OVERVIEW

- Current Significance
- Management Updates
  - Antibiotic Prophylaxis
  - Diagnostics
  - Antibiotic Treatment
  - Indications for Surgery
  - Timing of Surgery
- Endocarditis after TAVR
- Surgical Techniques
Significance

- Infective endocarditis (IE) affects 3-10 individuals/100,000 per year
- Average cost $120,000 per patient
- One-year mortality has not improved in over 2 decades
- Incidence rising
  - 40,000 to 50,000 new cases/year
In 21st century, IE healthcare-acquired in > 25% of cases

# Antibiotic Prophylaxis

**Table 2: ACC/AHA and ESC Guidelines on Use of Antibiotic Prophylaxis for the Prevention of IE**

<table>
<thead>
<tr>
<th>ACC/AHA</th>
<th>Class, Level of Evidence</th>
<th>ESC</th>
<th>Class, Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental procedures that involve manipulation of gingival tissue, manipulation of the periapical region of teeth, or perforation of the oral mucosa:</td>
<td></td>
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</tr>
<tr>
<td>1. Patients with prosthetic cardiac valves</td>
<td>IIA, B</td>
<td>1. Patients with any prosthetic valve, including a transcatheter valve, or those in whom any prosthetic material was used for cardiac valve repair</td>
<td>IIA, C</td>
</tr>
<tr>
<td>2. Patients with previous IE</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>3. Cardiac transplant recipients with valve regurgitation due to a structurally abnormal valve</td>
<td></td>
<td>3. Patients with CHD, including a. Any type of cyanotic CHD</td>
<td></td>
</tr>
<tr>
<td>4. Patients with CHD, including a. Unrepaired cyanotic CHD, including palliative shunts and conduits; b. Completely repaired CHD repaired with prosthetic material or device, whether placed by surgery or catheter intervention, during the first 6 months after the procedure; or c. Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device</td>
<td></td>
<td>b. Any type of CHD repaired with a prosthetic material, whether placed surgically or by using percutaneous techniques, up to 6 months after the procedure, or lifelong if residual shunt or valvular regurgitation remains</td>
<td></td>
</tr>
<tr>
<td>Vaginal delivery:</td>
<td></td>
<td></td>
<td>Not recommended. &quot;During delivery the indication for prophylaxis has been controversial and, given the lack of convincing evidence that infective endocarditis is related to either vaginal or caesarean delivery, antibiotic prophylaxis is not recommended&quot; (145).</td>
</tr>
<tr>
<td>1. Patients with prosthetic cardiac valve or prosthetic material used for cardiac valve repair</td>
<td>IIA, C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Patients with unrepaired and palliated cyanotic CHD, including surgically constructed palliative shunts and conduits</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*ACC/AHA guidelines on valvular heart disease 2014 and ESC guidelines on infective endocarditis 2015, TACC/AHA management of adults with congenital heart disease 2008 (146); and ESC management of cardiovascular diseases in pregnancy 2011 (145). Infective endocarditis prophylaxis at the time of vaginal delivery is controversial and not included as an indication in the ACC/AHA guidelines on valvular heart disease 2014 or the main ESC 2015 guidelines. CHD = congenital heart disease; IE = infective endocarditis.*

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DIAGNOSIS

- Timely diagnosis tied to improve outcomes
- Variegated clinical presentations
- Limitations of modified Duke criteria
Table 5. Definition of Terminology Used in the Duke Criteria

<table>
<thead>
<tr>
<th>Major criteria</th>
<th>Minor criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive blood culture</td>
<td>Predisposition: pre-existing heart condition or intravenous drug use</td>
</tr>
<tr>
<td>Typical microorganism</td>
<td>Fever: temperature &gt;38°C (100.4°F)</td>
</tr>
<tr>
<td>Viridans spp.</td>
<td>Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway lesions</td>
</tr>
<tr>
<td>Community-acquired</td>
<td>Immunologic phenomena: glomerulonephritis, Osler nodes, Roth spots, rheumatoid factor</td>
</tr>
<tr>
<td>Persistently positive</td>
<td>Microbiologic evidence: positive blood culture but not meeting major criterion as noted previously or serologic evidence of active infection with organism consistent with infective endocarditis</td>
</tr>
<tr>
<td>Blood cultures</td>
<td>Echocardiogram: consistent with infective endocarditis but not meeting major criterion as noted previously</td>
</tr>
<tr>
<td>All of 3 or more</td>
<td>New-onset heart failure</td>
</tr>
<tr>
<td>Evidence of endocarditis</td>
<td>New conduction disturbances</td>
</tr>
<tr>
<td>Positive echocardiographic evidence of abscess or</td>
<td>or serologic evidence of active infection with organism</td>
</tr>
<tr>
<td>New partial dehiscence of valve prosthesis</td>
<td>previously</td>
</tr>
<tr>
<td>New valvular regurgitation</td>
<td></td>
</tr>
</tbody>
</table>

