BONE & JOINT INFECTIONS

Henry F. Chambers, MD

I have nothing to disclose
Case

- 42 y/o female, unable to bear weight, L knee effusion, no fever
- Labs: CBC-14K WBCs; synovial fluid WBC 60K, Gram stain negative
- Best management in this case?
  1. Obtain CRP, d/c home on NSAID
  2. Ceftriaxone
  3. Vancomycin
  4. Vancomycin + ceftriaxone
## Microbiology of Septic Arthritis

<table>
<thead>
<tr>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Staph. aureus (40%)</td>
<td>• Staph. aureus (40%)</td>
</tr>
<tr>
<td>• Streptococci (30%)</td>
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</tr>
<tr>
<td>– S. pneumoniae</td>
<td>– GAS</td>
</tr>
<tr>
<td>– GAS</td>
<td>– S. pneumoniae</td>
</tr>
<tr>
<td>• Gram-negative bacilli (20%)</td>
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</tr>
<tr>
<td>– H. influenzae</td>
<td>– Enterics</td>
</tr>
<tr>
<td>• Neisseria sp.</td>
<td>• Neisseria sp.</td>
</tr>
</tbody>
</table>

Up to 1/3 culture-negative

## Clinical Presentations

- **Acute, monoarticular**
  - GC, Staph. aureus, Strep, Gram-negative bacilli
  - Gout, pseudogout
- **Chronic, monoarticular**
  - Brucella, mycobacteria, nocardia, fungi
- **Acute, polyarticular**
  - GC, Lyme, Staph. aureus, Pneumococci, GAS
  - SLE, ARF, reactive arthritis, viral, other non-infectious
Clinical Presentations

• Sternoclavicular, acromioclavicular
  – Staph. aureus
  – Pseudomonas aeruginosa

• Sacroileitis
  – Brucella
  – TB
  – S. aureus

• Symphysis pubis
  – Staph. aureus

Joints Affected in Septic Arthritis
Septic Arthritis: Presentation


Risk Factors for Septic Arthritis

### Serum Lab Values

<table>
<thead>
<tr>
<th>Factor</th>
<th>Likelihood Ratio Positive</th>
<th>Likelihood Ratio Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC &gt; 10,000</td>
<td>1.4</td>
<td>0.28</td>
</tr>
<tr>
<td>ESR &gt; 30 mm/h</td>
<td>1.3</td>
<td>0.17</td>
</tr>
<tr>
<td>CRP &gt; 100 mg/L</td>
<td>1.6</td>
<td>0.44</td>
</tr>
</tbody>
</table>


### Synovial Fluid Studies

<table>
<thead>
<tr>
<th>Factor</th>
<th>Likelihood Ratio Positive</th>
<th>Likelihood Ratio Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC &gt; 100,000</td>
<td>28</td>
<td>0.75</td>
</tr>
<tr>
<td>WBC &gt; 50,000</td>
<td>7.7</td>
<td>0.42</td>
</tr>
<tr>
<td>WBC &gt; 25,000</td>
<td>2.9</td>
<td>0.32</td>
</tr>
<tr>
<td>PMNs &gt; 90%</td>
<td>3.4</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Management Of Septic Arthritis

• Drain the joint (controversy as to which is better)
  – Arthrocentesis
  – Arthroscopy
  – Open drainage

• Empirical antimicrobial therapy
  – STD risk group
    • Gram stain negative or GN diplococci: Ceftriaxone 1 gm q24h
  – Low STD risk
    • Gram stain negative: Vancomycin 15-20 mg/kg q8-12h + Ceftriaxone 1 gm q24h or Cefepime 2 gm q8h
    • Gram stain with GPCs: Vancomycin 15-20 mg/kg q8-12h
    • Gram stain with GNRs: Cefepime or meropenem 1 gm q8h

