Vascular Graft Infections

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Mayo Clinic

Division of INFECTIOUS DISEASES
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Vascular Graft Infection

• History

• Definition
  • Extracavitary
  • Intracavitary

• Diagnosis
  • Clinical presentation
  • Imaging

• Management
  • Medical
  • Surgical

• Prognosis
Vascular Graft Infections

• Synthetic material first used in 1950s
  • France 1951
  • DeBakey – 1953
  • Early infection rate 30-80%
VAH HOSPITAL HOUSTON 1950’S
Vascular Graft Infections

Definition

• Extracavitary
  • Groin 80%
  • Peripheral 20%

• Intracavitary
  • Intra-abdominal 70%
  • Intrathoracic 30%
Vascular Graft Infections

• Frequency
  • Extracavitary 1.5-2%
    – Groin 3-6%
  • Intracavitary 1-5%
    – Duodenal – aorta fistula 1-2% with aortic reconstruction
PERCENTAGE INFECTION PROSTHESES

- Vascular graft: 64%
- Mechanical heart valve: 10%
- Pacemaker: 6%
- Ventricular assist device: 6%
- Fracture fixation device: 6%
- Neurosurgical-ventricular shunt: 8%
Vascular Graft Infections Microbiology

- **Extracavitary**
  - Coag-neg Staph. 40%
  - S. aureus 30%
  - Gram-negative bacillus 10%; Pseudomonas most common

- **Intracavitary**
  - Coag-neg Staph. 30%
  - S. aureus 30%
  - Gram-negative, polymicrobial 35%
Vascular Graft Infections
Pathogenesis

• Extracavitary
  • Wound infection in groin
  • Intraoperative contamination

• Intracavitary
  • Intraoperative contamination 50%
  • Enteric fistulae; duodenum 30%, rarely colon
  • Contiguous spread 10-15%
  • Bacteremia infection 5-10%
Vascular Graft Infections
Diagnosis – General Principles

• Index suspicion

• Different clinical presentations
  extracavitary, intracavitary

• Time of onset postop

• Physical findings

• Laboratory tests, cultures, draining sinus,
  perigraft fluid, surgical specimens

• Imaging
Vascular Graft Infections
Extracavitary - Diagnosis

• Clinical Presentation
  • Early onset - <2 months postop
    – Sepsis
    – Wound erythema
    – Sinus tract
    – Distal ischemia
    – Septic emboli
    – Graft rupture
Vascular Graft Infections
Extracavitary - Diagnosis

• Clinical Presentation
  • Late onset - >2 months
    – Less often present with sepsis
    – Indolent; groin erythema
    – Sinus tract
    – Erosion graft through skin
    – Pseudoaneurysm - rupture
Vascular Graft Infections
Extracavitary – Samson Classifications (Group 1-5)

Group

1  No deeper than dermis
2  Subcutaneous tissue
   No direct contact with graft
3  Body of graft but not anastomosis
4  Exposed anastomosis, no bleeding, no bacteremia
5  Anastomosis involved bleeding, bacteremia

*Samson et al: J Vas Surg 8:147, 1988
Vascular Graft Infections
Extracavitary - Diagnosis

• Imaging
  • Individualize
  • Combination often required
  • Sinograms – only in select patients; risk of introduction of infections, less useful than other imaging
  • Angiography – Not useful for diagnosis, used to define anatomy for revascularization; CTA used more commonly now
Vascular Graft Infections
Extracavitary – Diagnosis

• Local swelling groin; no drainage – Samson 1 or 2

Ultrasound

• Dermis only
  • Samson 1

• Subcutaneous abscess
• Does not extend to graft
• Ultrasound nondiagnostic
• CT/MRI
• I&D
• No graft involvement
  • Samson 2
Vascular Graft Infections
Extracavitary – Treatment

• Samson 1 – antibiotic therapy alone
• Samson 2 – I&D, antibiotic therapy
• Antimicrobial therapy 2-4 weeks
Vascular Graft Infections
Extracavitary – Diagnosis

- Open draining wound groin, sinus tract
  - Ultrasound, CT, MRI, PET/CT, Indium scan
  - I&D

Graft involved but not anastomosis
No bleeding from anastomosis

Infection surrounds graft
Anastomosis exposed
No bleeding
BC negative

Samson 3

Anastomosis involved bleeding
Pseudoaneurysm
BC positive

Samson 4

Samson 5
Vascular Graft Infections
Extracavitary – Treatment
Samson 3

• Aggressive I&D, irrigation
• Surgery
  • Preservation; in situ reconstruction
  • Wound coverage, VAC, flap
• Antimicrobial therapy 4-6 weeks
Vascular Graft Infections
Extracavitary – Diagnosis

- Open draining wound groin, sinus tract
  - Ultrasound, CT, MRI, PET/CT, Indium scan
  - I&D

<table>
<thead>
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<th>Graft involved but not anastomosis</th>
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<tr>
<td>No bleeding from anastomosis</td>
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Samson 4
Vascular Graft Infections
Extracavitary – Treatment

Samson 4

• Aggressive I&D, irrigation

• Surgery
  • Preservation; in situ reconstruction
  • Wound coverage, VAC, flap

• Antimicrobial therapy 4-6 weeks
Vascular Graft Infections
Extracavitary – Diagnosis

- Open draining wound groin, sinus tract
  - Ultrasound, CT, MRI, PET/CT, Indium scan
  - I&D

Graft involved but not anastomosis
No bleeding from anastomosis

Infection surrounds graft
Anastomosis exposed
No bleeding
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Samson 3

Anastomosis involved bleeding
Pseudoaneurysm
BC positive

Samson 4

Samson 5
SAMSON 5
Vascular Graft Infections
Extracavitary – Treatment
Samson 5

• Control bleeding

• Pseudomonas, MRSA, poor prognosis

• Surgery
  • Extravascular reconstruction
  • Graft excision
  • Wound coverage, VAC, flap

• Antimicrobial therapy 4-6 weeks, lifelong suppressive selected patients
Vascular Graft Infections
Extracavitary Prognosis

• Samson 1, 2 – excellent

• Samson 3-5
  • Operative mortality – 1-18%; Samson 5 – 15-18%
  • Amputation
    – Samson 3 – 1-2%
    – Samson 4 – 10-15%
    – Samson 5 – 15-18%
  • Recurrence infection – Depends on Samson classification
    – Samson 1, 2 – 1-2%
    – Samson 3-5 – 15-20%

Vascular Graft Infections
Definition

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  - Peripheral 20%

- Intracavitary
  - Intra-abdominal 70%
  - Intrathoracic 30%
Vascular Graft Infections
Intracavitary

- Intra-abdominal
  - Enteric fistulae
- Intrathoracic
Vascular Graft Infections
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Vascular Graft Infections
Intra-abdominal – Diagnosis

