Septic Joints: Diagnostics, Treatment and Outcomes

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Common equine emergency

- 3 Main Causes:
  1) Hematogenous spread (foals)
  2) Penetrating wound
  3) Iatrogenic

- Less commonly extension of peri-articular infection

Clinical signs

- Severe, NWB lameness
  - Lameness may be less severe if joint open & draining
- Joint effusion
- Peri-articular swelling
- Heat, pain on palpation

Pathophysiology

- Bacterial contamination of synovial space
- Inoculation dose depends on virulence & pathogenicity of organism
  - ~ $10^5$ CFU
  - Staph spp. require significantly fewer CFU
  - Adequan significantly decreases CFU needed
    (Gustafson et al., 1989)

- Colonization of synovium leads to marked synovial inflammatory response

Hematogenous route of infection

- Tortuous nutrient vessels (epiphyseal, metaphyseal, periosteal and terminal branches of nutrient artery)

- Foals can also develop thrombosis/osteonecrosis

Types of Septic Arthritis in Foals

- **S-Type**: Synovial fluid and membrane infected
- **E-Type**: Articular epiphysis also involved
- **P-Type**: Physis of long bone infected +/- joint infected
Etiological agents

- **Foals**
  - *Rhodococcus* (usually immune-mediated arthritis)

- **Adults**
  - Penetrating wound: Gram -ve > gram +ve
  - Iatrogenic: Gram +ve, *Strep, Staph aureus*

- **Other less common agents**
  - *Mycoplasma*
  - Fungal

Joint degradation

- **Inflammatory mediators**
  - Neutrophil infiltration
  - Activated synoviocytes & chondrocytes
  - Bacteria

- **Bacterial toxins**
  - Alpha- and gamma-cytolytic toxins

- **Degradative enzymes**
  - Hyaluronidase, MMPs, aggrecanases

Diagnostic considerations

- **Signalment**
- **History**
- **Hematology**
- **Synovial fluid analysis**
- **Imaging: radiographs, ultrasound**
- **Advanced imaging: nuclear scintigraphy, CT, MRI**

Diagnosis – Signalment & history

- **Foals (hematogenous)**
  - Prematurity
  - High sepsis score
  - Umbilical abscess
  - Partial or complete failure of passive transfer
  - 50-88% of foals with septic arthritis have FPT (Meijer et al. 2000)
  - Fever

- **Adults**
  - Penetrating wound
  - Iatrogenic: Injection
  - Post-op (rare ~1%)
  - Nearby infection (such as foot abscess or cellulitis)
  - Adults are not necessarily febrile

Hematology

- **CBC**
  - Normal in adults
  - Neutrophilia in foals

- **Fibrinogen**
  - Mild hyperfibrinogenemia in adults
  - Moderate hyperfibrinogenemia in foals

- **Serum amyloid A**
  - Usually increased

- **Blood culture for foals**
**Synoviocentesis**
- Site away from open wounds
  - Probably OK to sample through inflamed tissue
- Distend joint with sterile fluid to determine communication with wounds
-Inject joint with antibiotic sampling

***Always sample joint if you are concerned about communication or sepsis***

**Sample types**
- **Cytology**
- **Culture**
- **Culture broths**

**Diagnosis - Synovial fluid**
- **Synovial fluid analysis**
  - Viscosity changes rapidly with sepsis
  - Cloudy fluid suggests at least $30 \times 10^3$/dL cells

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Inflammation</th>
<th>Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Protein</strong></td>
<td>&lt;2.0 - &lt;2.5 g/dL</td>
<td>&lt;2.5 g/dL</td>
<td>&gt;4.0 g/dL</td>
</tr>
<tr>
<td><strong>WBC</strong></td>
<td>&lt;450 to &lt;5000</td>
<td>500 to 20,000</td>
<td>&gt;30,000/dL</td>
</tr>
<tr>
<td><strong>Cell Type</strong></td>
<td>&lt;10% neutrophils</td>
<td>10-20%</td>
<td>&gt;80% neutrophils</td>
</tr>
</tbody>
</table>

**Diagnosis – Importance of neutrophils**
- **Normal**: <10% neutrophils; > 90% lymphocytes, monocytes, macrophages
- **Septic**: >80% neutrophils almost always infected
  - <75% neutrophils suggests that the infection is resolving
- Early in infection the neutrophils are usually non-degenerate
**Diagnosis – Synovial fluid lactate and SAA**

- Increased lactate in synovial fluid > 4.9 mmol/L in 66% (van Petegem, 1979)
- Increased SAA common but can be normal (Jacks, 2003)

**Diagnosis – Serum SAA**

- Serum SAA may be useful to monitor response to treatment (Haltmayer et al., 2017)

**Diagnosis – Culture**

- Only ~50% of samples will have positive culture
- Positive culture correlate with decreased prognosis (Taylor et al., 2010)
- Synovial fluid vs. synovium
- Culture broth increases rate of positive culture (Dumoulin et al., 2010)
- Isolation of a single organism is almost always indicative of infection
- Antimicrobial sensitivity important