Management Of Septic Arthritis

• Drain the joint
• Definitive parenteral antimicrobial therapy
  – GC: Ceftriaxone 1 gm q24h
  – MSSA: Nafcillin or oxacillin 2 gm q4h or cefazolin 2 gm q8h
  – MRSA: Vancomycin 15-20 mg/kg q8-12h
  – Streptococci
    • 1st line: Pen G 2 mU q4h or ceftriaxone 2 gm q24h
    • 2nd line: Vancomycin 15-20 mg/kg q8-12h or linezolid 600 mg q12h (PO or IV)
  – GNRs
    • 3rd gen cephalosporin, carbapenem, FQ depending on susceptibility
Duration of Therapy

- For GC: 7 days
- For other bacterial etiologies
  - Duration not well established
  - Relapse is an unlikely occurrence
  - CRP may be useful for monitoring response
  - 14-21 day
    - Combination of IV (1-2 weeks) then orally active agent
    - Consider the longer duration for Staph. aureus, GNRs
  - For Staph. aureus septic arthritis with bacteremia treat for 4 weeks IV
  - For streptococci 2-3 weeks

Septic Arthritis - Summary

- Clinical features and patient risk factors are useful in assessing likelihood of septic arthritis
- WBC, ESR, and CRP have limited utility in diagnosis of septic arthritis
  - CRP may be useful for monitoring response
- Synovial fluid WBC and %PMNs are essential for assessment of likelihood of septic arthritis
- Duration of treatment 2-3 weeks except 7 days for GC.
Prosthetic Joint and Hardware Infections

Case

- 42 y/o female, s/p prosthetic joint replacement of R shoulder joint 4 months prior presents with 3 weeks of increasing pain, worse with movement, no fever
- Percutaneous aspirate of joint fluid with 1,200 WBCs, 95% PMNs
- Intraoperative cultures negative at 7 days
- Which organism is probably causing this infection
  1. No organism, patient does not have PJI
  2. Staph. aureus
  3. Pseudomonas aeruginosa
  4. Cutibacterium acnes
  5. Coagulase-negative staphylococcus
PJI Presentation

• Early onset (< 3 mo): subacute to acute onset; pain, effusion, wound breakdown, drainage; acquired at time of surgery
  – Staph. aureus, GNRs, mixed
• Delayed onset (3-12 mo): chronic onset of symptoms, pain, loosening of prosthesis, drainage; acquired at time of surgery
  – Cutibacterium sp, coag-negative staph, enterococci
• Late onset (> 12 mo): acute onset of symptoms, secondary to hematogenous seeding
  – Staph. aureus, streptococci, GNRs

PJI Presentation

• Signs of infection include wound drainage, sinus tract, acutely or chronically painful prosthesis
• Elevated CRP, ESR
• Synovial fluid counts > 1500 or 95% PMNs
• Imaging may or may not show evidence of osteomyelitis
• Intraoperative inspection and cultures required to establish the diagnosis
Principles of Diagnosis and Management

• Empirical therapy is NOT recommended prior to obtaining cultures
• Cutibacterium infection relatively common in shoulder PJI
  – Hold cultures for at least 10 days and blind subculture recommended
• Debridement and retention vs. removal and reimplantation of hardware

Device Retention vs Removal

Clin Infect Dis 56:e1, 2013
IDSA Prosthetic Joint Infection Treatment Guidelines

• Obtain cultures prior to starting Rx
• Treatment based on surgical option chosen
  – Debridement, hardware retention
  – 1-stage, direct exchange
  – 2-stage debridement later re-implantation

Clin Infect Dis 56:e1, 2013

Orthopedic Device Related MRSA Infections
Cumulative Treatment Failure Rate

Orthopedic Device Related MRSA Infections
Cumulative Treatment Failure Rate


Total Knee/Hip S. aureus Infections
Cumulative Treatment Failure Rate

Streptococcal PJI

- 42% failure rate with device retention
- Predictors of failure
  - RA, late post-surgical infection (> 3 months), bacteremia, infection with S. pyogenes
- Predictors of success
  - Exchange of removable components, use of rifampin within the first 30 days, a prolonged course (>21 days) of a beta-lactam antibiotic with or without rifampin


