Staphylococcal Bacteremia

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Chief of Infectious Diseases
San Francisco General Hospital

Outline of the Talk

- About blood cultures
- Management of line-related infections
- Management of S. aureus bacteremia
  - Choice of agents, duration of therapy
  - Use of echocardiography
  - Treatment failure
  - What to do when vancomycin MIC > 1 µg/ml

Case 1

- 38 y/o man, new CHF, alcoholic cardiomyopathy, Hct = 13
- Given PRBCs, diuretics, afterload reducers
- HD 6: upper + lower endoscopy
- Post-procedure T = 38°C, 2 peripheral blood cultures taken
- HD 7: afebrile but BC x1 = GPC in clusters
Case 1 – Appropriate Next Step?

1. Administer vancomycin 1 g q12h
2. Order a transthoracic echocardiogram
3. Order transesophageal echocardiogram
4. Repeat blood cultures, administer vancomycin 1 g q12h pending results of repeat culture
5. Repeat blood cultures, observe off therapy

How many blood cultures are needed?

<table>
<thead>
<tr>
<th>Organism (# BSI)</th>
<th>Cumulative % detected by culture number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td><em>Staph. aureus</em> (100)</td>
<td>93</td>
</tr>
<tr>
<td>Coag-neg staph (66)</td>
<td>64</td>
</tr>
<tr>
<td>Enterococcus (36)</td>
<td>67</td>
</tr>
</tbody>
</table>

How many blood cultures are needed?

Obtaining Blood Cultures

- Skin prep with alcohol-based or iodine antiseptic
- Draw at least 2 and preferably 3 blood cultures from peripheral vein
- For suspected catheter-related infections
  - No broth cultures of tip, “routine” cultures
  - Semi-quantitative roll-plate methods (> 15 cfu/5 mm segment)
  - Paired set of blood cultures through the line and peripherally

J Clin Microbiol 45:3546, 2007
Interpreting Blood Culture Results

- **Coagulase-negative staph**
  - Most common blood culture isolate (~40%)
  - Only 10-15% represent true bacteremia

- **Staphylococcus aureus**
  - Second most common isolate (~15%)
  - 93% represent true blood stream infection

- **Other organisms with high contamination rates**
  - Viridans strep (55%)
  - Corynebacterium (88%)
  - Bacillus, Micrococcus, Propionibacterium species (all > 90%)


Criteria for True BSI with CoNS

- Signs or symptoms of infection
- Two or more positive blood cultures
- Positive cath tip roll plate culture + positive blood culture
- Positive paired blood cultures through catheter and peripheral vein
  - Cath cfu > 3 x blood cfu
  - Cath culture positive 2 h before peripheral blood culture

Criteria for True BSI with CoNS

- Single positive culture should be presumed to be a contaminant
- Two or more positive blood cultures* plus
  1. Positive w/in 48h, temp > 38, chills, hypotension
     Sens = 91%, Spec = 11%, NPV = 30%
  2. No. 1 + identical antibiograms
     Sens = 76%, Spec = 26%, NPV = 27%
  3. No. 1 + identical species
     Sens = 91%, Spec = 52%, NPV = 67%
  4. Identical species
     Sens = 100%, Spec = 48%, NPV = 100%

* Gold standard of identical genotypes (74 of 101 cases)

Clin Microbiol Infect 17:569, 2011
Therapy of CoNS BSI

- **Antibiotic**
  - MRCS: vancomycin 15 mg/kg q12h
  - MSCS: beta-lactam
- **Duration**
  - No therapy: line out, no hardware, intravascular device, pre-treatment blood cultures negative
  - 3-5 days* or 5-7 days: line out
  - 10-14 days: line in and in combo with lock therapy


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Case 1

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- Given PRBCs, diuretics, afterload reducers
- HD 6: upper + lower endoscopy
- Post-procedure T = 38°C, 2 peripheral blood cultures taken
- HD 7: afebrile but BC x1 = GPC in clusters
- If blood culture yields CoNS, no therapy
- If blood culture yields *S. aureus*: 14 days of therapy
Management of *Staph. aureus* Bacteremia

What is the risk of a poor outcome?

