Endocarditis: Treatment & Prevention

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Overview

(I) Prevention
- Concept of antibiotic prophylaxis
- Updated 2007 AHA Guidelines

(II) Therapy
- Importance of bactericidal therapy
- Clinical scenarios
- Special pathogens
- New drugs and combinations

(III) Points about epidemiology & diagnosis

Clinical Scenario

- Patient with MVP scheduled to have wisdom teeth extracted. Has systolic murmur with mid-systolic click on exam. Gives vague history of rash with penicillin as a child. You should give:

(A) Oral clindamycin 60 minutes prior
(B) Oral amoxicillin 60 minutes prior
(C) IV ampicillin 30 minutes prior
(D) No antibiotic prophylaxis is required

Prophylaxis – The Concept
**Frequency of Bacteremia**

- Dental procedures: tooth extraction (10-100%), periodontal surgery (36-88%), teeth cleaning (up to 40%), & endodontic procedures (up to 20%)
- Routine: brushing & flossing (20-68%), use of toothpicks (20-40%), water irrigation devices (7-50%), & chewing food (7-51%)
- Average person <2 yearly dental visits, so risk much higher just from daily activities

**Cumulative Risk of Bacteremia**

- Guntheroth (Am J Cardiol, 1984) estimated cumulative 5370 minutes of bacteremia with 1 month chewing & brushing compared with 6-30 minutes after single tooth extraction
- Roberts (Pediatr Cardiol, 1999) estimated brushing twice daily for one year had 154,000 X risk of exposure compared to single tooth extraction...estimated 5.6 million X greater when including other daily activities

**Primary Reasons for the Revision of the IE Prophylaxis Guidelines**

- IE much more likely to result from frequent exposure to random bacteremias associated with daily activities than from bacteremia caused by a dental, GI tract, or GU tract procedure
- Prophylaxis may prevent exceedingly small number of cases of IE, if any, in individuals who undergo a dental, GI or GU tract procedure.
- Risk of antibiotic-associated adverse events exceeds the benefit, if any, from prophylactic antibiotic therapy.
- Maintenance of optimal oral health and hygiene may reduce the incidence of bacteremia from daily activities and is more important than prophylactic antibiotics for a dental procedure to reduce the risk of IE.

**AHA Guidelines Revised – 2007**

- Most IE not from invasive procedures but bacteremias from routine daily activities
- Previous recommendations based on scattered case reports, expert opinion, clinical experience, & descriptive studies
- Numerous publications over past 2 decades now bring efficacy into question
Cardiac Conditions Associated with the Highest Risk of Adverse Outcome from Endocarditis for which Prophylaxis with Dental Procedures is Reasonable

• Prosthetic cardiac valve or prosthetic material used for cardiac valve repair
• Previous IE
• Congenital heart disease (CHD)*
  - Unrepaired cyanotic CHD, including palliative shunts and conduits
  - Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure
  - Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)
• Cardiac transplantation recipients who develop cardiac valvulopathy

Principles of Management

• Begin counting therapy on the first day of negative blood cultures – be sure you clear!
• Give bactericidal therapy (use a β-lactam if you can...give aminoglycoside in enterococcal endocarditis)
• Early consultation with cardiac surgeon if: AoV endocarditis, prosthetic valve, heart failure, other indications for surgery

Clinical Scenario

Underlying MVP. Blood cultures growing viridans group streptococci and has MV vegetation on TEE. NKDA.

Penicillin MIC = 0.5 μg/mL...give:
(A) Penicillin plus gentamicin
(B) Ceftriaxone alone
(C) Vancomycin plus gentamicin
(D) Vancomycin alone
α-Hemolytic Streptococci

- Viridans group & *Streptococcus bovis*
- Community-acquired endocarditis in non-IVDUs
- Some strains (e.g., *Abiotrophia*) more tolerant to penicillin
- Treatment based on penicillin MIC
- If highly-susceptible (MIC <0.12) use penicillin or ceftriaxone alone, but if intermediate (MIC 0.12 – 0.5) include gentamicin for 2 weeks.
Clinical Scenario

57 year old man presents with F/C & new murmur. TEE shows MV vegetation. Blood cultures X 3 grow:

*Clostridium septicum*

Stable & doing well on antibiotic therapy. Next test?

A) Lower extremity dopplers  
B) Colonoscopy  
C) Panorex  
D) Toxicology screen

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Clinical Scenario

37 year old IVDU presents with native AoV endocarditis. Blood cultures growing methicillin-sensitive *Staphylococcus aureus*. Rash with penicillin as a child (no anaphylaxis). WORST option is:

A) Nafcillin (after desensitization)  
B) Daptomycin  
C) Cefazolin  
D) Vancomycin
Clinical Scenario

Patient had St. Jude prosthetic MV placed 3 years ago. Presents with F/C & confusion, and TEE shows a vegetation on the valve.

Blood cultures → Methicillin-resistant *Staphylococcus aureus* (MRSA)

What antibiotic therapy should you choose?

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Clinical Scenario

57 yo man with prostate cancer presents with a PCN-susceptible *Enterococcus faecalis* pyelonephritis. Has persistent bacteremia on vancomycin (PCN allergy) & TEE shows MV vegetation.

