borders
- Typically face, scalp, hands
Erysipelas
Treatment - Erysipelas

- Dicloxacillin – *S. aureus*/GAS
  - IV, PO based on severity
  - Macrolides alternative

- Duration – 7 to 10 days
Impetigo

• Group A streptococci (10% staph)
• More common in children
• Common during hot and humid weather
• Spread through close contact
• Vesicles – pus blister – rupture golden crust
Treat same as erysipelas –

Dicloxacillin
Emerging Pathogen: Outpatient MRSA

Four Pediatric Deaths from Community-Acquired MRSA

MMWR August, 20 1999.

Community MRSA in urban poor of San Francisco

Community MRSA infections in south Texas children

MRSA in a rural American Indian community
JAMA 2001;286:1201-5.
Figure 1. Epidemic-Curve Graph (Top) and Field Position Diagram (Bottom) of Cases of MRSA Infection among St. Louis Rams Professional Football Players in 2003.

Each box on the epidemic-curve graph and field diagram represents an MRSA infection; different colors designate different players; boxes of the same color thus represent recurrent infections. On the field diagram, X represents a defensive-player position and O an offensive-player position.
S. aureus Colonization
2001-2002 National Health and Nutrition Examination Survey (NHANES)

67.6% None
31.6% MSSA
0.8% MRSA

MRSA risks and Types
2001-2002 National Health and Nutrition Examination Survey (NHANES)

Risk factors
• Age <65, 0.3 (0.1-0.9)
• Men, 0.4 (0.2-0.6)
• Race
• Diabetes 2.6 (1.1-6.1)
• LTC 7.4 (2.5-21.8)

Types
• ½ hospital-related
  • SCCmec Type II
• ½ community-related
  • SCCmec Type IV
    • (USA 300)

Community onset
*S. aureus*
skin infections (n=389)

- **MRSA**
  - (n=279 [72%])
  - **CA-MRSA**
    - USA 300 / 400
    - (n=244 [87%])
  - “Other MRSA”
    - (n=35 [13%])
- **MSSA**
  - (n=110 [28%])

# Nationwide Infections

11 Emergency Rooms, August 2004

<table>
<thead>
<tr>
<th>Site</th>
<th>No. of Patients Enrolled (N=422)</th>
<th>MRSA (N=249)†</th>
<th>MSSA (N=71)</th>
<th>Other Bacteria (N=64)‡</th>
<th>No Bacterial Growth (N=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>number (percent)</td>
<td>number (percent)</td>
<td>number (percent)</td>
<td>number (percent)</td>
</tr>
<tr>
<td>Albuquerque</td>
<td>42</td>
<td>25 (60)</td>
<td>10 (24)</td>
<td>3 (7)</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Atlanta</td>
<td>32</td>
<td>23 (72)</td>
<td>4 (12)</td>
<td>3 (9)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Charlotte, N.C.</td>
<td>25</td>
<td>17 (68)</td>
<td>0</td>
<td>4 (16)</td>
<td>4 (16)</td>
</tr>
<tr>
<td>Kansas City, Mo.</td>
<td>58</td>
<td>43 (74)</td>
<td>6 (10)</td>
<td>4 (7)</td>
<td>5 (9)</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>47</td>
<td>24 (51)</td>
<td>6 (13)</td>
<td>8 (17)</td>
<td>9 (19)</td>
</tr>
<tr>
<td>Minneapolis</td>
<td>28</td>
<td>11 (39)</td>
<td>4 (14)</td>
<td>9 (32)</td>
<td>4 (14)</td>
</tr>
<tr>
<td>New Orleans</td>
<td>69</td>
<td>46 (67)</td>
<td>11 (16)</td>
<td>9 (13)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>New York</td>
<td>20</td>
<td>3 (15)</td>
<td>8 (40)</td>
<td>5 (25)</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Philadelphia</td>
<td>58</td>
<td>32 (55)</td>
<td>12 (21)</td>
<td>12 (21)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Phoenix, Ariz.</td>
<td>30</td>
<td>18 (60)</td>
<td>8 (27)</td>
<td>4 (13)</td>
<td>0</td>
</tr>
<tr>
<td>Portland, Oreg.</td>
<td>13</td>
<td>7 (54)</td>
<td>2 (15)</td>
<td>3 (23)</td>
<td>1 (8)</td>
</tr>
</tbody>
</table>

* A total of 31 cultures, including 10 cultures from which MRSA was isolated, were polymicrobial. Because of rounding, percentages may not total 100. MSSA denotes methicillin-resistant *Staphylococcus aureus*.