Complications in catheter-associated SAB

- Endocarditis, thrombosis
- Osteomyelitis, epidural abscess


Independent Predictors of Complicated SAB

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive f/u blood culture</td>
<td>5.6</td>
</tr>
<tr>
<td>Community onset</td>
<td>3.1</td>
</tr>
<tr>
<td>Persistent fever @ 72h</td>
<td>2.2</td>
</tr>
<tr>
<td>Skin lesions</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Fowler, Arch Intern Med 163:2066, 2003
What is the risk of a poor outcome?

1 point each for skin findings, fever > 72h, community onset
4 points for positive blood culture @ 48-96h

Fowler, Arch Intern Med 163:2066, 2003

Predictors of Poor Outcome for Staphylococcus aureus Bacteremia

- Septic shock
- Persistent focus of infection
- Secondary focus of infection
- Prolonged bacteremia on therapy (>48-72h)
- Elderly patient (age > 60 years)
- MRSA
- Use of vancomycin instead of a β-lactam
- Duration of treatment < 10-14 days

What antibiotic should be used?

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nafcillin or oxacillin</td>
<td>Highly effective</td>
<td>Poorly tolerated, inconvenient</td>
</tr>
<tr>
<td>2 g q4h IV</td>
<td></td>
<td>Inconvenient</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>Effective</td>
<td></td>
</tr>
<tr>
<td>2 g q6h IV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Well tolerated,</td>
<td>Less effective than β-lactams</td>
</tr>
<tr>
<td>1 g q12h IV</td>
<td>convenient</td>
<td></td>
</tr>
<tr>
<td>Dicloxacillin or</td>
<td>Convenient (oral)</td>
<td>Unknown efficacy, GI side effects,</td>
</tr>
<tr>
<td>cephalaxin</td>
<td></td>
<td>qid dosing</td>
</tr>
<tr>
<td>1 g qid PO</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Vancomycin vs. Beta-Lactams

**Study** | Regimens compared | Key findings
---|---|---
Fowler, et al (Clin Infect Dis 27: 478, 1998) | Vanco vs beta-lactam | **Lower cure rate (62% vs 84%) with vanco**<br>**Higher death rate (12% vs 6%) with vanco**
Schweizer, et al (BMC Infect Dis 11:279, 2011) | 30 mortality with MSSA for 1. Naf or cefazolin vs 2. Vanco + naf or cefazolin vs 3. Vanco | **Lowest mortality for 1 vs 2 vs 3 (3% vs. 7% vs 20%)**<br>**Naf vs vanco: adjusted HR=0.21**<br>**Switch to naf after vanco vs stay on vanco: adjusted HR=0.31**

Cefazolin vs. Nafcillin

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Cefazolin (n=41)</th>
<th>Nafcillin (n=41)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days resolution of fever (mean + sd)</td>
<td>4.1 ± 3.8</td>
<td>5.4 ± 9.5</td>
<td>NS</td>
</tr>
<tr>
<td>Death or clinical failure @ 4 wk (n)</td>
<td>4</td>
<td>4</td>
<td>NS</td>
</tr>
<tr>
<td>Death or clinical failure @ 12 wk (n)</td>
<td>6</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>Relapse @ 12 wk</td>
<td>1</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>Death @ 12 wk</td>
<td>1</td>
<td>5</td>
<td>0.22</td>
</tr>
<tr>
<td>Rx stopped for adverse drug event</td>
<td>0</td>
<td>7</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Duration of Therapy: *Staph. aureus* Bacteremia

<table>
<thead>
<tr>
<th>Duration</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>14 days</td>
<td>Fever resolves by day 3&lt;br&gt;Sterile blood culture after 2-3 days&lt;br&gt;Easily removed focus of infection&lt;br&gt;No metastatic infection (e.g., osteo)&lt;br&gt;Negative echo, no evidence of endocarditis&lt;br&gt;No predisposing valvular abnormalities&lt;br&gt;No implanted prosthetic devices (No DM, immunosuppression)</td>
</tr>
<tr>
<td>4-6 weeks (at least)</td>
<td>Failure to meet one of more of above criteria</td>
</tr>
</tbody>
</table>

Echocardiography for *Staph. aureus* Bacteremia (SAB)

- Generally recommended for all patients with SAB
  - Approx. 20% of all comers will have evidence of endocarditis
  - Compliance is low
  - TEE vs TTE?
- TTE may be adequate in low risk patients
  - Uncomplicated, prompt conversion of blood cultures to negative, no embolic phenomenon, no prosthetics/pacemaker, high quality study
- Echo may not needed in low risk patients with
  - Nosocomial bacteremia (prevalence of endocarditis 4-9%) AND no hemodialysis


When to Get an ECHO

![Flowchart indicating the decision-making process for echocardiography based on clinical suspicion and imaging outcomes.]