• Clinical presentation
  • May present months to years postop
  • Abdominal pain; sepsis
  • Duodenal fistulae – mixed polymicrobial, intermittent, bacteremia
  • GI bleeding – subtle or massive
  • Peripheral ischemia, emboli
Vascular Graft Infections
Intra-abdominal – Diagnosis

Clinical Presentation
Sepsis Syndrome

Monomicrobial bacteremia

Polymicrobial bacteremia; GI bleeding

CT first choice
• PET/CT
• Indium scan

EGD – duodenal fistulae
• MRI/PET/CT
• Indium scan
## Vascular Graft Infections
### Intra-abdominal – Diagnosis

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Intra-abdominal – Diagnosis

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PET-CT
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PET-CT; Indium Scan
Vascular Graft Infections
Intra-abdominal - Management

• Surgery
  • Graft excision; in situ reconstruction
    – Cryopreserved arterial allograft
    – Autogenous venous graft
    – Rifampin or silver coated grafts
  • Extra-anatomic reconstruction; then graft excision
Vascular Graft Infections
Intra-abdominal – Management

• Surgery
  • Aorto-enteric fistulae
    – Excision, in situ reconstruction
  • MRSA, Pseudomonas, multiply drug resistant
    – Extra-anatomic reconstruction; graft excision
Intra-Abdominal In Situ Reconstruction
Vascular Graft Infections
Intra-abdominal – Management

Antimicrobial Therapy
IV/oral 6 weeks; then oral 3-6 months

MRSA, Pseudomonas multi-resistant
Extra-anatomic reconstruction

Extensive perigraft infection
In situ reconstruction

Observe off antimicrobial therapy

Lifelong suppression
Vascular Graft Infections
Intra-abdominal – Prognosis

- **In situ**
  - Perioperative mortality – 13-15%
  - Two; five year survival – 97%; 82%

- **Extra-anatomic**
  - Perioperative mortality 20%
  - Amputation rate 5%
  - Early graft failure 20%
  - 30 month survival, with no amputation 50-60%
Vascular Graft Infections
Intrathoracic – Diagnosis

- Clinical presentation
  - Present like IE or PVE
  - Sepsis
  - Chest pain
  - Rupture with massive bleeding
Vascular Graft Infections
Intrathoracic – Diagnosis

Clinical Presentation

**IE/PVE**
- TEE
  - Nondiagnostic or extensive infection
- CT/MRI, PET/CT

**Aortic Graft**
- CT/MRI
  - Inconclusive
- TEE, PET/CT
- PET/CT/MRI
Vascular Graft Infections
Intrathoracic – Diagnosis

Clinical Presentation

IE/PVE
- TEE
  - Nondiagnostic or extensive infection
- CT/MRI, PET/CT

Aortic Graft
- CT/MRI
  - Inconclusive
- TEE, PET/CT
  - PET/CT/MRI
Vascular Graft Infections
Intrathoracic – Management

• Treat complications of IE, PVE
• In situ arterial allograft preferred
• Less experience with venous autograft
• Avoid rifampin synthetic graft because of risk infection
• Antimicrobial therapy 4-6 weeks; then 3-6 months, lifelong suppression in selected patients
Staphylococcus aureus Bacteremia: A Wolf that May Arrive in Sheep’s Clothing

Daniel J. Sexton MD FACP
Professor, Department of Medicine
Director, Duke Infection Control Outreach Network
Duke University Medical Center
Goals of This Talk

• To discuss relevant old and new literature
• To discuss general principles of management
• To discuss a few ongoing unresolved clinical and scientific questions
• To instill or reconfirm a sense of great respect for this frequently lethal sometimes curable infection
The Big Picture

• SAB is common and becoming more frequent
• SAB is lethal without proper treatment and outcomes are often poor even with proper treatment.
• The management of SAB requires careful bedside evaluation(s), knowledge about its natural history and pitfalls and clinical skill in therapy. (i.e. effective treatment is NOT simply a matter of matching the bug with a drug or treating for one moon cycle)
S. aureus
A Unique Organism

Cellular Composition of S. aureus

- **Cell Wall**
  - Peptidoglycans
  - Teichoic acid
  - Adhesins
  - Potential for “slime layer”

- **Genes**
  - SCC/mecA
  - Enzymes
    - Catalase/Coagulase
    - Beta-lactamases

- **Virulence Factors**
  - $\alpha$, $\beta$, $\gamma$, $\delta$, TSST toxins
  - Leukocidin (PVL)
  - Chemotaxis inhibitory protein

WTA=wall teichoic acid; PVL=Panton-Valentine leukocidin; CHIP=chemotaxis inhibitory protein.
Severe Sepsis—*S. aureus*
Tissue/BSI virulence factors

- Leukocidins/modulins
- Complement inhibitor proteins
- Fibrin clot formation
- Platelet traps
- Fibrinectin BP A/B
  - EC tethering
- Blocks opsonophagocytosis
- S. aureus α-toxin
  - EC barrier disruption

doi:10.1371/journal.ppat.1003871
http://www.plospathogens.org/article/info:doi/10.1371/journal.ppat.1003871
SAB: Epidemiology

• S. aureus is the leading cause of bacteremia in the US and in most community and tertiary care hospitals

• Good rule of thumb: \( \frac{1}{3} \) of all cases of SAB are true community-onset; \( \frac{2}{3} \) are healthcare-associated or hospital-onset
Etiologic Organism of Bacterial Infective Endocarditis
United States (1999-2007)

Cases Per 100,000 Inpatient Discharges

Year (by quarter)

P < 0.001

Federspiel et al Arch Intern Med, In press
Decreasing Rates of Central-Line Associated S. aureus Bacteremia

Deron et al. JAMA. 2009;301(7):727-736
SAB is BAD

- Mortality of S aureus IE in the preantibiotic era = 100%
- Mortality of SAB in the pre-antibiotic era was ~80% [Skinner, D. and Keefer, C. S. Arch.Intern.Med. 68, 851-75. 1941]
- Mortality of SAB in the antibiotic era: 11-43%--recent evidence shows that proper management leads to better outcomes
- *Mortality rate of IE due to S aureus largely unchanged from 1981-2015*
**S. aureus** Bacteremia Is A Bad Disease:
724 Prospectively Identified Patients
at DUMC (Fowler et al, CID 2005)

- Overall 12-week mortality: **24%**
- Metastatic infectious complication: **34%**
- IE: **12.2%**
- Relapse: **10%**
S. Aureus bacteremia cases, Duke Hospital, 2009-2013*

N = 1069**
**unique patients

*DEDUCE query 2/5/13
The Status Quo

• Failure to correctly treat SAB both empirically (before cultures return) and with directed therapy (after cultures return) is a common important problem in the US.

• Our treatment options for SAB in general are suboptimal.