Synopsis of IDSA Treatment Guidelines

- Prosthesis retained
  - Staph: use iv/po rifampin combo for 4-6 mo
  - Others: iv/po regimen for 4-6 weeks
- 1-stage procedure
  - Staph: use iv/po rifampin combo for 4 mo
  - Others: iv/po regimen for 4-6 weeks
- 2-stage procedure
  - Staph: use iv/po rifampin combo for (4)-6 weeks
  - Others: iv/po regimen for 4-6 weeks
OSTEOMYELITIS

Case

• 55 y/o man with T10-T12 MRSA vertebral osteomyelitis
• What is the preferred duration of therapy
  1. 4 weeks
  2. 6 weeks
  3. 8 weeks
  4. 12 weeks
Classification

- **Acute osteomyelitis**
  - First episode at given site
  - Potentially cured with antibiotics alone within 6 weeks
  - Bone remains viable
- **Chronic osteomyelitis**
  - Evolves from acute osteomyelitis
  - Present > 6 weeks
  - Often indolent with few systemic signs/symptoms
  - Fistula formation, dead bone, refractory clinical course
- **Orthopedic device-related osteomyelitis**

Diagnosis

**ESR, CRP, and WBC**

- Case series of patients with osteomyelitis
  - ESR “elevated” in apx. 90% of patients
  - C-reactive protein “elevated” > 90% of patients
- ESR virtually worthless: less predictive of clinical course; longer period of elevation
- CRP levels which are slow to resolve may predict complicated course
- WBC: worthless
Microbiology

- Staphylococcus aureus (50-60%)
- Streptococci, coagulase-negative staphylococci (orthopedic implants)
- Enteric gram-negative rods, Pseudomonas aeruginosa

Diagnosis

Microbiological Confirmation

- Gold standard = bone culture
- Histopathology may give dx if cultures negative
- Swabs from sinus tracts unreliable
  - Isolation of Staph. aureus is more predictive but not sensitive
Imaging

- Conventional radiography
  - Relatively insensitive (~50-75%), non-specific
  - Initial imaging of choice for symptoms > 2 weeks
- CT scan
  - More sensitive than conventional x-ray
  - Less sensitive than MRI
- MRI
  - Best sensitivity and specificity
  - Imaging modality of choice
- Nuclear imaging study
  - PET-CT, 3-phase bone scan, Indium-labelled WBC scan
  - May be an alternative to MRI

Treatment of Hematogenous Vertebral Osteomyelitis
Antibiotic treatment for 6 weeks versus 12 weeks in patients with pyogenic vertebral osteomyelitis: an open-label, non-inferiority, randomised, controlled trial

Louis Bernard, Aurélien Dinh, Idir Ghout, David Simo, Valérie Zeller, Bertrand Issartel, Vincent Le Moing, Nadia Behmatou, Philippe Lensort, Jean-Pierre Bru, Audrey Thony, Damien Bouhass, Eric Dénès, Alexia Deband, Catherine Civroux, Karine Fribou, Michel Dupon, Philippe Agertter, Denis Malfessen, on behalf of the Duration of Treatment for Spontaneous Scoliosis (DOTS) study group


Patient Characteristics

- Unblinded, non-inferiority (10% margin) RCT:
  - 6 wks (n=176) versus 12 wks (n=175) IV/PO Rx
- Patients: all culture positive
  - 68% blood culture positive, 20% with endocarditis
    - S. aureus 41% (only 13 MRSA cases), CoNS 17%, Strep 18%
  - 19% with abscess, only 3/68 needed
  - 5% perioperative specimen
- Other characteristics
  - 15% with diabetes
  - 89% with single vertebral body
  - 16% with neurological signs
PO and IV Therapy

- **IV therapy**
  - Median of 14 days (IQR 7-27)
  - 26% for < 1 week
- **PO therapy**
  - 73% received FQ or RIF, or the combination
    - 44% received FQ + RIF
  - 28% received oral aminopenicillin