Case 2

- 57 y/o man, fevers, aching all over
- Exam
  - VS: 39.5, 130/70, 140, 18
  - 2/6 systolic murmur
  - Tender, 1 cm hemorrhagic lesions both great toes
- Labs:
  - WBC = 22,000, remainder unremarkable
  - CXR: normal
  - Blood cultures pending
- RX: Vancomycin + ceftriaxone
Case 2 - Hospital Course

<table>
<thead>
<tr>
<th>Day</th>
<th>Tmax</th>
<th>BC</th>
<th>Vanco</th>
<th>MIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>39.5</td>
<td>1/1</td>
<td>+</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>38.3</td>
<td>4/4</td>
<td>+</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>39.8</td>
<td>1/2</td>
<td>+</td>
<td>0.5</td>
</tr>
<tr>
<td>4</td>
<td>39.2</td>
<td>4/4</td>
<td>+</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>38.4</td>
<td>1/2</td>
<td>+</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>37.1</td>
<td>2/2</td>
<td>+</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Management Questions
1. Would you change antibiotics?
2. If so, to what?
3. And if so, when?

Management Issues
- What is the appropriate dosing for vancomycin?
- Is this a vancomycin failure?
- What is the reason for failure?
- How does the MIC affect the decision?
- At what point in therapy should one consider changing therapy? 

Choose the answer that best indicates what you would do.
1. Continue vancomycin as a single agent.
2. Add gentamicin to vancomycin on day 5 or 7.
3. Add rifampin to vancomycin on day 5 or 7.
4. D/C vanco, switch to alternative on day 8.
5. D/c vanco, switch to alternative on day 5.
Recommended Vancomycin Dosing

- For serious infections (pneumonia, bacteremia)
  - 15-20 mg/kg IV q8-12h
  - Target trough concentrations of 15-20 µg/ml
  - Adjust for renal function
- For less serious infections (SSTI):
  - 15 mg/kg q12h (1 gm q12h)
  - Routine measurement of trough not necessary


Vancomycin MIC Breakpoints in S. aureus

<table>
<thead>
<tr>
<th></th>
<th>Old</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susceptible</td>
<td>≤ 4</td>
<td>≤ 2</td>
</tr>
<tr>
<td>Intermediate</td>
<td>8-16</td>
<td>4-8</td>
</tr>
<tr>
<td>Resistant</td>
<td>≥ 32</td>
<td>≥ 16</td>
</tr>
</tbody>
</table>

Clinical and Laboratory Standards Institute January 2006.

What is Persistent SAB?

Duration of Positive Blood Cultures on Therapy

<table>
<thead>
<tr>
<th>Study</th>
<th>Regimen</th>
<th>MSSA*</th>
<th>MRSA*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Korzenowski, 1982**</td>
<td>Naf</td>
<td>3</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>Naf + gent</td>
<td>2</td>
<td>--</td>
</tr>
<tr>
<td>Levine, 1991**</td>
<td>Vanco</td>
<td>--</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Vanco + rif</td>
<td>--</td>
<td>9</td>
</tr>
<tr>
<td>Fowler, 2006**</td>
<td>Vanco or naf + 4d gent</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Daptomycin</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Khatib, 2006</td>
<td>Beta-lactam, vanco</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Neuner, 2010</td>
<td>Vanco</td>
<td>--</td>
<td>2</td>
</tr>
</tbody>
</table>

*Median or mean duration of positive blood cultures in days
**Endocarditis
Persistent Bacteremia: Risk Factors