Table 6. Duke Criteria for Diagnosis of Infective Endocarditis

**Definite infective endocarditis**

Pathological criteria:
- Microorganisms: demonstrated by culture or histological examination of a vegetation, or in a vegetation that has been embolized, or in an intracardiac abscess, or
- Pathologic lesions: vegetations or intracardiac abscess present, confirmed by histological examination showing active endocarditis

Clinical criteria, using specific definitions listed in Table 5
- 2 Major criteria or
- 1 Major criterion and 3 minor criteria or
- 5 Minor criteria

Rejected
- Firm alternate diagnosis for manifestations of endocarditis or
- Resolution of manifestations of endocarditis, with antibiotic therapy for ≤4 d or
- No pathological evidence of infective endocarditis at surgery or autopsy after antibiotic therapy for ≤4 d

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**Transthoracic Echocardiography (TTE)**

- **Native valve endocarditis**
  - 50-90% sensitivity, 90% specificity
- **Prosthetic valve endocarditis**
  - 40-70% sensitivity
- Can be better than TEE for visualizing anterior prosthetic aortic valve abscesses
Transesophageal Echocardiography (TEE)
- Indicated when TTE is positive or non-diagnostic
- Native valve endocarditis
  - 90-100% sensitivity, 90% specificity
- Prosthetic valve endocarditis
  - 86% sensitivity
- Superior to TTE for detection of complications
  - Perforations
  - Abscesses
  - Fistulae
Computed Tomography

- Key adjunctive imaging modality when echocardiography unclear
- Possibly superior in detecting paravalvular complications
- Less subject to prosthetic valve artifacts
- Concurrent coronary angiography

Combining CT with metabolic imaging (i.e., $^{18}$FDG-PET, SPECT) may enhance diagnosis in “possible” IE or device infection

- $^{18}$FDG-PET plus CT had 73% sensitivity and 80% specificity
- Adding “abnormal prosthetic valve $^{18}$FDG-PET signal” as a diagnostic criterion increased sensitivity of modified Duke criteria from 70% to 95%
- Reduced the frequency of “possible IE” from 56% to 32%.

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Limitations/Drawbacks:

- Metabolic imaging cannot accurately discriminate between sterile inflammation and infection.
- False-positives for PET/CT reported after cardiac surgery.
- Access to advanced imaging is limited.
- Identifying which patients stand to benefit remains to be determined.
DIAGNOSIS: MICROBIOLOGY WHAT’S NEW?

- *Staphylococcus aureus* now most common pathogen in IE (30% of cases)
  - Aggressive disease
  - Increased risk of embolism, stroke, persistent bacteremia, death
  - Most common cause of PVE
    - Reoperations
    - Mortality rates approaching 50%

- 10% to 20% have negative blood cultures → rigorous testing
  - Serologic testing
  - Blood PCR
  - Causative organism can be identified in 2/3 of culture negative patients
TREATMENT: ANTIBIOTICS

WHAT’S NEW?

- Organism-specific antibiotic protocols (AHA Guidelines¹)
- Traditional requirement for 4-6 weeks of intravenous antibiotics
- Balancing treatment efficacy versus toxicity
  - New evidence supporting short-course/stepped-down antibiotic treatment in selected groups (e.g., uncomplicated oral Streptococci)
    - Post-surgical patients with negative valve culture findings
    - Earlier transition to oral antibiotics
  - Increasing data suggesting that aminoglycosides may cause harm without clear benefit
    - Aminoglycosides removed or reduced in current treatment guidelines

Novel strategies to prevent and treat biofilm-forming strains of multidrug-resistant organisms (e.g., S. aureus)

- Inhibition of bacterial adhesion
- Disruption of biofilm architecture

Association of nontuberculous mycobacterial infections in cardiac surgical patients

Pathogen identified in heater-cooler devices used in extracorporeal circulation

Chronic colonization despite adherence to manufacturer cleaning recommendations

Attributed to biofilm formation


Ann Thorac Surg 2017; 104:1237-1242
SURGERY

- Performed in 50% to 60% of patients
- 6-month survival rates > 80%
# SURGERY: CURRENT INDICATIONS