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Results

<table>
<thead>
<tr>
<th></th>
<th>6 wk RX</th>
<th>12 wk RX</th>
<th>Δ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT, N</td>
<td>176</td>
<td>175</td>
<td></td>
</tr>
<tr>
<td>Cured &amp; alive @ 6 mo</td>
<td>156 (88.6%)</td>
<td>150 (85.7%)</td>
<td>2.9 (-4.2, 10.1)</td>
</tr>
<tr>
<td>Cured, no further Rx</td>
<td>142 (80.7%)</td>
<td>141 (80.6%)</td>
<td>0.1 (-8.3, 8.5)</td>
</tr>
<tr>
<td>Back pain @ 1 yr</td>
<td>44/145 (30%)</td>
<td>41/138 (30%)</td>
<td></td>
</tr>
</tbody>
</table>

Failure associated with age > 75 yr and *S. aureus* infection
Conclusions

• 6 weeks as good as 12 weeks for relatively uncomplicated infections
• Predominantly PO therapy effective
• Limitations:
  – Not much MRSA, other multiple drug resistant organism
  – Few cases with larger abscesses, multiple vertebral bodies or other subgroups that may require longer courses of therapy
Study Design

- Observational cohort study of patients with hematogenous vertebral osteo (HVO) at 5 Korean tertiary hospitals
- 314 patients, microbiologically confirmed HVO evaluated for risk factors associated with recurrence
- Patients stratified into 2 groups, 1) no risk factor present and 2) 1 or more risk factors present and analyzed for recurrence as a function of duration of therapy

Study Population

- Positive blood cultures: 78.3%
- Epidural abscess: 38.2%
- Paravertebral or psoas abscess: 67.8%
- Microbiology
  - Staph aureus: 58.8% (43.3% of these MRSA)
  - Gram-negative bacilli: 21.7%
  - Streptococcal species: 11.3%
## Risk Factors Associated with Recurrence

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Adjusted Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-stage renal disease</td>
<td>6.58 (1.63-26.5)</td>
</tr>
<tr>
<td>MRSA infection</td>
<td>2.61 (1.16-5.87)</td>
</tr>
<tr>
<td>Undrained paravertebral/psoas abscess</td>
<td>4.09 (1.82-9.19)</td>
</tr>
</tbody>
</table>

## Probability of Recurrence-Free Survival

![Graph A](image1.png)

**log-rank test, $P = .04$**

- ≥6 weeks (n = 166)
- <6 weeks (n = 255)

![Graph B](image2.png)

**log-rank test, $P = .002$**

- ≥6 weeks (n = 73)
- <8 weeks (n = 50)

- No risk factor
- 1 or more risk factors
Effect of Treatment Duration on Recurrence by Risk Factor

Numbers are denominator for each group
Recommended Treatment Durations for Vertebral Osteomyelitis

• 6 week po/IV regimen
  – No MRSA, no abscess, no end-stage renal disease
  – No benefit of 12 week duration in this group
• Any one of MRSA, undrained abscess, or ESRD
• > 8 weeks po/IV regimen

MRI for Osteomyelitis
Beware the routine follow-up exam

Intravenous or Oral Therapy?

2009 and 2013 Cochrane Reviews
Treatment of Chronic Osteomyelitis

• No difference in outcome between oral and parenteral therapy
• Adverse events similar
• No recommendations on duration of therapy or impact of bacterial species or disease severity on outcome
Oral Agents: Advantages and Disadvantages

Conclusions - 1

- Oral therapy is probably as effective as parenteral therapy (OVIVA trial results pending), preferred in children ([JAMA Pediatr 169:120, 2015])
- 6-8 weeks of therapy generally effective in cases of acute/hematogeneous/vertebral osteo
- Monitoring response to therapy
  - CRP: persistently elevated CRP is suggestive of persistent osteomyelitis
  - Routine MRI: findings often do not correlate with clinical status (although worsening soft tissue abnormalities may be significant)
Conclusions - 2

• Gram negative oral options
  – Quinolones or TMP-SMX

• Anaerobic oral choices
  – Metronidazole > clindamycin

• Gram positive oral options
  – TMP-SMX, clindamycin, linezolid
  – Rifampin in combination for Staph. aureus

• Beta-lactams preferable to vancomycin for MSSA