<table>
<thead>
<tr>
<th>Study</th>
<th>Khatib ScanJID 2006</th>
<th>Hawkins Arch IM 2007</th>
<th>Neuner DMID 2010</th>
<th>Yoon JAC 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design, N</td>
<td>Cohort 245</td>
<td>Case-control 236</td>
<td>Cohort 196</td>
<td>Case-control 63</td>
</tr>
<tr>
<td>Scope</td>
<td>MSSA, MRSA</td>
<td>MSSA, MRSA</td>
<td>MRSA</td>
<td>MRSA</td>
</tr>
<tr>
<td>Persistence</td>
<td>&gt; 3d</td>
<td>&gt;7d v &lt; 3d</td>
<td>&gt; 5d</td>
<td>&gt;7d v &lt; 3d</td>
</tr>
<tr>
<td>Predictors</td>
<td>Endovascular source</td>
<td>Endocarditis</td>
<td>Endocarditis</td>
<td>Retained device</td>
</tr>
<tr>
<td></td>
<td>– Cardiac prosthesis</td>
<td>– CVC/foreign body</td>
<td>– Metastatic foci</td>
<td>– Septic shock</td>
</tr>
<tr>
<td></td>
<td>– Metastatic foci</td>
<td>– MRSA</td>
<td>– MRSA</td>
<td>– Metastatic foci</td>
</tr>
<tr>
<td></td>
<td>– DM</td>
<td>– Renal failure</td>
<td>– Vanco MIC = 2</td>
<td>– Vanco MIC = 2</td>
</tr>
<tr>
<td></td>
<td>– Vancomycin</td>
<td></td>
<td>(6/120 v 12/76)</td>
<td>(4/32 v 14/31)</td>
</tr>
<tr>
<td>Not predictors</td>
<td>Fever, MRSA</td>
<td>Vanco trough, AUC</td>
<td>Vanco trough, AUC/MIC</td>
<td></td>
</tr>
</tbody>
</table>

Predictors of Vancomycin Failure in S. aureus Bacteremia

- 320 patients
- 52.5% vancomycin failure
- Predictors of failure
  - Infective endocarditis
  - Nosocomial infection
  - Vancomycin MIC > 1 µg/ml (E-test)
  - AUC/MIC > 421

Clin Infect Dis 52:975, 2011

What is an E-test Anyway?

MIC = 1.5 µg/ml
MIC and Probability to Obtain Target Attainment

1. Trough ~10 $\mu$g/ml
   - 15 mg/kg q 12 h, 70 kg individual, nl RF
   - $AUC_{24} = 318 \pm 111 \mu$g/24h/ml

2. Trough ~20 $\mu$g/ml
   - 30 mg/kg q 12 h, 70 kg individual, nl RF
   - $AUC_{24} = 418 \pm 152 \mu$g/24h/ml

Jeffries MN et al. Critical Care Med. 2006;130:947
Mohr J & Murray B. Clin Infect Dis. 2007 44:1536

Limitations of Current MIC Methods

- Compared to CLSI reference broth microdilution, Etest yields one dilution higher vancomycin MIC
  - Etest: MIC of 2 $\mu$g/ml reported in 20-37% of isolates
  - Microdilution: MIC of 2 $\mu$g/ml reported in 3% of isolates
- MRSA USA300 (reference microdilution MIC = 1 $\mu$g/ml) sent to > 2000 laboratories as the CAP challenge organism:
  - Microscan and BD Phoenix: Majority MIC = 2 $\mu$g/ml
  - Vitek: Majority MIC as ≤ 0.5 or 2 $\mu$g/ml
  - Vitek 2: Most accurate method, majority MIC = 1 $\mu$g/ml
- No commercially available methods detect hVISA

Prakash V AAC 2008; Personal communication, Ronald Jones
How Should the Vancomycin MIC Be Used to Guide Therapy?