**Diagnosis – Radiographs**

- Radiographic lytic changes can occur in less than 1 week
  - Most changes are seen at 7-10 days post infection
- Evaluate for fracture, gas in joint, lytic changes, foreign bodies
  - 59% of foals have osteomyelitis/bone necrosis concurrently

**Foal with septic physisis**

One month old Thoroughbred foal who recently developed severe swelling in the right stifte and associated lameness

Horses with <24hr history of penetrating wound responding to 1 surgery

Horses with >24hr history of penetrating wound requiring >1 surgery
Thoroughbred gelding with RF fetlock effusion

Thoroughbred gelding that stepped on a nail several hours prior to presentation

Specialty diagnostics

- Nuclear scintigraphy
  - Can be very useful in subclinical infections

- MRI
  - Sensitive for osteomyelitis
  - Fluid and bone may be affected

Advanced techniques

- Molecular diagnostics - PCR
  - Detects bacterial/viral DNA (MicroGen-DX, Texas)
  - Specific primers (e.g. 16S ribosomal RNA)
  - Can be multiplexed (multiple genes in one mix)

  Advantages
  - Rapid (<8 hours)
  - No interference from antibiotics
  - Sensitive (10 CFU/mL)

  Disadvantages
  - Equipment
  - Contamination by skin or environmental bacteria

Stahl et al., 2000
Yang et al., 2006
Kim et al., 2010

Treatment principles

1. Sterilize the joint

   - Systemic antimicrobials
     - Broad spectrum IV to begin

   - Local antimicrobials:
     - Intra-articular
     - IV regional perfusion
     - Intraosseous
     - Elution from antibiotic beads
**Intra-articular antimicrobials**

- High levels directly into joint
- Most effective after lavage (vs. in lavage fluids)
- IA drains can be used to deliver antibiotics

**Physiological considerations in septic arthritis**

- Hypervascularity due to inflammatory response which influences pharmacokinetics:
  - Greater rate of transfer of antibiotics from serum to synovium
  - More persistence of the drug in the diseased joint

Semi-logarithmic plot of average serum and synovial concentrations for six arthritic horses after i.v. administration of 40 mg AMX/kg body mass

**Regional limb perfusion**

**Advantages**
- Reaches infected tissue / joints by diffusion
- Far greater concentration (>10 fold) than systemic IV
- Concentrations remain higher for longer

**Disadvantages**
- May not work if tourniquet not functional
- Venous thrombosis
- Difficult in limb with cellulitis

**RLP - Antimicrobials**

- Amikacin most common
- Cephalosporins, ticarcillin, vancomycin, enrofloxacin, imipenem
- Dose of antimicrobials:
  - 1/3 systemic dose?
  - 2-3g amikacin

**RLP - Antimicrobials**

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Dosage</th>
<th>Methods of delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin</td>
<td>1g</td>
<td>All</td>
</tr>
<tr>
<td>Cefazolin+ceftaxone</td>
<td>2g</td>
<td>RLP, IA</td>
</tr>
<tr>
<td>Penicillin/ampicillin</td>
<td>1/4 – 1/2 systemic dose</td>
<td>RLP, IA</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>0.5 – 1g</td>
<td>1/3 systemic dose</td>
</tr>
<tr>
<td>Amikacin</td>
<td>1-3g</td>
<td>All</td>
</tr>
<tr>
<td>Ceftiofur</td>
<td>1g</td>
<td>RLP, IA</td>
</tr>
<tr>
<td>Ticarcillin+clavulanate</td>
<td>500mg – 1g</td>
<td>All</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>300mg</td>
<td>RLP, beads</td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td>500mg</td>
<td>All</td>
</tr>
<tr>
<td>Imipenem</td>
<td>500mg</td>
<td>RLP, IA</td>
</tr>
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</table>
Intraosseous perfusion
- More invasive/painful than IV regional
- Hole drilled into long bone and a cannula is used to deliver infusion
- Requires tourniquet like IV regional

Antibiotic-impregnated materials
- Non-absorbable
  - Polymethylmethacrylate (PMMA)
  - Normally need to be removed
  - Elution of antibiotics is longest (months)
- Absorbable
  - Collagen
  - Gelatin
  - DL lactide-glycolide copolymers
  - Plaster of Paris
  - Elution over days to weeks

2. Drainage
- Lavage with balanced physiological solution
- Arthroscopy
- Arthrotomy
- Removal of necrotic tissues

If significant amount of fibrin or thick synovial fluid or bony lesion, more aggressive drainage is selected:
- Arthroscopy
- Arthrotomy

Arthroscopy vs. Arthrotomy
- Experimentally, both eliminate the infection equally but arthrotomy was faster
- Arthrotomy has increased risk of ascending infection