• Many patients with SAB do poorly even with seemingly appropriate treatment. WHY?
The Deadly Toll of Invasive MRSA Infections (Kaye et al 2008)

- 1 in 3 patients with MRSA bacteremia (n=564) died during their initial hospitalization
- 57% were dead within a year of their bacteremia and
- 36% of survivors were re-hospitalized within 90 days of their MRSA bacteremia
- The mean duration of hospitalization for 374 patients with SAB who survived their initial hospitalization was 17.3 days
- Not surprisingly those who initially received effective therapy less often died (OR 3.2 p<0.001). **Note: only 38% of patients with SAB rec’d effective Rx during the 24 hr period after blood cultures were drawn.**
Key Principle

Is SAB complicated or uncomplicated?
Uncomplicated
SAB
Uncomplicated SAB: Definition

- Endocarditis excluded (often by echocardiography)
- Fever gone within 72h
- Follow-up blood cultures negative after 72h
- No prosthetic material (pacer, valve, arthroplasty)
- No evidence of metastatic infection

TREATMENT: at least 2 weeks with an appropriate agent
Use of a Simple Criteria Set for Guiding Echocardiography in Nosocomial S. aureus Bacteremia


**Table 2. Clinical Prediction Criteria Associated With Increased Risk of Infective Endocarditis (IE) in Patients With Nosocomial Staphylococcus aureus Bacteremia.**

<table>
<thead>
<tr>
<th>Clinical prediction criterion</th>
<th>All patients (n=304)</th>
<th>Patients without IE (n=291)</th>
<th>Patients with IE (n=13)</th>
<th>P&lt;sup&gt;a&lt;/sup&gt;</th>
<th>All patients (n=432)</th>
<th>Patients without IE (n=392)</th>
<th>Patients with IE (n=40)</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Prolonged bacteremia (&gt;4 days)</td>
<td>83 (27.3)</td>
<td>83 (28.5)</td>
<td>0</td>
<td></td>
<td>125 (28.9)</td>
<td>124 (31.6)</td>
<td>1 (2.5)</td>
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<tr>
<td>Intracardiac devices (PV, ICD, PCM)</td>
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<td>Hemodialysis dependence</td>
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<tr>
<td>Spinal infection or nonvertebral osteomyelitis</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>No criteria fulfilled</td>
<td>221 (72.7)</td>
<td>208 (71.5)</td>
<td>13 (100)</td>
<td></td>
<td>307 (71.1)</td>
<td>268 (68.4)</td>
<td>39 (97.5)</td>
<td></td>
</tr>
<tr>
<td>≥1 criterion fulfilled</td>
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**NOTE.** Data are shown for 304 patients in the Invasive S. aureus Infection Cohort (INSTINCT) and 432 patients in the S. aureus Bacteremia Group (SABG) with complete follow-up. More than 1 criterion may be present.

<sup>a</sup> Determined using the 2-sided Fisher exact test.

- Prolonged bacteremia >4 days
- Intracardiac devices (PV, ICD, PCM)
- Hemodialysis dependence
- Spinal infection/nonvertebral osteomyelitis
Relative frequency of infective endocarditis by number of positive criteria in patients with nosocomial SAB

TAKE HOME PAY:
Uncomplicated SAB

• If you think someone has it and if you treat someone for it, be sure you are right.
Complicated MRSA Bacteremia
Complicated SAB is Common

Frequency in 724 consecutive Duke patients with SAB

43%

Complicated SAB is Complicated

Patients (%)*

- Infective endocarditis: 12%
- Septic arthritis: 7.4%
- Deep-tissue abscess: 5.7%
- Vertebral osteomyelitis: 3%
- Epidural abscess: 2.4%
- Septic thrombophlebitis: 2.2%
- Psoas abscess: 1.7%
- Meningitis: 2.4%
- Other complications: 2.4%

Identifying Complicated *S. aureus* Infection
Identifying Complicated SAB:
Physical Exam Matters

- Helpful when Present
- Not Always Present
Factors Associated With Complications in Patients with SAB

- Fever > 72 hours *Clin Infect Dis* 1992
- Positive follow-up blood cultures *Clin Infect Dis* 1992
- Pain
- Abnormal Echocardiogram (especially TEE) *Arch Intern Med* 87, *J Am Coll Cardiol* 97
- Presence of prosthetic device
Independent Predictors of Complicated SAB

- Positive follow-up blood culture OR 5.6
- Community-onset OR 3.1
- Persistent fever @ 72 hrs OR 2.2
- Skin lesions OR 2.0
Risk factors for complications* in SAB

- **Community acquisition:**
  - Risk of complications 43% in CASAB vs 21% in noso SAB (CID 1993:16:567) [retrospective study n=281]

- **Absence of an identifiable focus**
  - Risk of complications was 51% without an identifiable focus vs 24% with a known focus (CID above)

*complications=metastatic infection, IE, relapse, or death
Identifying Complicated SAB

**Scoring Systems Matter**

1 point  Community-acquired
Skin examination suggesting acute systemic infection
Persistent fever at 72 hours

2 points  Positive follow-up blood cultures at 48-96 hours

SAB + Arthroplasty = 28% Joint Infection

SAB + Prosthetic Valve = 51% Valve Infection

SAB + Pacemaker/ICD = 45% Device Infection
Chamis *Circulation* 2001; 104: 1029

SAB + Central Catheter = 71% Thrombophlebitis
Crowley *Crit Care Med* 2008;36:385-90
Lessons Learned: Clinical Identifiers of Complicated SAB

- Things to bank on:
  *All SAB is Complicated SAB until Proven otherwise*

- Things to always do:
  - Get Follow-up Blood cultures
  - Get an Echo

- Things to look for:
  - Persistent Bacteremia
  - Persistent Fever
  - Community acquisition
  - Clinical Evidence of complications
  - Post-operative State

- Things to Fear:
  - Pain
  - Prostheses
Expertise Matters

**ID Consultants Improve Outcome of S. aureus Bacteremia**

Fowler *Clin Infect Dis* 1998; 27(3):478-86. Prospective cohort of 244 patients. Compliance with IDC associated with less recurrent SAB (P<0.01).

Jenkins *Clin Infect Dis.* 2008;46:1000-8. Institutional IDC for SAB- 234 patients 4 standards of care more frequent with routine IDC (p<0.001).

Lahey *Medicine* 2009; 88: 263-7. Retrospective cohort of 241 patients with SAB. IDC associated with lower mortality (hazard 0.46; p = 0.03).

Reig *J Infection* 2009; 59: 232-9. Retrospective cohort of 521 German SAB patients. IDC associated with lower mortality (OR 0.6, CI 0.4-1.0).

Honda *Am J Med* 2010; 123: 631-7. Prospective cohort of 341 patients with SAB. IDC associated with lower mortality (adj hazard: 0.44; 95% CI, 0.22-0.89).
What about telephone consultation?

