Choosing the Right Antibiotic
The Art and The Science

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The Science

Recurrent Cellulitis

- Randomized, double blind, placebo controlled trial of 12 months of oral penicillin VK 250 mg bid to prevent recurrent cellulitis
- Primary outcome
  - Time to next occurrence of medically documented cellulitis
- Secondary outcomes
  - Proportion of subjects with repeat episodes during prophylaxis and follow-up
  - Number of repeat episodes
  - Hospital days
  - Adverse events

Thomas, et al. NEJM 368:1695, 2013

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pen VK (n=136)</th>
<th>Placebo (n=138)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to recurrence (days)</td>
<td>626</td>
<td>532*</td>
</tr>
<tr>
<td>Recurrence during Rx</td>
<td>30 (22%)</td>
<td>51 (37%)*</td>
</tr>
<tr>
<td>Number of repeat episodes</td>
<td>149</td>
<td>164*</td>
</tr>
<tr>
<td>Recurrence after Rx</td>
<td>26/97 (27%)</td>
<td>22/81 (27%)</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>30</td>
<td>28</td>
</tr>
<tr>
<td>Adverse event</td>
<td>37</td>
<td>48</td>
</tr>
</tbody>
</table>

Number needed to treat to prevent 1 episode = 5

Predictors of prophylaxis failure: BMI > 33, ≥3 prior episodes of cellulitis, edema

Thomas, et al. NEJM 368:1695, 2013
Antimicrobial Prophylaxis for Vascular Surgery

- Procedures for which prophylaxis **HAS NOT** been shown to reduce infection rate
  - Brachiocephalic procedures w/o prosthetic graft
- Procedures for which prophylaxis **HAS** been shown to reduce infection rate
  - Aneurysm repair
  - Implantation of prosthetic material
  - Thromboendarterectomy
  - Vein bypass
  - Dialysis access

- Microbial etiology
  - *S. aureus* (33%)
  - Enterococci (10%)
  - Coagulase-negative staphylococci (8%)
  - Gram-negative enterics (24%)
  - *Ps. aeruginosa* (8%)

- Should be given prior to procedure
- Redosing may be needed for procedures > 4 hours
- No added benefit of > 24h duration vs single dose or < 24h


### Antimicrobial Prophylaxis for Vascular Surgery

#### Antibiotic Dose Timing Repeat Strength

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose</th>
<th>Timing</th>
<th>Repeat dose</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefazolin</td>
<td>2 g</td>
<td>60 min prior to incision</td>
<td>4h</td>
<td>A</td>
</tr>
<tr>
<td>(3g ≥120 kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td>15 mg/kg</td>
<td>120 min prior to incision</td>
<td>Not needed</td>
<td>A</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>900 mg</td>
<td>60 min prior to incision</td>
<td>6h</td>
<td>A</td>
</tr>
</tbody>
</table>

| **Alternatives** | | | |
|------------------| | | |

Vancomycin

- Inferior to beta-lactams (nafcillin, cefazolin) for methicillin-susceptible *S. aureus* infection
- Still drug of choice for treatment of MRSA
- Dosing (?)
  - Loading dose: 25-30 mg/kg for serious infections
  - Maintenance dose: 15-20 mg/kg every 8-12 hours
  - Target trough: 15-20 μg/mL
- Toxicity
  - Higher troughs associated with toxicity
  - Avoid in combination with aminoglycosides
The Art

Parachutes reduce the risk of injury after challenge but their effectiveness has not been proved with randomized controlled trials.

Rifampin

- Good oral bioavailability
- Highly active against *S. aureus*
- Resistance rapidly emerges if used as a single agent to treat active infection (must be used in combination)
- Optimal dose not established
  - 600 mg once daily, 300 mg bid, 450 bid
- Hepatotoxic (cholestatic pattern)
- Numerous drug interactions (potent inducer of cytochrome P450)
Rifampin - Uses

• Impregnation of vascular grafts
  – Probably safe
  – Clinical efficacy not established (only case series)
• Treatment of graft and device infections (must be used in combination) (Grade B II/III mostly)
  – Rationale: active in biofilms, works great in animals
  – MRSA osteomyelitis
  – Device related infections (bone and joint)
  – Prosthetic valve endocarditis
  – Septic cavernous sinus thrombosis

References

  – Meta-analysis of antibiotic prophylaxis, impregnated grafts, other prevention methods
  – IDSA MRSA treatment guidelines
  – Review of case series of antibiotic-impregnated grafts
  – Poor quality study
  – Review of rifampin use to treat S. aureus infections

Done!