• An alternative to vancomycin is recommended for the treatment of isolates with a vancomycin MIC > 2 µg/mL (e.g., VISA, VRSA)
• Due to the limitations of susceptibility testing, clinical and microbiologic correlation with MIC results is recommended if MIC < 2

Management of Persistent MRSA Bacteremia on Vancomycin Therapy

• Median time to clearance of MRSA bacteremia is 7-9 days
• Persistent bacteremia around day 7 of therapy should prompt assessment to determine if a change in therapy is indicated:
  – Search for and remove other foci of infection
  – Evaluate clinical response
  – Assess micro data (vanco MIC, results of f/u bld cx)

Consider change if:
1) Unsatisfactory clinical response, regardless of MIC
2) Vanco MIC > 2

No change if:
1) Clinically responding and
2) Vanco MIC < 2

Day of vancomycin therapy
**Vancomycin Alternatives**

- Trimethoprim-sulfamethoxazole
- Quinupristin/dalfopristin (Synercid™)
- Linezolid (Zyvox™)
- Daptomycin (Cubicin™)
- Tigecycline (Tygacil™)
- Telavancin (Vibativ™)
- Ceftaroline (Teflaro™)

**Additives**

- Rifampin
- Gentamicin
- Beta-lactams
- TMP-SMX
- Linezolid, daptomycin, quinupristin/dalfopristin

**Daptomycin vs Vancomycin for BSI Due to MRSA with High Vancomycin MICs**

- Retrospective, case control
  - MRSA with E-test MICs > 1.5 µg/ml
  - 118 vanco cases, 59 dapto cases
- Vanco trough target 10-20 µg/ml
- Dapto dose 6-12 mg/kg per 24h
- 58/59 dapto-treated subjects switched
- 91% of whom were on vanco
- Mean time to switch 5 days (60% *not improving, 48% with positive blood cultures

*Clin Infect Dis 54:51, 2012*
### Daptomycin vs Vancomycin for BSI Due to MRSA with High Vancomycin MICs

<table>
<thead>
<tr>
<th></th>
<th>Vanco</th>
<th>Dapto</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical failure*</td>
<td>37/118</td>
<td>10/59</td>
<td>0.084</td>
</tr>
<tr>
<td>60-day mortality</td>
<td>24/118</td>
<td>5/59</td>
<td>0.046</td>
</tr>
<tr>
<td>Failure, MC 1.5</td>
<td>31/102</td>
<td>6/25</td>
<td>0.530</td>
</tr>
<tr>
<td>Failure, MIC 2</td>
<td>6/16</td>
<td>4/34</td>
<td>0.065</td>
</tr>
</tbody>
</table>

* Composite endpoint of 60-day mortality, microbiological failure, relapse


### Daptomycin vs Vancomycin for BSI Due to MRSA with High Vancomycin MICs

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<td>0.065</td>
</tr>
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* Vanco was an independent predictor of failure by logistic regression with adjusted OR = 3.13 (95% CI 1.00-9.76)

§ Composite endpoint of 60-day mortality, microbiological failure, relapse


### Daptomycin MIC Distribution for Vancomycin Non-Susceptible Strains

Do we have the right dose for daptomycin?

- Dose was chosen based on concerns for toxicity, not guarantee of efficacy
- Daptomycin has concentration dependent killing
- Higher dose may provide protection against emergence of resistance
- IDSA guidelines committee recommends that if daptomycin is used for treatment failure, it be used at a dose of 10 mg/kg/d

Vancomycin vs TMP-SMX
Matched Case-control Study of SAB

<table>
<thead>
<tr>
<th></th>
<th>TMP-SMX (n=38)</th>
<th>Vancomycin (n=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay (d)</td>
<td>21.5</td>
<td>25</td>
</tr>
<tr>
<td>Persistent + BC</td>
<td>2 (5%)</td>
<td>5 (7%)</td>
</tr>
<tr>
<td>Relapses</td>
<td>1 (3%)</td>
<td>9 (12%)</td>
</tr>
<tr>
<td>30 d mortality</td>
<td>13 (34%)</td>
<td>31 (41%)</td>
</tr>
</tbody>
</table>

Goldberg JAC 2010

Linezolid Salvage for Persistent Bacteremia

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Attempts (N)</th>
<th>% Neg BC @ 72h</th>
<th>Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>Add rif or gent to vanco</td>
<td>12</td>
<td>2 (17%)</td>
<td>0</td>
</tr>
<tr>
<td>Switch to linezolid</td>
<td>16</td>
<td>12 (75%)</td>
<td>14 (88%)</td>
</tr>
</tbody>
</table>