- Forsblom *Clin Infect Dis* 2013; 56:527-35. in 342 Finnish patients with MSSA bacteremia (all MRSA patients excluded…. N=5).
  - 72% formal IDC, 18% phone, 10% no consultation
  - Deep focus of infection identified in 78% formal, 53% phone, 29% no consult cases
  - In regression analysis, factors independently associated with death were pneumonia, steroid use, ICU care, no ID consult, and phone consultation (OR 2.31, 95% CI 1.22-4.38)

- From the accompanying editorial:

  “Most ID clinicians lack sufficient time or motivation to provide comprehensive advice when they receive an unsolicited call from another physician who intends to manage a problem as complex as SAB without a formal bedside consultation. Such calls are not rare even in tertiary care centers.”
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

SAB Therapy: General Comments

• Antibiotics are like golf clubs: good clubs won’t keep a bad player from shooting a bad score
• Rx usually starts as empiric treatment; later it becomes directed treatment.
• Even appropriate Rx may fail. However, treatment failure and complications are much more likely with inappropriate Rx
• Little details (about Rx) can have big consequences (e.g. validity of allergy history, MIC, dose)
Delayed Antibiotic Treatment of Hospital-Acquired SAB (CID 2003)

• 167 Patients with SAB studied in a Detroit hospital
• Delayed Rx was defined as >45 hours from the time the first BC was obtained and the institution of effective Rx
• Infection-related death occurred in 16/48 (33%) patients with delayed Rx vs 23/119 (19%) with “early Rx” \( p=0.05 \)
• Mean LOS after SAB was 17.6 days in delayed Rx group vs 14.9 days in early Rx group (NS)
• Note: 42 of 46 patients with delayed Rx had MRSA
The Deadly Toll of Invasive MRSA Infections (Kaye et al 2008)

• 1 in 3 of 564 patients with MRSA bacteremia died during their initial hospitalization
• 57% were dead within a year of their bacteremia and
• 36% of survivors were re-hospitalized within 90 days of their MRSA bacteremia
Impact of Methicillin Resistance on Outcome of *S. aureus* Bacteremia:

**WORSE OUTCOME**

- Romero-Vivas *Clin Infect Dis* 1995
- Conterno *Infect Control Hosp Epidemiol* 1998
- Gonzalez *Clin Infect Dis* 1999

**NO CHANGE IN OUTCOME**

- Mylotte *Infect Control Hosp Epidemiol* 1996
- Soraino *Clin Infect Dis* 2000
SAB: Treatment Options

- Semi-synthetic penicillins (Nafcillin, Oxacillin)
- Penicillin-Penicillinase Inhibitors (Augmentin, Unasyn, Zosyn,)
- Cephalosporins
- Vancomycin
- Daptomycin
- Linezolid
- TM/SXT
- Tetracycline (minocycline, tigecycline)
Decreasing Susceptibilities to Vancomycin over Time


\[ \chi^2_{\text{trend}} = 15.46; \text{ df } = 1; P < .001 \]
Relationship Between Vancomycin MIC and Outcome of MRSA Bacteremia (AAC 2008)

- Retrospective study of 92 hospitalized adult patients with hospital-onset MRSA bacteremia
- 66/92 patients had MIC of 1.5 or greater; 26 had MRSA strains with MICs of 1 or less
- 30-day mortality: 18.2% v 11.5%
- Microbiologic failure: 9% v 0
- Recurrence within 60 days: 17% v 4%
- Mean hospital LOS: 21 days v 11.5 days
What does an elevated MIC to Vancomycin really mean?

• It is true that patients with high MICs to vancomycin do worse on vancomycin than those with low MICs

• However, patients with MSSAB who have a high vancomycin MIC who are treated with B-lactams also do worse than patients with a low vancomycin MIC who are treated with B-lactams
Managing SAB: Critical Steps

1. First give empirical therapy *pronto*
2. Determine extent of the Staphylococcal infection
3. Be sure to order an appropriate drug and route of administration
4. Assess response to treatment
5. Give therapy for an appropriate length of time (while continuing to assess response)
• Perform a careful clinical assessment when SAB is detected:
  – Do a careful clinical exam:
    • Cardiac assessment for murmurs
    • Look for signs of metastatic infection/emboli
    • Carefully evaluate any pain(s)
    • Percuss the spine
    • Examine/assess any IV lines
    • Assess vital signs
    • Determine if prosthetic material is in the patient
    • Prior history of S aureus infection?
SAB: A Suggested Approach-2

• Reassess antimicrobial Rx (drug, dose, route) when sensitivity results return
• If an IV catheter is present assess whether it can or should be removed
• Arrange for follow-up blood cultures
• At 72-96 hrs decide upon the duration of Rx:
  – Assess clinical response (repeat exam)
  – Assess need for an echocardiogram
• At the end of treatment: decide if post treatment follow-up is needed
Key Historical Points

• Setting in which bacteremia was acquired
• Previous endocarditis
• Recent IV procedures, line placement
  – Dialysis (huge risk)
• Heart structure/valve abnormalities
• Presence of hardware
  – Intravascular
  – Other (>25% of pts with prosthetic joints and SAB have PJI)
  – Removeable, removed

Key Physical Exam Findings

• Skin
• Eyes
  – Fundi
  – Conjunctivae
• Heart
• Other – *S. aureus* can infect any tissue
  – Lungs
  – Bones/Muscles/Joints
  – Kidneys
  – Liver/Spleen
  – Other
Key Laboratory Tests

• Remember the primary objective:
  – Differentiate uncomplicated from complicated *S. aureus* bacteremia

• Urinalysis in patients without a Foley catheter

• Follow-up Blood Culture
Other Imaging

• Xrays
  – Chest
  – Bone

• CT
  – Very useful for abscess/osteo/other
  – Many more emboli than clinically apparent
    • Usefulness of these data unclear

• Imaging
  – MRI
  – 3D echo
Identifying *S. aureus* IE: TTE

* *Curr ID Reports ’99*

- Sensitivity: 57%*
- Specificity: 97%*

*447 patients in 11 studies*
Echocardiograms

• TTE vs TEE
  – Important (often ignored) factors
    • Physical impediments to clear images
    • Technical expertise of physician

• Rosen: TEE cost effective

Rosen A et al  Ann Int Med 130: 810, 1999
“Within the limitations of existing empirical data, these data suggest that for patients with clinically uncomplicated catheter-associated S. aureus bacteremia, the use of TEE to determine therapy duration is a cost-effective alternative to 2 or 4 week empirical therapy.”
Length of Treatment

2 weeks in well-defined patients with ALL of the following

– Catheter-associated bacteremia / catheter removed
– Follow-up BC negative
– Patient is afebrile within 72 hours of starting Rx
– TEE normal (not negative)
– No prosthetic material in joints or intravascular space
– No evidence of thrombophlebitis
– No symptoms suggestive of metastatic infection
## Progressive Algorithm

