Endocarditis

February 10, 2017 by Josh Farkas

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when to suspect endocarditis

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at-risk patients

- IV drug use
- Hemodialysis
- Valvular heart disease (e.g., prior endocarditis, mitral valve prolapse, aortic valve calcification)
- Any endovascular hardware, for example:
  - Prosthetic valve, pacemaker
• Large vessel stent
• Subcutaneous port used for chemotherapy
• Transcatheter aortic valve replacement (TAVR)

**Clinical presentation of left-sided endocarditis**

- Fever (e.g. Strep viridans causing *subacute* bacterial endocarditis)
  - Fever in someone using IV drugs carries nearly a 15% risk of endocarditis!\(^1\)
- Flu-like, nonspecific illness (e.g. chills, night sweats, headache)
- Septic shock (e.g. Staph aureus causing *acute* bacterial endocarditis)
- Acute heart failure from valve regurgitation
- Systemic emboli (e.g. ischemic stroke, kidney infarction)
  - Stroke in a young patient with IVDU is a classic endocarditis presentation.
  - Delirium due to multifocal emboli (with no clinically obvious focal neurologic lesion).

**Clinical features of right-sided endocarditis**

- Highest risk patients:
  - Most commonly: IV drug use
  - Endovascular hardware (pacemaker, chemotherapy port, etc.)
- Fever
- Septic pulmonary emboli
  - Will often initially mimic pneumonia (respiratory failure, pulmonary infiltrates, fever).
  - May eventually lead to hemoptysis or pneumothorax
  - Radiographically seen as multiple pulmonary nodules which eventually cavitate.

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**Traditional examination findings**

- Fever (~85% sensitive)
- New regurgitant murmur
- Signs of local infection at the site of a pacemaker or indwelling catheter
- Classic findings for endocarditis are each <5% sensitive (more commonly seen in subacute endocarditis):
  - Splinter hemorrhages
  - Conjunctival petechiae
- Janeway lesions (red/blue macules on palms and soles)
- Osler's nodes (painful swelling in pulp of fingers)

point-of-care echocardiography findings

- Most sensitive findings:
  - (1) Color doppler shows regurgitation. This raises a concern for endocarditis, but must be interpreted in clinical context:
    - Regurgitation is more worrisome if severe and found in a young patient with no prior cardiac disease (who shouldn't have regurgitation).
    - Regurgitation is most worrisome if there is a recent echocardiogram without any regurgitation.
    - Mild/trace regurgitation is nonspecific, especially in older patients.
  - (2) Valve looks "funny" (thickened, etc).
- More specific findings:
  - (1) Vegetation visualized
  - (2) Prosthetic valve partial dehiscence

lab workup

peripheral blood cultures

- Single most important test to order for suspected endocarditis. Cultures must be obtained prior to starting antibiotics in suspected endocarditis, even if this causes a short treatment delay.
- Number of cultures
  - One "set" of cultures = two bottles (anaerobic & aerobic) drawn from a single location.
  - Ideally three sets should be obtained from three different locations (two sets are OK if this isn't possible).
- Location of cultures
  - Ideally cultures should be obtained from a fresh peripheral stick.
  - If this isn't feasible, obtain blood wherever you can get it. For example, obtaining blood from a freshly placed central line is OK – but ideally, obtain blood from different locations.
- Timing
  - Traditionally, usually recommended to spread out cultures (e.g. over 60-90 minutes).
  - In endocarditis, bacteremia is generally constant, so there is little rationale to spread cultures out over time.
  - Don't worry too much about the timing of cultures – the key thing is to get a lot of cultures and fill the culture bottles fully. (Get a lot of blood; more blood removed = higher likelihood of capturing a causative pathogen).

additional culture of any indwelling lines
In addition to the above peripheral cultures, any indwelling lines in place >48 hours should also be cultured. The intention here is to determine if there is an infection of the line.

**other labs which may be considered (but not terribly helpful)**

- Acute-phase reactants (ESR, CRP)
  - Reasonably sensitive for endocarditis (>95%)
  - These tests don't generally help guide initial patient management. They may be useful for subsequent follow-up to help determine if the infection is responding adequately to therapy.
- Urinalysis consistent with glomerulonephritis (proteinuria, microscopic hematuria) is seen in ~60% of cases.