Jang CID 2009
### Linezolid Salvage for Persistent SAB

<table>
<thead>
<tr>
<th>Primary Regimen</th>
<th>Salve success</th>
<th>Mortality</th>
<th>Days + BC</th>
<th>Vanco levels</th>
<th>MIC = 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vanco</strong></td>
<td>0/12</td>
<td>10/19</td>
<td>12 ± 4</td>
<td>16 ± 19</td>
<td>N=1</td>
</tr>
<tr>
<td>Vanco only</td>
<td>6/14</td>
<td>12 ± 4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ rif + gent</td>
<td>4/5</td>
<td>17 ± 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Linezolid</strong></td>
<td>14/16</td>
<td>4/16</td>
<td>26 ± 39</td>
<td>19 ± 5</td>
<td>N=2</td>
</tr>
<tr>
<td>Linezolid only</td>
<td>2/7</td>
<td>33 ± 55</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ penem</td>
<td>2/9</td>
<td>20 ± 10</td>
<td></td>
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</tr>
</tbody>
</table>

Jang CID 2009

Vanco levels (+ s.d.) and MIC in µg/ml; days and vanco levels are mean + s.d.

### Case Reports of Salvage Therapy for SAB

- **Daptomycin + rifampin** (Ahmed Ann Pharmacother 2010)
  - 19 days of MRSA bacteremia (occult, post-cystoscopy)
  - Vnco 10 d, Dapto 9 d, emergence of dapto NS isolate (MIC =2)
  - Resolution with addition of rifampin

- **Linezolid + rifampin** (Schwalm Can JID 2004)
  - Vanco + rif failure (bone and joint)

- **Telavancin**
  - 15 days of bacteremia, emergence of VISA (Marcos AAC 2010)
  - Pacemaker, epidural abscess, initial vanco MIC = 2
  - Daptomycin failure, emergence of dapto NS isolate (MIC>2)
  - 8 days of bacteremia, MRSA (Nace JAC 2010)
  - TCV endocarditis
  - Negative blood cultures after 1 day of televancin

### Treatment of Bacteremia and Other Serious Staph Infections

- Use a beta-lactam for MSSA infections whenever possible
- Vancomycin has issues....
  - High clinical and microbiological failure rate (25-50%)
  - May be nephrotoxic at the higher doses required to achieve recommended troughs of 15-20 µg/ml (Lodise, AAC 52:1330, 2008)
- No alternative agents(s) has been shown to be superior to vancomycin alone
  - In fact, they have been found to be "not inferior"
Summary

- Define and eliminate source of bacteremia
- Document clearance of bacteremia with follow-up blood cultures
- Use of vancomycin for MRSA
  - Few data supporting utility of drug combinations
  - Precisely define the vancomycin MIC
  - Maintain vancomycin troughs of 15-20 µg/ml
  - Treatment failures are common
- Switch to alternative agents in non-responders
  - Do not "add on" to vancomycin, switch
  - Use a drug combination whenever possible
  - If daptomycin is used
    - Check daptomycin MIC
    - Dose daptomycin at 10 mg/kg and in combination
    - Role of newer agents unknown

Hospital Course

<table>
<thead>
<tr>
<th>Day</th>
<th>Tmax</th>
<th>BC</th>
<th>Vanco MIC</th>
<th>Other info</th>
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<tbody>
<tr>
<td>1</td>
<td>39.5</td>
<td>1/1+</td>
<td>1</td>
<td>Vanco started</td>
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<tr>
<td>2</td>
<td>38.3</td>
<td>4/4+</td>
<td>2</td>
<td>TEE = AV veg</td>
</tr>
<tr>
<td>3</td>
<td>39.8</td>
<td>1/2</td>
<td>0.5</td>
<td>VancoT = 20 µg/ml</td>
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<tr>
<td>4</td>
<td>39.2</td>
<td>4/4+</td>
<td>2</td>
<td>Stable</td>
</tr>
<tr>
<td>5</td>
<td>38.4</td>
<td>1/2+</td>
<td>1</td>
<td>Δ to dapto 10 mg/kg + gent 3 mg/kg/d</td>
</tr>
<tr>
<td>8</td>
<td>37.1</td>
<td>2/2+</td>
<td>1</td>
<td>Stable</td>
</tr>
<tr>
<td>10</td>
<td>37.1</td>
<td>2/2-</td>
<td>n/a</td>
<td>Stable</td>
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