† P<0.001 for the test for homogeneity of MRSA prevalence across sites.

‡ Other bacteria isolated were as follows: MSSA (17 percent), streptococcus species (7 percent), coagulase-negative staphylococci (3 percent), and *Proteus mirabilis* (1 percent).

Nationwide Infections
11 Emergency Rooms, August 2004

97% USA 300
59% of all infections MRSA
76% of all infections S. aureus

## Susceptibility Differences

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>CA-MRSA %</th>
<th>HCA-MRSA %</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>79%</td>
<td>16%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>83%</td>
<td>44%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>44%</td>
<td>9%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>92%</td>
<td>92%</td>
<td>NS</td>
</tr>
<tr>
<td>TMP/SMX</td>
<td>95%</td>
<td>90%</td>
<td>.13</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>100%</td>
<td>100%</td>
<td>-</td>
</tr>
</tbody>
</table>

JAMA. 2003;290(22):2976-84.
### Importance of Correct Antibiotics?

#### 2003-2006 Little Rock, AR

#### Table 3. Comparison of clinical characteristics between patients who received active versus patients who received inactive antimicrobial therapy (for 531 episodes)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Episodes in active therapy recipients (n = 312)</th>
<th>Episodes in inactive therapy recipients (n = 219)</th>
<th>OR (95% CI)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of infection</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abscess</td>
<td>209 (67)</td>
<td>152 (69)</td>
<td>1.12 (0.77–1.62)</td>
<td>&gt; 2&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Furuncle or carbuncle</td>
<td>26 (8)</td>
<td>28 (13)</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>77 (25)</td>
<td>39 (18)</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>Incision and drainage performed at zero time</td>
<td>249 (80)</td>
<td>178 (61)</td>
<td>0.91 (0.59–1.41)</td>
<td>&gt; 2</td>
</tr>
<tr>
<td><strong>Site of infection</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head and neck</td>
<td>26 (8)</td>
<td>18 (6)</td>
<td>0.99 (0.53–1.85)</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Trunk</td>
<td>40 (13)</td>
<td>23 (11)</td>
<td>0.80 (0.46–1.38)</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Upper extremity&lt;sup&gt;b&lt;/sup&gt;</td>
<td>47 (15)</td>
<td>46 (21)</td>
<td>1.50 (0.96–2.35)</td>
<td>0.08</td>
</tr>
<tr>
<td>Genitoperineal/perirectal</td>
<td>21 (7)</td>
<td>17 (6)</td>
<td>1.17 (0.60–2.27)</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Lower extremity&lt;sup&gt;b&lt;/sup&gt;</td>
<td>114 (37)</td>
<td>82 (37)</td>
<td>1.34 (0.73–2.49)</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Hand or foot</td>
<td>11 (4)</td>
<td>12 (6)</td>
<td>0.38 (0.43–1.09)</td>
<td>0.11</td>
</tr>
<tr>
<td>Duration of symptoms of illness (days)</td>
<td>5 (1)</td>
<td>6 (1)</td>
<td>…</td>
<td>0.14&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Abnormal leukocyte count&lt;sup&gt;f&lt;/sup&gt;</td>
<td>1 (3)</td>
<td>2 (1)</td>
<td>…</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Health care-associated infection</td>
<td>7 (2)</td>
<td>14 (7)</td>
<td>0.49 (0.18–1.28)</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>MRSA susceptible to all antibiotics except for macrolides</td>
<td>208 (67)</td>
<td>147 (67)</td>
<td>1.01 (0.70–1.46)</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Treatment failure</td>
<td>16 (5)</td>
<td>29 (13)</td>
<td>2.82 (1.49–5.34)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Median no. of follow-up visits within 14 days</td>
<td>2</td>
<td>2</td>
<td>…</td>
<td>&gt; 2&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

**NOTE.** Data are no. (%) of episodes, unless otherwise indicated. MRSA, methicillin-resistant *Staphylococcus aureus*.

- Determined by the \( \chi^2 \) test, unless otherwise indicated.
- For abscess vs. nonabscess.
- Including axilla but not including the hand.
- Including the buttocks but not including the foot.
- Determined by Wilcoxon rank sum test.
- Defined as total leukocyte count >12 \times 10<sup>9</sup> cells/L or <4 \times 10<sup>9</sup> cells/L. Data are for 348 episodes.
Empiric Antibiotics
CA-MRSA Skin Infections