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**echocardiography**

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**performance**

- Sensitivity of trans-thoracic echocardiogram (TTE) is ~70% for native valve endocarditis or 50% for prosthetic valve endocarditis.
- Sensitivity of trans-esophageal echocardiogram (TEE) is ~96% for native valve endocarditis and ~92% for prosthetic valve endocarditis.
- Specificity isn't perfect. For example, false-positive vegetation may occur due to thrombi or marantic (non-infectious) vegetations.
  - Note: These numbers are population averages. The sensitivity of TTE is best appreciated by reviewing the images.
    - If the images are crystal clear, then the sensitivity is higher (and the added value of a TEE thus lower).
    - If the windows are poor and images are limited, then the sensitivity is poor.

**advantages of trans-thoracic echocardiogram**

- Noninvasive, useful to obtain as a baseline study.
- Easier to repeat serially if patient deteriorates.

**advantages of trans-esophageal echocardiogram**

- Greater sensitivity for endocarditis diagnosis, especially prosthetic valve endocarditis.
- Greater sensitivity for complications of endocarditis (e.g. aortic ring abscess, valve perforation).

**2015 AHA/ACC guideline for which study to obtain**

- (1) Everyone gets a baseline TTE to start.
- (2) TEE is usually indicated in the following situations.
  - TTE is negative and persistent suspicion for endocarditis remains.

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Figure. An approach to the diagnostic use of echocardiography (echo). Rx indicates prescription; TEE, transesophageal echocardiography; and TTE, transthoracic echocardiography. For example, a patient with fever and a previously known heart murmur and no other stigmata of infective endocarditis (IE). High initial patient risks include prosthetic valve heart valves, many congenital heart diseases, previous endocarditis, new murmur, heart failure, or other stigmata of endocarditis. High-risk echocardiographic features include large or mobile vegetations, valvular insufficiency, suggestion of perivalvular extension, or secondary ventricular dysfunction (see text). Modified from Baddour et al. Copyright © 2005, American Heart Association, Inc.
- TTE is positive and shows high-risk features (large/mobile vegetations, valvular insufficiency, suggestion of perivalvular extension, or secondary ventricular dysfunction).
- Patient has prosthetic valves or complex congenital heart disease.
- Patient has poor transthoracic imaging windows.

**repeat echo: consider for hemodynamic deterioration or failure to improve clinically. Look for:**

- Worsening valvular dysfunction
- Development of aortic ring abscess
- Enlarging vegetations despite antibiotics (associated with complications, need for surgery)

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**diagnostic strategies & Duke criteria**

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**Approach to the diagnosis of endocarditis**

- **Basic evaluation**
  - History & physical, basic laboratory tests
  - Blood cultures x3 (plus any indwelling lines)
  - Transthoracic echo (TTE)

- **Diagnostic certainty** (ruled in or excluded)

- **Ongoing uncertainty**

- **Further testing** (one or more of the following tests depending on clinical context)
  - Subject triqsus endocarditis (e.g. IV drug use)
  - Concern for left-sided Endocarditis. Higher yield with altered mental status.
  - Any patient with unclear diagnosis who can tolerate endoscopy
  - May consider depending on availability & symptoms

- **Chest CT scan**
  - Multiple embolic infarctions may support right-sided endocarditis.

- **Brain MRI**
  - Multiple embolic infarctions supports left-sided endocarditis.
  - Sensitivity of MRI is ~70% for left-sided endocarditis.

- **Trans-esophageal echo**
  - Possibly single best test for endocarditis
  - Invasive

- **Advanced imaging**
  - Cardiac CT
  - PET/CT or Leukocyte-labelled SPECT/CT
  - Additional imaging for embolic events (e.g. whole-body CT)
  - Transesophageal echo

**Continue aggressive investigation until satisfied with diagnosis**

- **Serial physical examination** to look for emerging evidence of any alternative primary source of infection or (more commonly) emergence of metastatic infection at distant sites (e.g. spine, joints).
- **Image and biopsy/sample aggressively** to evaluate for any alternative source of infection or potential embolic/metastatic infection.
- **Consider serology or PCR studies** to evaluate for fastidious organisms which cannot be cultured with standard media.
- **Exclude all alternative sites of infection**

Generally transesophageal echocardiography is the most definitive study. However, for right-sided endocarditis a high-quality CT scan showing multifocal embolic disease with cavitation can be nearly diagnostic. More advanced imaging modalities (e.g. PET/CT or leukocyte-labelled SPECT/CT) are unavailable at most centers in the USA but will likely become more important in the future. If the diagnosis is uncertain, continue to aggressively search for additional information which may help secure the diagnosis (or at least exclude other possible foc of infection).