<table>
<thead>
<tr>
<th>Table 3: Indications for Surgery in AHA and ESC Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heart Failure</strong></td>
</tr>
<tr>
<td>Early surgery* is indicated in patients with IE who present with valve dysfunction resulting in symptoms or signs of HF</td>
</tr>
<tr>
<td>Early surgery* is indicated in patients with PVE with symptoms or signs of HF resulting from valve dehiscence, intracardiac fistula, or severe prostatic valve dysfunction</td>
</tr>
<tr>
<td><strong>Uncontrolled Infection</strong></td>
</tr>
<tr>
<td>Early surgery* is indicated in patients when IE is complicated by heart block, annular or aortic abscess, or destructive penetrating lesions</td>
</tr>
<tr>
<td>Early surgery* is reasonable for patients with relapsing PVE</td>
</tr>
<tr>
<td>Early surgery* should be considered, particularly in patients with IE caused by fungi or highly resistant organisms (e.g., VRE, multidrug-resistant gram-negative bacilli)</td>
</tr>
<tr>
<td>Early surgery* is indicated for evidence of persistent infection (manifested by persistent bacteremia or fever lasting &gt;5-7d, and provided that other sites of infection and fever have been excluded) after the start of appropriate antimicrobial therapy</td>
</tr>
<tr>
<td><strong>Prevention of Embolism</strong></td>
</tr>
<tr>
<td>Early surgery* is reasonable in patients who present with recurrent emboli and persistent or enlarging vegetations despite appropriate antibiotic therapy</td>
</tr>
<tr>
<td>Early surgery* is reasonable in patients with severe valve regurgitation and mobile vegetations &gt;10mm</td>
</tr>
<tr>
<td>Early surgery* may be considered in patients with mobile vegetations &gt;10mm, particularly when involving the anterior leaflet of the mitral valve and associated with other relative indications for surgery</td>
</tr>
</tbody>
</table>

*Defined as “during initial hospitalization and before completion of a full course of antibiotics.” †Defined as: emergency surgery — performed within 24 h; urgent surgery — within a few days; elective surgery — after at least 1 to 2 weeks of antibiotic therapy.

HACEK — Haemophilus species, Aggregatibacter species, Cardiobacterium hominis, Eikenella corrodens, and Kingella species; HF — heart failure; NVE — native valve infective endocarditis; PVE — prosthetic valve infective endocarditis; VRE — vancomycin-resistant Enterococcus; other abbreviations as in Tables 1 and 2.

Predictors of Surgical Treatment among patients with Indications for Surgery\textsuperscript{1}

\begin{table}[h]
\centering
\begin{tabular}{|l|l|}
\hline
Variable & OR (95\% CI) \\
\hline
History of COPD & 0.57 (0.31–1.05) \\
History of heart failure & 0.61 (0.35–1.06) \\
History of cancer & 0.54 (0.29–1.02) \\
History of moderate/severe liver disease & 0.16 (0.04–0.64) \\
Transfer from another hospital & 2.70 (1.75–4.15) \\
Severe aortic regurgitation & 2.38 (1.30–4.20) \\
\textit{Staphylococcus aureus} etiology & 0.50 (0.30–0.85) \\
New heart failure, NYHA class III or IV & 1.59 (0.96–2.64) \\
Abscess before surgical decision & 1.95 (1.15–3.29) \\
Stroke before surgical decision & 0.54 (0.32–0.90) \\
Embolization before surgical decision & 1.70 (1.01–2.86) \\
STS quintile 2 & 1.36 (0.66–2.78) \\
STS quintile 3 & 0.59 (0.30–1.18) \\
STS quintile 4 & 0.83 (0.41–1.66) \\
STS quintile 5 & 0.93 (0.46–1.89) \\
\hline
\end{tabular}
\caption{Multivariable Model\textsuperscript{*} Predicting Surgery Among Patients With Surgical Indications}
\end{table}

In the “real-world” many patients with a guideline indication for intervention do not undergo surgery\(^1\)

The perceived operative risk dictates the threshold for surgery (overall in-hospital mortality of 20% or higher)

Balancing Act
- Delay allows increased antibiotic course and “stabilization”, but runs risk of disease progression (e.g., abscess, heart block, embolism)

Recent trend towards “Early Surgery”
- Still controversial; more RCTs needed
- No proven benefit in delaying surgery once an indication has been established

Endocarditis complicated by stroke in 20% to 40% of cases

Independent risk factor for postoperative mortality in IE patients

Risk of stroke highest at diagnosis and decreases rapidly after initiation of antibiotic therapy

Risk factors for embolism
- Vegetation size (> 10 to 15 mm)
- Mitral valve involvement
- Vegetation mobility
- *Staphylococcus aureus*

Timing of surgery after stroke controversial
Early studies identified high mortality rates among patients who underwent surgery soon after stroke, but they were small and not risk-adjusted.

Still, there is a reluctance to perform surgery immediately after stroke.

