Give the Right Antibiotics in Trauma

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Learning Objectives

• Evaluate specific traumatic injuries where presumptive antibiotics are indicated

• Incorporate guidelines and evidence to make recommendations that balance the risks and benefits of presumptive antibiotics
Disclosure

• No financial conflicts of interest to disclose related to this subject manner

• Discuss off-label uses of medication therapy
Antibiotics in Trauma Patients

**Prophylaxis**
- Bacterial contamination: No
- Established infection: No

**Presumptive**
- Bacterial contamination: Yes
- Established infection: No

**Treatment**
- Bacterial contamination: Yes
- Established infection: Yes

Presumptive Antibiotics in Trauma

**Benefits**
- Prevent infection / sepsis
- Morbidity
- Mortality

**Risks**
- Antimicrobial resistance
- Adverse drug reactions
- Superinfection

Specific Traumatic Injuries

- Penetrating abdominal trauma
- Open extremity fractures
- Facial, sinus, skull fractures
- Penetrating brain injury
Penetrating Abdominal Injury (PAI)

- **Infection**
  - Post-op wound infection
  - Intra-abdominal abscess
- **Incidence:** 30-70% → 7-11%
- **Risk factors for infection**
  - Injury mechanism (e.g. velocity)
  - Number of organs
  - Presence of shock
  - Antibiotic spectrum
- **Common pathogens**
  - Gram negative
    - *Escherichia coli*
    - *Enterobacter cloacae*
    - *Klebsiella species*
  - Anaerobes: *Bacteroides*
  - Gram positive
    - *Enterococcus faecalis*
    - *Staphylococcus aureus*

Evidence for Presumptive Antibiotics?

- Has been used since the 1970’s yet no placebo controlled trials

<table>
<thead>
<tr>
<th>Reference and Design</th>
<th>Population</th>
<th>Treatment: % Infections</th>
<th>Pearls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thadepalli 1973</td>
<td>PAI</td>
<td>Cephalothin: 27%</td>
<td>Difference from greater number of anaerobic infections</td>
</tr>
<tr>
<td>RCT single site</td>
<td></td>
<td>Cephalothin + clindamycin: 10%</td>
<td></td>
</tr>
<tr>
<td>Kirton 2000</td>
<td>N=317 PAI HVI</td>
<td>Ampicillin/Sulbactam 3 g q6h 24 hr: 8% 5 days: 10% p=0.74</td>
<td>Antibiotics should NOT be continued &gt;24 hours with HVI (level 1)</td>
</tr>
<tr>
<td>RCT at 4 sites</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HVI: hollow viscous injury

REC: Penetrating Abdominal Trauma

• Preoperative dose with aerobic and anaerobic coverage indicated
  – Cefazolin + metronidazole
  – Clindamycin + gentamicin 5 mg/kg q24h

• Duration:
  – No hollow viscus injury: single pre-operative dose
  – Hollow viscus injury: less than 24 hours

• Clinical pearls:
  – Avoid ampicillin / sulbactam due to poor E. Coli coverage
  – Anaerobe resistance increasing for clindamycin and cefoxitin
Open Extremity Fractures

• Gustilo & Anderson Classification
  – I: open, wound <1 cm, clean
  – II: open, wound >1 cm, no extensive soft tissue injury
  – III: open, >10 cm, extensive STI
• Incidence: 1.8-52%
• Risk factors for infection
  – Grade III injuries
  – Poor vasculature / vascular injury
  – Limited soft tissue coverage (e.g. tibia)

• Common pathogens
  – Gram positive
    • *Streptococcus* species
    • *Staphylococcus aureus*
  – Gram negative (grade III)
    • Enterobacteriaceae
    • *Pseudomonas* species