<table>
<thead>
<tr>
<th>Description</th>
<th>n</th>
<th>Cure n (%)</th>
<th>Recurrence n (%)</th>
<th>Attributable mortality n (%)</th>
<th>Non-S. aureus related mortality n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) ANY SAB</td>
<td>1282</td>
<td>804 (63)</td>
<td>131 (10)</td>
<td>135 (11)</td>
<td>150 (12)</td>
</tr>
<tr>
<td>b) a + non community-acquired</td>
<td>598</td>
<td>348 (58)</td>
<td>50 (8)</td>
<td>79 (13)</td>
<td>95 (16)</td>
</tr>
<tr>
<td>c) b + no prosthetic device</td>
<td>357</td>
<td>223 (62)</td>
<td>26 (7)</td>
<td>47 (13)</td>
<td>51 (14)</td>
</tr>
<tr>
<td>d) c + catheter-associated</td>
<td>167</td>
<td>132 (79)</td>
<td>8 (5)</td>
<td>9 (5)</td>
<td>17 (10)</td>
</tr>
<tr>
<td>e) d + ≤ 14 d parenteral Ab Rx</td>
<td>105</td>
<td>80 (76)</td>
<td>4 (4)</td>
<td>8 (8)</td>
<td>13 (12)</td>
</tr>
<tr>
<td>f) e + defervesce within 72h</td>
<td>72</td>
<td>55 (76)</td>
<td>3 (4)</td>
<td>4 (6)</td>
<td>10 (14)</td>
</tr>
<tr>
<td>g) f + neg f/u blood cx at d 2-4</td>
<td>50</td>
<td>43 (86)</td>
<td>2 (4)</td>
<td>0 (0)</td>
<td>5 (10)</td>
</tr>
<tr>
<td>h) g + any echo</td>
<td>36</td>
<td>31 (86)</td>
<td>2 (6) (1 reinfection)</td>
<td>0 (0)</td>
<td>3 (8)</td>
</tr>
<tr>
<td>i) h + TEE</td>
<td>26</td>
<td>23 (88)</td>
<td>1 (4) (1 reinfection)</td>
<td>0 (0)</td>
<td>2 (8)</td>
</tr>
</tbody>
</table>
Vancomycin v Nafcillin for MSSA

• Vancomycin is inferior:
  – Less rapidly bactericidal in vitro
  – Longer duration of bacteremia after Rx is started
  – More complications in patients with MSSA IE
  – Short duration Rx of MSSA right-sided IE fails with vancomycin but is successful with nafcillin
### What antibiotic should be used?

#### Outcomes of dialysis pts with MSSA bacteremia:

<table>
<thead>
<tr>
<th></th>
<th>Vancomycin</th>
<th>Cefazolin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure</td>
<td>24%</td>
<td>6%</td>
</tr>
<tr>
<td>Death</td>
<td>8%</td>
<td>2%</td>
</tr>
<tr>
<td>Recurrence</td>
<td>16%</td>
<td>4%</td>
</tr>
</tbody>
</table>

Stryjewski et al. CID 2007
A Few Words about Daptomycin

- Studies have shown it to be equivalent to Vancomycin and Nafcillin (not better)
- Prior Rx with Vancomycin may lead to higher MICs to Daptomycin
- Resistance to Daptomycin may occur in selected patients
- Not effective in S aureus pneumonia
- Controversy exists about the optimal dose
- Toxicity can be severe (muscle, lung)
A Few Words About Linezolid

• Studies have shown it is “not inferior” to Vancomycin
• A recent open-labeled randomized trial of Linezolid v Vancomycin or Nafcillin in patients with catheter-associated SAB was discontinued prematurely
• Prolonged therapy with Linezolid can lead to hematologic and neurologic toxicity
Avoidable Mistakes in Patients with SAB

- Leaving “removable foci” of infection in place during treatment (e.g. PCs, CVCs, pacemakers)
- Giving therapy for too short a time period
- Assuming that long-term Rx will cure all metastatic infections and any prosthetic-related Staphylococcal infection
- Wrong route of Rx
- Assuming clinical response can be a surrogate for microbiologic response or assuming a good clinical response means short-term Rx is fine
- Not assuring follow-up after Rx has been completed
- Failure to diagnose concurrent or subsequent IE and its secondary complications
SAB: Odds and Ends

- Disseminated staphylococcal infections may occur in the absence of IE
- Disciitis commonly manifests after SAB is detected; ditto for other metastatic infections
- Prolonged SAB may occur in patients who look and feel surprisingly good
- Not knowing that a complication of SAB has occurred can lead to preventable further complications (e.g. paralysis, embolism)

- *Doing right is more important than being right*
SAB: Odds and Ends-2

• Late relapses may be due to the presence of biofilms (on devices) and/or the formation of small colony variants

• Strains of S aureus associated with invasive disease and/or relapse appear to have important genetic differences from strains associated with uncomplicated bacteremia

• Healthy previously well patients who develop SAB can end up dead or badly damaged
Clinical Pearls

• Pay close attention to any complaints of pain (pain is the diagnostician’s friend)

• Remember Hickum’s Dictum, but be highly suspicious that a poor response to Rx means there is a complication due to Staphylococcus

• Metastatic infections sometimes first manifest late in the course of illness or after even a long-course of Rx has been completed
Clinical Pearls

- Always inform patients about the possibility of relapse at the completion of treatment. Ask them to stay alert and seek care if ANYTHING goes wrong in the following 90 days—longer if a pacemaker is present.

- If recurrent bacteremia occurs in the next 90-180 days immediately suspect a RELAPSE rather than a reinfection
SAB: Speculations about the Future

• Vancomycin will become less useful and less commonly used

• Daptomycin and Linezolid resistance will become bigger problems

• We will eventually understand why some patients with SAB have complications and others don’t. The answer will be more in the bug than the host

• Better diagnostic methods will be developed
Take Home Pay

• Respect and understand the enemy (SAB)
• Look for complications early AND during Rx--
  Do serial assessments while on Rx (and during
  followup after Rx)
• Be sure you have the right drug, the right
dose, right route and right duration of Rx
• Educate your patient about the possibility of
early or late relapse Make no warranties
Infective Endocarditis in Adults
Diagnosis, Management, and Prevention
Financial Disclosures

• UpToDate, Inc.
  • Authorship

• Massachusetts Medical Society
  • Editor-in-Chief (NEJM Journal Watch Infectious Diseases)

• Email address: baddour.larry@mayo.edu
2015 AHA Statement

• Update for 2005 Statement
  • Start up call date – 8/16/2012
  • Reviewed by AHA (SACC) and IDSA (endorsement)
  • Embargoed currently

• Other AHA-related Statements
  • “IE Prophylaxis” – 2007
  • “CIED Infections” – 2010
  • “IE in Pediatrics” - 2015
Infective Endocarditis