No definitive studies have confirmed that it is safe to perform surgery within 7 days after stroke or if it is better to postpone.
More recent studies suggest better outcomes for endocarditis patients presenting with ischemic stroke when they undergo early cardiac surgery. Time elapsed between the stroke and cardiac surgery does not impact rates of perioperative neurologic complications or neurologic recovery. Mortality was higher when surgery was performed within 4 weeks of hemorrhagic stroke compared with delayed surgery (75% versus 40%).


Current AHA Recommendations

Valve Surgery in Patients With Prior Emboli/Hemorrhage/Stroke

Recommendations

1. Valve surgery may be considered in IE patients with stroke or subclinical cerebral emboli and residual vegetation without delay if intracranial hemorrhage has been excluded by imaging studies and neurological damage is not severe (ie, coma) (Class IIb; Level of Evidence B).

2. In patients with major ischemic stroke or intracranial hemorrhage, it is reasonable to delay valve surgery for at least 4 weeks (Class IIa; Level of Evidence B).

SURGERY: TAVR - ENDOCARDITIS

- 1 year incidence 0.1% to 3.0%
- Causative antecedent procedure identified in about 50%
- *Enterococcus, Staphylococcus*
- < 20% underwent open heart surgery or transcatheter valve-in-valve procedure
- Antibiotic therapy with poor results
  + In-hospital mortality from 47% to 64%
  + 1-year mortality from 66% to 75%

researchgate.net
NATIVE MITRAL ENDOCARDITIS
Surgical Techniques: Mitral Valve

- Lends itself more often to reparative procedures
- Severe mitral insufficiency, especially with congestive signs and symptoms, dictates surgical intervention
- Look out for ventriculoatrial discontinuity
- Annular abscess: all infected tissue must be removed and annulus reconstructed with pericardium

SURGICAL TECHNIQUES: MITRAL VALVE

Murasita et al. West Virginia Univ. CTSNet

Cleveland Clinic Foundation, 1998
NATIVE AORTIC ENDOCARDITIS
SURGICAL TECHNIQUES: AORTIC VALVE

- Leaflet destruction
- Generally requires aortic valve replacement
- No conclusive evidence favoring tissue over mechanical prosthesis
- Inspect aortic root for abscess
- Inspect mitral valve anterior leaflet for “drop lesions”
- Involvement of anterior mitral leaflet and intravalvular fibrous body may require homograft reconstruction
SURGICAL TECHNIQUES: AORTIC VALVE

- Sometimes aortic endocarditis extends onto aortomitral continuity requiring more complicated reconstruction
- Homograft reconstruction of intravalvular fibrous body using attached aortomitral continuity, ascending aorta, and left atrial dome
- Reimplantation of coronary buttons
- Mitral annuloplasty
AORTIC ROOT ABSCESS

SURGICAL TECHNIQUES: AORTIC ROOT

- Generally requires aortic root replacement
- Biologic conduit preferred
- Occasionally, can get by with debridement patch repair
Surgical Techniques: Aortic Root

- Patch Repair
SURGICAL TECHNIQUES: AORTIC ROOT
SURGICAL TECHNIQUES: AORTIC ROOT

- Infected Sinus of Valsalva Aneurysm
SURGICAL TECHNIQUES: AORTIC ROOT

- Infected Sinus of Valsalva Aneurysm
PROSTHETIC VALVE ENDOCARDITIS

- Best assessed by TEE; much higher sensitivity than TTE
- Suggestive findings:
  - “Rocking” valve indicating dehiscence
  - Moderate to severe perivalvular leak
  - Abnormal leaflet motion
  - Perivalvular abscess
  - Vegetation(s)
- *Staphylococci, Streptococci, and Enterococci* are frequent isolated species
- Fungal species also seen, especially in immunocompromised

Tuna IC, Harrison MR. NEJM 2001:344:275
PROSTHETIC VALVE ENDOCARDITIS
Incidence of infective endocarditis (IE) rising, affecting a wider demographic with new antibiotic resistances and new cardiac devices

Multimodality diagnostic approaches may improve diagnostic accuracy of IE

Antibiotic IE prophylaxis has been revised, focusing on highest risk patients

Shorter-course antibiotic treatment regimens for selected patients

Earlier, more aggressive surgical treatment of IE, with proper indications, associated with better outcomes

Earlier surgical treatment of IE after non-hemorrhagic stroke may be associated with improved clinical outcomes.

Reasonable to defer surgery in patients suffering from hemorrhagic stroke for four weeks

Cornerstone of surgical therapy of IE is to remove all infected tissue, even if it results in a more extensive operation

Homografts generally preferred for aortic root replacement for IE