# Evidence for Presumptive Antibiotics?

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<tr>
<th>Reference Design</th>
<th>Population</th>
<th>Treatment: % Infections</th>
<th>Pearls</th>
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<tbody>
<tr>
<td>Patzakis 2000 RCT single site</td>
<td>N=163 I: 40% II: 33% III: 32%</td>
<td>Grade I &amp; II: cipro 5.8% vs. cef+gent 6% (p=1) Grade III: cipro 31% vs. cef+gent 7.7% (p=0.08)</td>
<td>FLQ may cause delayed fracture healing</td>
</tr>
<tr>
<td>Dunkel 2013 Retrospective</td>
<td>N=1,492 I: 44% II: 25% III: 21%</td>
<td>MV analysis to predict infection 1 day antibiotics: reference 2-3 days: OR 0.6 (0.2-2) 4-5 days: OR 1.2 (0.2-4.9) &gt;5 days: OR 1.4 (0.4-4.4)</td>
<td>1 day may suffice for all grades 70% of grade III infections not covered by empiric regimen</td>
</tr>
</tbody>
</table>

REC: Open Extremity Fractures

• Systemic antibiotics administered as soon as possible after injury
  – All types: target gram positive organisms with cefazolin (clinda if allergy)
  – Type III: additional gram negative coverage indicated with gentamicin q24h

• Duration
  – Type I & II: no more than 24 hours
  – Type III: no more than 24 hours after soft tissue coverage (72 hour max)

• Clinical pearls
  – Fecal contamination (e.g. farm): cover *Clostridium* species with ampicillin/sulbactam
  – Once-daily aminoglycosides not associated with AKI, but warrant caution
Facial, Sinus and Skull Fractures

- Infection
  - Wound infection / sinusitis
  - Meningitis
- Incidence: 10-50%
- Risk factors for infection
  - Mandible fractures (tooth-bearing)
  - Open
  - Proximity to oral/nasal cavity
  - Basilar skull fracture (CSF leak)
- Common pathogens
  - Gram positive
    - Streptococcus
    - *Staphylococcus aureus*
  - Oral anaerobes
    - *Peptostreptococcus*
    - *Propionibacterium*
  - Gram negative
    - *Prevotella*
Evidence for Presumptive Antibiotics?

- Numerous, small conflicting trials with no guidelines

<table>
<thead>
<tr>
<th>Reference Design</th>
<th>Population Fracture location</th>
<th>Treatment duration: % Infections</th>
<th>Pearls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mottini 2014</td>
<td>N=399 Zygomatic: 42% Orbital floor: 33.5% Mandibular: 23%</td>
<td>Amoxicillin / clavulanic &gt;5 after surgery: 3.3% 1 day after: 4% (p=0.77)</td>
<td>Prolonged post-operative antibiotics did not prevent infections</td>
</tr>
<tr>
<td>Domingo 2016</td>
<td>N=359 Mandibular fracture</td>
<td>Post op antibiotics: 14.6% No post op antibiotics: 9.7%</td>
<td>Post-op antibiotics do not provide additional benefit</td>
</tr>
</tbody>
</table>

REC: Facial, Sinus and Skull Fractures

• Preoperative dose with aerobic & anaerobic coverage
  – Cefazolin + metronidazole or ampicillin/sulbactam (clinda if allergy)
  – May forgo for maxilla, zygoma, mandibular condyle region or closed skull

• Duration:
  – Limit to pre-operative doses?
  – < 24 hours post op

• Clinical pearls
  – Little guidance if delayed fixation

Penetrating Brain Injury

- Little data in the civilian population
- Microbiology of potential organisms
  - Skin, hair, bone fragments
  - Trajectory of bullets through sinus cavity's
- Extrapolated from known benefit in clean neurosurgery
  - Ampicillin / sulbactam or ceftriaxone ± metronidazole
  - Duration: pre-operative dose or longer with retained fragments (e.g. 5 days)