Which is not a treatment option?
(A) Ampicillin + gentamicin (desensitized)
(B) Pencillin + gentamicin (desensitized)
(C) Vancomycin + gentamicin
(D) Quinupristin-dalfopristin (Synercid®)

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**Table 1. Therapy for Prosthetic Valve Endocarditis Caused by Staphylococcus aureus**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dose* and Route</th>
<th>Duration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methicillin-resistant strains</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td>30 mg/kg in 3 or 4 equally divided doses</td>
<td>2 wk</td>
<td>↓*</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>3 mg/kg per 24 h <em>IV</em> in 2 equally divided doses</td>
<td>2 wk</td>
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**Enterococcus**

- Remember, you need bactericidal therapy in infective endocarditis.
- β-lactams or vancomycin not bactericidal by themselves against *Enterococcus*.
- Must include aminoglycoside for FULL course (4-6 weeks):
  - Ampicillin or PCN or vancomycin PLUS gentamicin.
If resistant to gentamicin, streptomycin may be an alternative.

HACEK

- *Haemophilus aphrophilus*
- *Actinobacillus*
- *Cardiobacterium*
- *Eikenella*
- *Kingella*

Traditionally common in culture-negative endocarditis, but easily isolated in current blood culture systems at 5 days. Most produce β-lactamases, but sensitive to ceftriaxone, ampicillin/sulbactam, and fluoroquinolones.
Culture-Negative Endocarditis

- No etiology with 3 negative blood cultures at 7 days incubation
- Most frequent cause → prior antibiotics
- Inadequate collection techniques, such as small volume of blood drawn into bottles
- Fastidious organisms: Fungi (e.g. Histoplasma), Coxiella, Brucella, Chlamydia, Legionella, Mycoplasma, Bartonella, Tropheryma whippelii, HACEK, Abiotrophia (NVS)
- Non-infectious endocarditis: myxoma, rheumatoid nodules, SLE, NBTE in malignancy

### Special Tests in Culture-Negative Endocarditis

- Serology: Bartonella, Coxiella burnetii, Brucella, Mycoplasma, Chlamydia, Legionella, consider RF or ANA in some
- Lysis centrifugation blood cultures: *Brucella*, fungi
- Hold blood cultures for 14 days
- Special stains and PCR on valve tissue

**History is Vital**

- Underlying valvular abnormality
- Procedures (e.g. dental extraction, colonoscopy with biopsies)
- IVDU
- Trauma
- Exposure to animals
Patients remain at high risk due to new valvular abnormality
Guidelines recommend establishing a new baseline at completion of therapy
Look at size of vegetations, LV function, valvular insufficiency
TTE adequate and preferred

Follow-up Echocardiography

Pathogens - Traditional Teaching

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Streptococci</td>
<td>60-80%</td>
</tr>
<tr>
<td>Staphylococci</td>
<td></td>
</tr>
<tr>
<td>S. aureus</td>
<td>10-25%</td>
</tr>
<tr>
<td>Coagulase (-)</td>
<td>1-3%</td>
</tr>
<tr>
<td>Enterococci</td>
<td>5-18%</td>
</tr>
<tr>
<td>Gram (-) Rods</td>
<td>2-13%</td>
</tr>
<tr>
<td>Fungi</td>
<td>2-4%</td>
</tr>
<tr>
<td>Other Bacteria</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Mixed Infections</td>
<td>1-2%</td>
</tr>
<tr>
<td>Culture Negative</td>
<td>&lt;5%</td>
</tr>
</tbody>
</table>
Approach to Initial Echocardiography

<table>
<thead>
<tr>
<th>Initial TTE</th>
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<tbody>
<tr>
<td>IE SUSPECTED</td>
<td>Low Initial Patient Risk and Low Clinical Suspection</td>
</tr>
<tr>
<td></td>
<td>High Initial Patient Risk, Moderate to High Clinical Suspection or Difficult Imaging Candidate</td>
</tr>
</tbody>
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Complications of Infective Endocarditis

- Conduction disturbances
- Heart failure
- Septic emboli (lungs, CNS, coronaries)
- Mycotic aneurysm
- Splenic abscess
- Immune phenomena (glomerulonephritis)

Clinical Scenario

- Patient with F/C & new systolic and diastolic murmurs over right upper sternal border.
- Here is the rhythm strip.
- What is going on? What should you do?

Table 1. Microbiologic Etiology in 1779 Patients With Definite Endocarditis

<table>
<thead>
<tr>
<th>Organism/Group</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus</td>
<td>558 (31.6)</td>
</tr>
<tr>
<td>S. aureus</td>
<td>186 (10.5)</td>
</tr>
<tr>
<td>Coagulate-negative staphylococci</td>
<td>319 (18.0)</td>
</tr>
<tr>
<td>Viridans group streptococci</td>
<td>114 (6.6)</td>
</tr>
<tr>
<td>Streptococcus bovis</td>
<td>91 (5.1)</td>
</tr>
<tr>
<td>Enterococci</td>
<td>38 (2.1)</td>
</tr>
<tr>
<td>Non-HACEK gram-negative bacteria</td>
<td>32 (1.8)</td>
</tr>
<tr>
<td>Polymicrobial</td>
<td>23 (1.3)</td>
</tr>
<tr>
<td>Other</td>
<td>56 (3.1)</td>
</tr>
<tr>
<td>Culture negative</td>
<td>144 (8.1)</td>
</tr>
</tbody>
</table>

Indications for Surgery

- Heart failure related to valve dysfunction
- Persistent bacteremia (>7 days) despite appropriate antibiotics
- Recurrent emboli
- Perivalvular abscess or fistula

Relative indications: fungal endocarditis, highly-resistant organism, relapse after “adequate” course, culture-negative IE with persistent fever >10 days after starting therapy

Important Points

- Thorough H&P...social history matters
- Epidemiology changing → more *Staph aureus*
- Need bactericidal therapy
- Generally, need parenteral therapy
- Know complications & when to call a surgeon
- Revised AHA Guidelines for prophylaxis → indicated in many fewer patients