<table>
<thead>
<tr>
<th></th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lavage</strong></td>
<td>- Can be done anywhere</td>
<td>- Unable to remove fibrin, infected synovium</td>
</tr>
<tr>
<td></td>
<td>- Less expensive</td>
<td>- Unable to examine joint</td>
</tr>
<tr>
<td></td>
<td>- Can be done standing</td>
<td></td>
</tr>
<tr>
<td><strong>Arthroscopy</strong></td>
<td>- Excellent exam and removal of fibrin &amp; synovium</td>
<td>- Increase costs</td>
</tr>
<tr>
<td></td>
<td>- Debridement of bony lesion</td>
<td>- General anesthesia</td>
</tr>
<tr>
<td><strong>Arthrotomy</strong></td>
<td>Best drainage</td>
<td>- Ascending infection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Premature closure</td>
</tr>
</tbody>
</table>
Benefit of arthroscopic lavage

3. Restoration of joint health
- Anti-inflammatories
  - NSAIDS
  - HA
  - Bandaging
- Additional pain control
  - Epidurals
  - IA anesthetics
  - Bandaging
  - Support of contralateral limb

Sodium hyaluronate (HA)
- Anti-inflammatory properties
- Decreases:
  - Cellular infiltration
  - Granulation tissue
  - Total glycosaminoglycans loss (p>0.05)

Epidural analgesia
- Combination of opioid and α-2 agonist most effective
- Single injection or indwelling catheter
- Best for hindlimb

Table 1

<table>
<thead>
<tr>
<th>Drug Regimen</th>
<th>Volume (mL)</th>
<th>Site of Injection</th>
<th>Duration of Effect (Hours)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Drug</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lidocaine 0.5%–2%</td>
<td>5–8</td>
<td>Epidural/intratechal, rapid onset</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mepivacaine 2%</td>
<td>5–8</td>
<td>Epidural/intratechal, rapid onset</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ropivacaine 0.1%–0.5%</td>
<td>5–10</td>
<td>Epidural/intratechal, less ataxia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupivacaine 0.1%–0.5%</td>
<td>5–8</td>
<td>Epidural/intratechal, more ataxia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xylazine 0.17 mg/kg</td>
<td>10</td>
<td>Epidural/intratechal, sedation/ataxia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detomidine 20–40 mg/kg</td>
<td>5–10</td>
<td>Epidural/intratechal, sedation/ataxia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medetomidine 2–5 mg/kg</td>
<td>10–30</td>
<td>Epidural/intratechal, sedation/ataxia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine 0.05–0.2 mg/kg</td>
<td>10–30</td>
<td>Epidural ONLY, useful for CRI mL/h via epidural catheter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methadone 0.1 mg/kg</td>
<td>20</td>
<td>Epidural, similar to morphine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol 1 mg/kg</td>
<td>10–30</td>
<td>Epidural, similar to morphine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketamine 0.5–2.0 mg/kg</td>
<td>10–30</td>
<td>Epidural, some ataxia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>10–30</td>
<td>Epidural, similar to morphine</td>
<td></td>
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</tbody>
</table>

Drug Combinations (Balanced Regional Analgesia)
<table>
<thead>
<tr>
<th>Drug 1</th>
<th>Volume (mL)</th>
<th>Site of Injection</th>
<th>Duration of Effect (Hours)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine 2%</td>
<td>1 xylazine 0.17 mg/kg</td>
<td>5–8</td>
<td>Epidural/intratechal, 4–6</td>
<td></td>
</tr>
<tr>
<td>Lidocaine 2%</td>
<td>1 morphine 0.1–0.2 mg/kg</td>
<td>5–8</td>
<td>Epidural/intratechal, 4–6</td>
<td></td>
</tr>
<tr>
<td>Bupivacaine 0.125%</td>
<td>1 morphine 0.1–0.2 mg/kg</td>
<td>10–30</td>
<td>Epidural/intratechal, 8–&gt;12 Also useful for CRI (0.5–2 mL/h) via epidural catheter</td>
<td></td>
</tr>
<tr>
<td>Xylazine 0.17 mg/kg</td>
<td>1 morphine 0.1–0.2 mg/kg</td>
<td>10–30</td>
<td>Epidural/intratechal, 12</td>
<td></td>
</tr>
<tr>
<td>Detomidine 10–30 mg/kg</td>
<td>1 morphine 0.1–0.2 mg/kg</td>
<td>5–10</td>
<td>Epidural/intratechal, 24–48</td>
<td></td>
</tr>
</tbody>
</table>

Use lower doses/volumes of the less concentrated drugs for intratechal injection. Intratechal (subarachnoid) injection potentially increases the risk of infections and inflammation (spinal cord and meninges).

~70% for life & return to athleticism
- Decreased with positive bacterial culture
- Decreased long-term px with Staph aureus

~50% for life and athleticism
- Decreased with comorbidities including septicemia, osteomyelitis

Prognosis
Worse prognosis in foals vs. adults

- Usually associated with failure of passive transfer & septicemia
- Often multiple joints (racing prognosis decreases) Neil et al., 2010
- Septic osteitis/osteomyelitis or physitis

Summary

- Septic arthritis is an emergency
- Early, aggressive treatment is best
- Treatment can be prolonged and expensive

- Prognosis
  - Foals 50%
  - Adults 70-80%

- Combination treatment
  - Systemic and local antibiotics
  - Anti-inflammatories
  - Lavage
  - Restoration of joint health
  - Pain control

Questions?