• Infections w/pus or abscesses
  • Trimethoprim-Sulfamethoxazole
    • 160/800mg PO BID
  • Doxycycline
    • 100mg PO BID
  • Clindamycin
    • 300-450mg PO QID
Bite wounds

- Dogs and cats
  - *Pasteurella multocida*
  - Prophylactic abx controversial

- Human bites are most infectious
  - Prophylaxis warranted
  - Need to cover oral anaerobes
Diabetic Foot Infections

- Significance - diabetics
  - 20% of hospitalizations – foot
  - ¼ of soft tissue infections
  - 55,000 admissions/year – 50% non-trauma
Diabetic Foot - Factors

- Neuropathy
- Angiopathy & ischemia
- Immunologic defects – ↓ cell mediated
Pathogens

• 4-6 isolates / culture
  • 45% Gram (+) aerobes
    • S. aureus, streptococci, enterococci
  • 24% Gram (-) aerobes
    • Proteus, Enterobacter, E. coli, Klebsiella
  • 31% Anaerobes
    • Peptococcus, Peptostreptococcus, Bacteroides

• Superficial cultures inadequate
Diabetic Foot - Severity

Ulcers

Osteomyelitis
General Treatment – DM Foot

- **Goals:** ↔ function & ↓ complications
- **Wound care**
  - Debridement
  - Drainage
  - Amputation
- **Diabetes care**
  - Control glucose – healing time
Antibiotic Treatment

• Mild – oral therapy (outpatient?)
  • Amoxicillin/clavulanate
  • FQ plus metronidazole / clindamycin

• Moderate / Severe
  • IV then Oral
  • BL/BL-inhibitors
  • Carbapenems
  • ? Vancomycin for MRSA
Diabetic Foot – Duration Abx

- **Mild**
  - 10-14 days
- **Moderate / Severe**
  - 21+ days
- **With osteomyelitis**
  - 6 - 12 weeks
Bone and Joint Infections
Osteomyelitis

• Definition: inflammation of the bone caused by an organism

• Classified: route of infection and duration of the disease
Osteomyelitis: Classification

• Route of bone infection
  
  • Hematogenous: spread of bacteria via bloodstream from a distant infection site
  
  • Contiguous: direct infection of the bone from an adjacent or contiguous source of infection
Osteomyelitis: Classification

• Duration of Disease
  • Acute <1 week
  • Chronic >1 month
Age of Onset

- Children and adults less than 20
  - Metaphysis
  - Pooling of blood, seeding by bacteria
  - Inflammatory response, sequestrum, necrotic bone
- Adults >50
Neonates (<1)

- **Site**
  - Long bones and joints (femur, tibia, humerus, fibula)
- **Risk factors**
  - prematurity, use of IV lines, RDS, perinatal asphyxia
- **Organisms**
  - *S. aureus*, group B Strep, *E. coli*
Children (1-20)

- **Site**
  - Long bones

- **Risk factors**
  - infection (pharyngitis, cellulitis), trauma, puncture wounds

- **Organisms**
  - *S. aureus, H. flu, Streptococci*
Adults – Site & Risk

- Adults - >50
  - Vertebrae – Lumbar
- Risk factors
  - Prosthetic devices
  - Immunosuppression
  - DM
  - Trauma
  - Infections (UTIs)
  - IVDU
Hematogenous Osteomyelitis

- Common Organisms:
  - All pt. populations:  S. aureus
  - Neonates:  S. aureus, GBS, E. coli
  - Children: S. aureus (60-90%), H. influenzae, P. aeruginosa
  - Adults:  S. aureus, E. coli, M. tuberculosis
    - IVDA: P. aeruginosa (78%)
    - Sickle Cell:  Salmonella (66%)
Hematogenous Osteomyelitis

- Clinical Features:
  - Tenderness of the infected area
  - Pain
  - Swelling
  - Fever, Chills
  - Decrease Motion
  - Malaise
S. aureus growing in bone
Contiguous Osteomyelitis

• Age of onset: > 50 years

• Risk Factors
  • Fractures, penetrating wounds, surgery
  • Soft tissue infections

• Pathogens
  • S. aureus, streptococci, staphylococci
  • GNR
  • Anaerobes
Vascular Insufficiency

- Mixed flora – aerobes / anaerobes
- DM – as with diabetic foot
Contiguous Osteomyelitis