# Freshwater and Saltwater Injuries

- Assume to be contaminated with aquatic pathogens

<table>
<thead>
<tr>
<th>Source</th>
<th>Unique microbiology (in addition to skin flora)</th>
<th>Clinical Syndrome</th>
<th>Treatment (in addition to)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freshwater</td>
<td>Aeromonas hydrophilia</td>
<td>Fever, Leukocytosis, Lymphadenopathy</td>
<td>Doxycycline + Cephalosporin (3rd or 4th generation) Fluoroquinolones</td>
</tr>
<tr>
<td>Saltwater</td>
<td>Vibrio species</td>
<td>Vomiting, Fever, Hypotension</td>
<td>Cephalosporin (3rd or 4th generation) Fluoroquinolones</td>
</tr>
</tbody>
</table>

Antibiotic Resistance

- >2,000,000 infected with antibiotic resistant organisms
- ~23,000 death annually
- Culture of antibiotic overuse
  - 20-50% inpatient inappropriate
  - Consistently associated with development of resistance
- Duration matters!!!


“But Timmy, you have to eat your antibiotics or you’ll never become a big strong bacteria.”
Conclusion

- Presumptive antibiotics indicated for many traumatic infection
- Growing literature that prolonged postoperative durations may not be beneficial
- J Trauma 2016;81:765

<table>
<thead>
<tr>
<th>Injury</th>
<th>Preferred Agent(s)</th>
<th>Alternate Agent(s) (Severe Penicillin and Cephalosporin Allergy)</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penetrating abdominal injury</td>
<td>Cefazolin 1-3 g IV every 8 h + metronidazole 500 mg IV/PO every 8 h</td>
<td>Clindamycin 600-900 mg IV every 8 h</td>
<td>3-5 d</td>
</tr>
<tr>
<td>Open extremity fractures Type I</td>
<td>Cefazolin 1-3 g IV every 8 h</td>
<td>Clindamycin 600-900 mg IV every 8 h</td>
<td>24 h after wound closure</td>
</tr>
<tr>
<td>Type II</td>
<td></td>
<td></td>
<td>24 h after wound closure</td>
</tr>
<tr>
<td>Type III</td>
<td>Cefazolin 1-3 g IV every 8 h + IV/PO every 8 h</td>
<td>Clindamycin 600-900 mg IV every 8 h</td>
<td>24 h after wound closure</td>
</tr>
<tr>
<td>Penetrating head injury</td>
<td>Ampicillin/sulbactum 3-4.5 g IV every 6 h</td>
<td>None</td>
<td>If retained fragment(s) immediately following injury and for 5 d postoperatively</td>
</tr>
<tr>
<td>Facial, sinus, and skull fractures Open</td>
<td>Cefazolin 1-3 g IV every 8 h + metronidazole 100 mg IV/PO every 8 h</td>
<td>None</td>
<td>If no retained fragment(s) at least one dose preoperatively</td>
</tr>
<tr>
<td>Facial, sinus, and skull fractures Closed</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Sinus fractures Open/closed</td>
<td>See recommendations for facial fractures</td>
<td>See recommendations for facial fractures</td>
<td>All sinus fracture types: single preoperative dose</td>
</tr>
<tr>
<td>Skull fractures Open</td>
<td>See recommendations for facial fractures</td>
<td>See recommendations for facial fractures</td>
<td>Single preoperative dose</td>
</tr>
<tr>
<td>Closed</td>
<td>Not routinely recommended</td>
<td>Not routinely recommended</td>
<td>N/A</td>
</tr>
<tr>
<td>Freshwater and saltwater injuries Freshwater</td>
<td>Cefazolin 1 g IV every 6 h</td>
<td>Piperacillin 400 mg IV every 6 h</td>
<td>Based on injury type, source control, and patient condition</td>
</tr>
<tr>
<td>Saltwater/submerged</td>
<td>Cefazolin 1 g IV every 6 h + doxycycline 100 mg IV/PO BID</td>
<td>Cefazolin 400 mg IV every 8 h + doxycycline 100 mg IV/PO BID</td>
<td>Based on injury type, source control, and patient condition</td>
</tr>
<tr>
<td>Human and animal bites</td>
<td>Amoxicillin/clavulanate 875 mg PO BID</td>
<td>Doxycycline 300 mg IV/PO BID</td>
<td>3-5 d</td>
</tr>
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