2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease

Nishimura RA, et al. JACC 2014;63:e57-185
<table>
<thead>
<tr>
<th>Size of Treatment Effect</th>
<th>Class I</th>
<th>Class IIA</th>
<th>Class IIB</th>
<th>Class III No Benefit or Class III Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefit &gt;&gt;&gt; Risk Procedure/Treatment <strong>SHOULD</strong> be performed/ administered</td>
<td>Benefit &gt;&gt; Risk Additional studies with focused objectives needed <strong>IT IS REASONABLE</strong> to perform procedure/ administer treatment</td>
<td>Benefit &gt; Risk Additional studies with broad objectives needed; additional registry data would be helpful Procedure/Treatment <strong>MAY BE CONSIDERED</strong></td>
<td></td>
<td>Procedure/ test</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>COR III:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No benefit</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Not Helpful</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No proven Benefit</td>
</tr>
<tr>
<td><strong>LEVEL A</strong></td>
<td>Multiple populations evaluated*</td>
<td>• Recommendation that procedure or treatment is useful/effective</td>
<td>• Recommendation’s usefulness/efficacy less well established</td>
<td>• Recommendation’s usefulness/efficacy less well established</td>
</tr>
<tr>
<td></td>
<td>Data derived from multiple randomized clinical trials or meta-analyses</td>
<td>• Sufficient evidence from multiple randomized trials or meta-analyses</td>
<td>• Greater conflicting evidence from multiple randomized trials or meta-analyses</td>
<td>• Greater conflicting evidence from multiple randomized trials or meta-analyses</td>
</tr>
<tr>
<td><strong>LEVEL B</strong></td>
<td>Limited populations evaluated*</td>
<td>• Recommendation that procedure or treatment is useful/effective</td>
<td>• Recommendation’s usefulness/efficacy less well established</td>
<td>• Recommendation’s usefulness/efficacy less well established</td>
</tr>
<tr>
<td></td>
<td>Data derived from a single randomized trial or nonrandomized studies</td>
<td>• Evidence from single randomized trial or nonrandomized studies</td>
<td>• Greater conflicting evidence from single randomized trial or nonrandomized studies</td>
<td>• Greater conflicting evidence from single randomized trial or nonrandomized studies</td>
</tr>
<tr>
<td><strong>LEVEL C</strong></td>
<td>Vey limited populations evaluated*</td>
<td>• Recommendation that procedure or treatment is useful/effective</td>
<td>• Recommendation’s usefulness/efficacy less well established</td>
<td>• Recommendation’s usefulness/efficacy less well established</td>
</tr>
<tr>
<td></td>
<td>Only consensus opinion of experts, case studies, or standard of care</td>
<td>• Only expert opinion, case studies, or standard of care</td>
<td>• Only diverging expert opinion, case studies, or standard of care</td>
<td>• Only diverging expert opinion, case studies, or standard of care</td>
</tr>
<tr>
<td><strong>COR III: No Benefit</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suggested phrases for writing recommendations</td>
<td>should be recommended</td>
<td>is reasonable</td>
<td>may/might be considered</td>
<td>COR III:</td>
</tr>
<tr>
<td></td>
<td>is indicated</td>
<td>can be useful/ effective/beneficial</td>
<td>may/might be reasonable</td>
<td>No Benefit</td>
</tr>
<tr>
<td></td>
<td>is useful/effective/beneficial</td>
<td>is probably recommended or indicated</td>
<td>usefulness/ efficacy is unknown/unclear or not well established</td>
<td>potentially harmful</td>
</tr>
<tr>
<td></td>
<td>Comparator effectiveness phrases†</td>
<td>treatment/strategy A is recommended/indicated in preference to treatment B</td>
<td>treatment/strategy A is probably recommended/indicated in preference to treatment B</td>
<td>it is reasonable to choose treatment A over treatment B</td>
</tr>
<tr>
<td></td>
<td>treatment A should be chosen over treatment B</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful effective.

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIA; level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.
IDSA Guidelines

~ 55% are consensus-based

• Khan AR, et al. CID 2010;51:1147-56
• Deresinski S. CID 2010;51:1157-59
• Lee DH, Vielemeyer O. Arch Intern Med 2011;171:18-22
• Deresinski S, File TM. Arch Intern Med 2011;171:1402-3
Infective Endocarditis

Prospective, randomized trials since 2005

  - ~22% of cases were IE (predominately right-sided)
- Cosgrove SE, et al. Initial Low-Dose Gentamicin for Staphylococcus aureus Bacteremia and Endocarditis is Nephrotoxic. CID 2009;48:718-21
Infective Endocarditis
Team Management

- Protocol development
  - Standardized care
    - Labs
    - Medical
    - Surgical
    - Other
- Multispecialty involvement in each case
- “Tumor Board” approach

Infective Endocarditis
Diagnosis

• Duke criteria – 1994
  • Initially drafted for use in trials and epidemiological studies
    • Used in individual patient management
• Modified – 2002
  • Li JW, et al. CID 2000;30:633-638
Infective Endocarditis

Diagnosis

- Modified Duke criteria
  - Molecular screening – criterion??
- TTE and TEE are complementary
  - TTE more readily available in some centers (as compared to TEE)
  - Right-sided lesions, prosthetic aortic valve
- Quantifying:
  - Hemodynamic dysfunction manifested by valvular dysfunction
  - Ventricular dysfunction
  - L and R elevated filling pressures and PA pressure
Infective Endocarditis
Microbiology

• “The Big Three”
  • All 3 groups are gram-positive cocci
    • Viridans group streptococci
    • *Staphylococcus* species
    • *Enterococcus* species

• Other pathogens
  • Broad range of bacteria and fungi
Infective Endocarditis
Enterococcal

Combination therapy

• Amp/PCN plus gentamicin
• Amp plus ceftriaxone (high dose)
  • 6 weeks in 2 non-randomized trials
• Amp/PCN plus gentamicin
  • 2 weeks of gentamicin
  • Swedish/Danish studies
    • Olaison L, and Schadewitz K, et al. CID 2002;34:159-66
    • Danish Cardiology guidelines - 2007
Infective Endocarditis
VRE

- Few cases
- No defined optimal regimen
Infective Endocarditis
Streptococcal

VGS common pathogen

• Ceftriaxone vs. PCN
  • High cure rates
  • Broad vs. narrower spectrum
  • Convenience
  • Cost
  • Adverse events

• PCN resistance
Infective Endocarditis

VGS IE

• 1999 – 2013 (Olmsted County, MN)
  • 96.3% (26/27 isolates) were sensitive (MIC ≤0.12 µg/mL) to penicillin

• DeSimone D, et al. Unpublished data
Infective Endocarditis
Staphylococcal

Native valve

- Gentamicin x 3-5 days
  - Avoid
  - Cosgrove SE, et al. Initial Low-Dose Gentamicin for *Staphylococcus aureus* Bacteremia and Endocarditis is Nephrotoxic. CID 2009;48:718-21

- Aqueous crystalline penicillin G
  - Avoid
  - Clinical labs are not able to confirm penicillin susceptibility
Infective Endocarditis
Culture-Negative Endocarditis