• Clinical Features:
  • Localized pain
  • Occasional fever
  • Erythema
  • Redness
Contiguous Osteomyelitis Due to Vascular Insufficiency
Osteomyelitis: Diagnostics

- Radiologic
  - X-Rays: changes > 10 days after infection
  - CT, bone scan
- Laboratory
  - Erythrocyte Sedimentation Rate (ESR)
  - ↑WBC
  - Bone/abscess: gram strain, C&S
  - Blood cultures
Osteomyelitis: Treatment

- **Antibiotic bone penetration - Rabbits**

<table>
<thead>
<tr>
<th>Abx</th>
<th>Serum (μg/mL)</th>
<th>Inf. Bone (μg/g)</th>
<th>%Serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinda</td>
<td>12.1</td>
<td>11.9</td>
<td>98.3</td>
</tr>
<tr>
<td>Vanco</td>
<td>36.4</td>
<td>5.3</td>
<td>14.5</td>
</tr>
<tr>
<td>Nafcillin</td>
<td>21.8</td>
<td>2.1</td>
<td>9.6</td>
</tr>
<tr>
<td>Tobra</td>
<td>14.3</td>
<td>1.3</td>
<td>9.1</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>67.2</td>
<td>4.1</td>
<td>6.1</td>
</tr>
</tbody>
</table>

Table 91-2. Mandell, Douglas, Bennett
Osteomyelitis: Treatment

- Antibiotic bone penetration
- Duration of therapy
  - 4-6 weeks
  - Adjust for ESR, signs and symptoms
- Route of administration
  - Usually IV
Osteomyelitis: Oral Treatment

- Requirements for oral therapy
  - Confirmed osteomyelitis
  - Known C & S results
  - Suitable oral agent available
  - Compliance assured
  - Suitable candidates
    - Children with response to IV therapy
    - Adults without DM or PVD
Osteomyelitis: Empiric Treatment

- Neonate
  - Organisms: S. aureus, E. coli, GBS
  - First line: cefazolin
- Children < 5 years of age
  - Organisms: S. aureus, H. influenzae, Streptococcus
  - First Line: Cefuroxime
  - Alternatives: vancomycin + gentamicin
Osteomyelitis: Empiric Treatment

- **Children > 5 years**
  - Organisms: *S. aureus*
  - First Line: cefazolin, nafcillin

- **Adults**
  - Organisms: *S. aureus*
  - First line: cefazolin, nafcillin
  - Alternatives: vancomycin, clindamycin
Osteomyelitis: Empiric Treatment

- IVDA
  - Organisms: S. aureus, P. aeruginosa
  - First Line: FQs + tobramycin, ceftazidime + tobramycin

- Postoperative/Post Trauma
  - Organisms: gram positive and negative
  - First Line: Nafcillin + ceftazidime
  - Piperacillin/tazobactam
Osteomyelitis: Empiric Treatment

- Vascular Insufficiency
  - Organisms: gram positive & negative, anaerobes
  - First Line: Nafcillin or cefazolin (+ ceftazidime)
  - Anaerobes: Cefoxitin
    Clindamycin + ceftazidime
Prosthetic Joint Infections (PJI)
Route, Risk, & Pathogenesis

- **Route of Infection**
  - Intraoperative contamination
  - Hematogenous spread
- **Risk Factors**
  - Advanced age, RA, DM, Corticosteroid use
- **Pathogenesis**
  - Adherence of bacteria in biofilm
Etiology

- Early (29%) – up to 3 months
  - S. aureus, coag (-) staph, GNR, beta hemolytic strep
- Delayed (41%) – 4-12 months
  - Coag (-) staph, S. aureus, skin commensals
- Late (30%) - >12 months
  - Coag (-) staph, S. aureus, skin commensals, GNR, anaerobes, M. tuberculosis
Principles of Therapy

1. Consistent cure requires removal of prosthesis
2. Treat according to C&S results
3. Extended length of treatment
   • 6-8 weeks
Diagnosis – Septic Arthritis and PJI

- Radiographic Studies
- Lab Studies
  - Aspiration of joint fluid and culture
  - Histopathologic
    - Microscopic tissue changes
Monitoring – Osteo & Joints

- Cultures – only at initiation of abx
- WBC – once to twice a week
- ESR – weekly (may take several weeks)
- Clinical signs – daily at start
- Compliance – reinforce at every chance