• “Empirism begets empirism”
  - Common - recent antimicrobial use

• Conundrum – “optimal” treatment
  - Focus on epidemiology

• Operative tissue, if available
  - “Send out” for 16S rRNA gene sequencing
Infective Endocarditis
Early Surgery

W/in 48 hours s/p randomization

• Inclusions
  • Native, left-sided, >10 mm veg, severe valve disease

• Exclusions
  • Prosthetic, mod-severe HF, heart block, annular or aortic abscess, destructive lesions requiring urgent surgery, fungal, >80 y/o, coexisting major embolic stroke with hemorrhagic risk, serious co-existing disease

Infective Endocarditis
Early Surgery

Limitations

• N = 76
• Mean age ~47 years
• ~60% streptococcal
• ~11% S. aureus
• ~22% CNE

# Clinical End Points

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Conventional treatment (n=39)</th>
<th>Early surgery (n=37)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary end point – no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-hospital death or embolic event at 6 weeks</td>
<td>9 (23)</td>
<td>1 (3)</td>
<td>0.01</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td>1.00</td>
</tr>
<tr>
<td>Embolic event at 6 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>8 (21)</td>
<td>0</td>
<td>0.005</td>
</tr>
<tr>
<td>Cerebral</td>
<td>5 (13)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Coronary</td>
<td>1 (3)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Popliteal</td>
<td>1 (3)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Splenic</td>
<td>1 (3)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Secondary end points at 6 months – no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>11 (28)</td>
<td>1 (3)</td>
<td>0.003</td>
</tr>
<tr>
<td>Death</td>
<td>2 (5)</td>
<td>1 (3)</td>
<td>1.00</td>
</tr>
<tr>
<td>Embolic event</td>
<td>8 (21)</td>
<td>0</td>
<td>0.005</td>
</tr>
<tr>
<td>Recurrence of infective endocarditis</td>
<td>1 (3)</td>
<td>0</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Infective Endocarditis
Early Surgery – PVE – S. aureus

• Within the first 60 days of hospitalization
• Left-sided, no IDU
• N=168 patients (ICE- Prospective Cohort Study)
  • 74 (44.3%) underwent surgery
  • 1-year mortality unchanged – risk ratio, 0.67 [95% CI, .39-1.15; P=.15]

“The decision to pursue EVS should be individualized for each patient……”

Chirouze C, et al. CID 2015;60:741-9
Infective Endocarditis
Surgery

Prospective cohort – ICE-PLUS

• 1,296 patients with left-sided IE (25% PVE)
• 9/1/08 – 12/31/12
• 52% - hospital transfers
• 57% underwent surgery w/in 7 days (median)
• 24% w/o surgery – though with an indication
  • Nonsurgical cohort
    • Mod/severe liver disease
    • Stroke before surgical decision
    • S. aureus

Erbel R. Circulation 2015;131:121-3
Infective Endocarditis
Management

• Short-term follow-up
  • Drug adverse events
  • PICC removal
  • Monitor for IE relapse
    • Importance of fever
    • BCs for fever and not as “routine”
    • New baseline echocardiography

• Long-term follow-up
  • Ongoing dental care
  • BCs for fever, systemic manifestations
Infective Endocarditis
Transcatheter Valve Replacement

• “Valvulation”
• Aortic
• Pulmonic
• IE
  • Early (< 1 year)
  • TAVR – Enterococci
  • Surgical management – TPVR>>TAVR
  • Mortality – TAVR>>TPVR
IE Prophylaxis
Advocated for > 50 Years

• No prospective trial data
• Cochrane Database review (2005)
  • “… no evidence that antibiotic prophylaxis
    is either effective or ineffective….”.
• # of editorials > # of EBD trials
• “Emotive”, “litigious”, “controversial”
## IE Prophylaxis – AHA Guidelines

<table>
<thead>
<tr>
<th>Year</th>
<th>Regimens (dental)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1955, 1957, 1960</td>
<td>Antibiotics for five days</td>
</tr>
<tr>
<td>1965, 1972</td>
<td>Antibiotics for three days</td>
</tr>
<tr>
<td>1977</td>
<td>Three doses antibiotics</td>
</tr>
<tr>
<td>1984</td>
<td>Two doses antibiotics</td>
</tr>
<tr>
<td>1990</td>
<td>Two doses antibiotics</td>
</tr>
<tr>
<td>1997</td>
<td>One dose</td>
</tr>
</tbody>
</table>
AHA Guideline
Prevention of Infective Endocarditis: Guidelines From the American Heart Association

A Guideline From the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group
AHA Guidelines 2007

Impact

Favorable
• ~90% reduction in antibiotic prophylaxis use
• Simplify guidelines

Unfavorable
• Endocarditis epidemic
AHA Guidelines – 1997
Moderate-Risk Category

- Most other congenital cardiac malformations (other than above and below)
- Acquired valvar dysfunction (eg, rheumatic heart disease)
- Hypertrophic cardiomyopathy
- Mitral valve prolapse with valvar regurgitation and/or thickened leaflets

AHA Guidelines 2007
Prevention

- Focus on oral health
- Limitations of antibiotic administration for prophylaxis
  - $$
  - Adverse drug events
  - Selection for resistance
  - “Ripple Effect”
IE Prophylaxis
Oral Health Importance

Oral hygiene and gingival bleeding

- Mean plaque and calculus scores
- Conclusion:
  - “Bacteremia after toothbrushing is associated with poor oral hygiene and gingival bleeding.”

Lockhart PB, et al. JADA 2009;140:1238-44
IE Prophylaxis
“Ripple Effect”

Prosthetic total joint replacement

• ADA/AAOS (1997; updated 2003) “Advisory Statement”
  • With an accompanying legal perspective
• AAOS 2009 “Information Statement”
• ADA/AAOS 2013 “Clinical Practice Guideline”
IE Prophylaxis
“Ripple Effect”

- Electrophysiologic devices
- Breast implants
- Vascular (prosthetic) grafts
- Tunneled catheters
- CSF shunts
- Penile implants
IE Prophylaxis
Microbiologic Issues

Not addressed in 2007 AHA document

- Impact on development of resistance
  - PCN
  - Macrolides
  - Clindamycin
IE Prophylaxis
Antibiotic Costs – Dental Prophylaxis

• Estimates for 15 medical conditions and devices

• Annual, United States
  • ~20,000,000 people
  • Estimated cost – between $19,880,279 and $143,685,823

IE Prophylaxis – Dental Procedures

- Prosthetic cardiac valve
- Previous infective endocarditis

IE Prophylaxis – Dental Procedures
Congenital Heart Disease (CHD)*

- Unrepaired cyanotic congenital heart disease, including those with palliative shunts and conduits
- Completely repaired CHD with prosthetic material or device either by surgery or catheter intervention during the first six 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
Dental Procedures

All dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa*

*The following procedures and events do not need routine prophylaxis: routine anesthetic injections through noninfected tissue, taking dental radiographs, placement of removable prosthodontic or orthodontic appliances, adjustment of orthodontic appliances, placement of orthodontic brackets, shedding of deciduous teeth and bleeding from trauma to the lips or oral mucosa.
### IE Prophylaxis Regimens

<table>
<thead>
<tr>
<th>Situation</th>
<th>Agent</th>
<th>Regimen – Single dose 30-60 min before procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Adult</td>
</tr>
<tr>
<td>Oral</td>
<td><strong>Amoxicillin</strong></td>
<td>2 gm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unable to take oral medication</td>
<td>Ampicillin OR Cefazolin or ceftriaxone</td>
<td>2 g IM or IV*</td>
</tr>
<tr>
<td><strong>or other first or second generation oral cephalosporin in equivalent adult or pediatric dosage.</strong></td>
<td>1 g IM or IV</td>
<td>50 mg/kg IM or IV</td>
</tr>
<tr>
<td>†Cephalosporins should not be used in an individual with a history or anaphylaxis, angioedema, or urticaria with penicillins or ampicillin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## IE Prophylaxis Regimens

<table>
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<th>Situation</th>
<th>Agent</th>
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<tbody>
<tr>
<td>Allergic to penicillins or ampicillin (Oral)</td>
<td>Cephalexin**† OR Clindamycin OR Azithromycin or Clarithromycin</td>
<td><strong>Adult</strong>&lt;br&gt;2 g&lt;br&gt;600 mg&lt;br&gt;500 mg&lt;br&gt;<strong>Children</strong>&lt;br&gt;50 mg/kg&lt;br&gt;20 mg/kg&lt;br&gt;15 mg/kg</td>
</tr>
<tr>
<td>Allergic to penicillins or ampicillin (unable to take oral meds)</td>
<td>Cefazolin/Ceftriaxone† OR Clindamycin</td>
<td><strong>Adult</strong>&lt;br&gt;1 g IM or IV&lt;br&gt;600 mg IM or IV&lt;br&gt;<strong>Children</strong>&lt;br&gt;50 mg/kg IM or IV&lt;br&gt;20 mg/kg IM or IV</td>
</tr>
</tbody>
</table>
GI or GU Tract Procedures

The administration of prophylactic antibiotics solely to prevent endocarditis is **not** recommended for patients who undergo GU or GI tract procedures.
IE Prophylaxis
AHA Guidelines

Future Considerations

“Studies are necessary to monitor the effects, if any, of these recommended changes in IE prophylaxis.”

Infective Endocarditis

“Before and After Studies”
Infective Endocarditis
Infective Endocarditis
Three Countries
IE Prophylaxis

• “NICE” impact
  • March 2008 guidelines (dental)
    • NO ANTIBIOTIC FOR ANY PATIENT
    • “Before and after study” – England

• January 2000 – April 2010
  • 78.6% reduction in prescribing of prophylaxis
  • No increase in IE cases (oral strep)

Thornhill MH et al. BMJ 2011;342:d2392
IE Prophylaxis

• “NICE” impact
  • March 2008 guidelines (dental procedures)
    • NO ANTIBIOTIC FOR ANY PATIENT
    • “Before and after study” – England

• Updated analysis
  • Jan 1, 2004 – March 31, 2013

Figure 1

(a) Number of Prescriptions of Amoxicillin 3g or Clindamycin 600mg

- Amoxicillin
- Clindamycin

(b) Number of Prescriptions of Amoxicillin 3g or Clindamycin 600mg

- Dentists
- GPs
- Hospitals
- Nurses
Figure 2

Incidence of Infective Endocarditis

Cases (Superspells) and Deaths, 10 Million / Month

IE Incidence: Change in level = -0.45, CI -2.54-1.63, p=0.670; change in slope = 0.11, CI 0.05-0.16, p=0.0001
IE mortality: Change in level = -0.09, CI -0.52-0.37, p=0.689; change in slope = 0.01, CI -0.01-0.02, p=0.394
IE Prophylaxis

• Adverse events
  • England
    • Amoxicillin – 3 gm oral dose
      • 0 fatal reactions/1,000,000 scripts
      • 22.62 non-fatal/1,000,000 scripts
    • Clindamycin – 600 mg oral dose
      • 13 fatal reactions/1,000,000 scripts
      • 149 non-fatal reactions/1,000,000 scripts

IE Prophylaxis

- 2002 French prophylaxis guidelines
  - Restricted use
- Population-based surveys
    - (24% of population, ≥20 years of age)
    - Overall IE incidence – stable
    - Oral streptococcal IE incidence – stable
    - Increase in staphylococcal IE
      - In those w/o known native valvulopathy

IE Prophylaxis
2007 AHA Guidelines

• Population-based (Olmsted County, MN) survey
  • Before and after 2007
    • 1999 through 2010, ≥18 years of age
• Nationwide Inpatient Sample database
  • 1999 through 2009
  • ~20% of stratified sample – US community hospitals
• ICD-9-CM codes

DeSimone DC, et al. Circulation 2012;126:60-64
NIS Database – VGS IE

Total number of discharges

Years

IE Prophylaxis
Olmsted County, MN

Update

• 2011-2013
• No VGS incidence increase
• Limitation
  • ~150,000 population
  • Small # of IE cases/year

DeSimone D, et al. Unpublished data
IE Prophylaxis
2007 AHA Guidelines

Pediatric Health Information Systems Database

• 37 centers, 2003-2010
• 1157 IE cases
• 68% had CHD

• Results
  • Oral streptococci – trend (P=0.05) toward decreased hospital admissions over time

IE Prophylaxis
2007 AHA Guidelines

- Medicare database (1999-2010)
- Principal or secondary dx of IE
- Hospitalizations
  - Per 100,000 person-years
- 30-day and 1-year mortality rates

IE Prophylaxis – Medicare database (JACC 2013)

Hospitalizations (per 100,000 person-years)

New AHA guidelines (2007 September)
IE Prophylaxis
Clinician Survey

“NICE guideline 64”

• 99% of respondents aware of guideline
• 36% of dentists have provided prophylaxis
• 1/3 of dentists have cases in whom prophylaxis was prescribed by other clinicians

IE Prophylaxis
AVERT

Silzone™ coating – mechanical valve

• 4400 patients in 17 centers
• July 1998 – recruitment
• January 21, 2000 – stopped
  • Perivalvular leak
    • Inhibited normal fibroblast response
  • Rates of IE in both groups – same

Infective Endocarditis

Conclusions

Many areas of controversy

• MRI brain – For all?
• Optimal timing of surgery?
• Daptomycin vs. vancomycin – MRSA/MRSE left-sided IE?
• Wholesale adoption of double beta-lactam therapy for enterococcal IE?
• Role of newer agents
  • Oritavancin, dalbavancin?
• Benefit of dental prophylaxis?
• Clinical trials are needed