[Internet Book of Critical Care, by @PulmCrit](https://emcrit.org/wp-content/uploads/2017/02/diagendo.pdf) approaches to the diagnosis of endocarditis?

- The modified Duke criteria are increasingly obsolete (especially for newer entities such as pacemaker-associated endocarditis). These criteria are shown below, but in practice aren’t terribly helpful.
- The schematic above shows a more clinically useful approach to the diagnosis of endocarditis. Improvements in diagnostic radiology are increasingly helpful in ambiguous situations. When in doubt, further imaging data should be aggressively sought both to evaluate the diagnosis of endocarditis and also to look for competing diagnoses.
modified Duke criteria for “definite” endocarditis

- Two major criteria
- One major criteria + 3 minor criteria
- Five minor criteria

major criteria

- [1] Microbiologic data: any of the following
  - i) Two separate cultures with organisms typically involved in endocarditis
    - Strep viridans, Strep bovis (now renamed Strep gallolyticus)
    - Staph aureus
    - Community-acquired enterococci without primary focus
    - Haemophilus species
    - Aggregatibacter species
    - Cardiobacterium hominis
    - Eikinella corrodens
    - Kingella species
  - ii) Single culture of Coxiella burnetti or anti-phase 1 IgG antibody titer >1:800
- [2] Echocardiographic data: any of the following
  - i) vegetation or myocardial abscess
  - ii) new valve regurgitation or dehiscence of prosthetic valve

minor criteria

- Patient at-risk for endocarditis (defined at top of this chapter)
- Temperature >38C
- Vascular phenomena
  - Major arterial emboli (e.g. ischemic stroke)
  - Septic pulmonary emboli
  - Janeway lesions
  - Conjunctival hemorrhage
- Immunologic phenomena
  - Glomerulonephritis
  - Osler's nodes
  - Positive rheumatoid factor
- Blood culture positivity not reaching the level of a major criterion

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**evaluation & management of metastatic infection**

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**endocarditis is often accompanied by metastatic infection, especially:**

- Joint infection(s)
- Spinal infection, including discitis
- Splenic abscess

Recognizing distant sites of infection is important, because these may require surgical drainage. Furthermore, such drainage should ideally be performed prior to valve replacement surgery, to avoid infection of the fresh valve.

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**empiric therapy**

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### epidemiologic associations with endocarditis due to unusual pathogens

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<th>Risk factor</th>
<th>Possible pathogens</th>
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<tbody>
<tr>
<td>IV drug use</td>
<td>Staph aureus (including MRSA), coag-negative staph, beta-hemolytic strep, fungi, GNB including pseudomonas, polymicrobial</td>
</tr>
<tr>
<td>Indwelling cardiovascular device</td>
<td>Staph aureus, coag-negative staph, fung, gram-negatives, Corynebacterium sp.</td>
</tr>
<tr>
<td>Genitourinary disorders, infection (including pregnancy, delivery, abortion)</td>
<td>Enterococcus, Group B streptococci (S agalactiae), Listeria monocytogenes, GNB, Neisseria gonorrhoeae</td>
</tr>
<tr>
<td>Chronic skin disorders</td>
<td>Staph, beta-hemolytic strep</td>
</tr>
<tr>
<td>Poor dental health, dental procedures</td>
<td>Viridans group streptococci, nutritionally variant streptococci, Abiotrophia defectiva, Granulactella sp., Gemella sp., HACEK organisms</td>
</tr>
<tr>
<td>Alcoholism, cirrhosis</td>
<td>Bartonella sp., Aeromonas sp., Listeria sp., Strep pneumonae, Beta-hemolytic strep</td>
</tr>
<tr>
<td>Burn</td>
<td>Staph aureus, GNB including pseudomonas, fungii</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Staph aureus, beta-hemolytic strep, Strep pneumonae</td>
</tr>
<tr>
<td>Prosthetic valve early (&lt;1 year)</td>
<td>Coag-neg staph, Staph aureus, GNB, fungii, Corynebacterium sp., Legionella sp.</td>
</tr>
<tr>
<td>Prosthetic valve late (&gt;1 year)</td>
<td>Coag-neg staph, Staph aureus, Viridans group strep, Enterococcus spp., Fungi, Corynebacterium spp.</td>
</tr>
<tr>
<td>Dog/cat exposure</td>
<td>Bartonella sp., Pasteurella sp., Capnocytophaga sp.</td>
</tr>
<tr>
<td>Contaminated milk</td>
<td>Brucella sp., Coxiella burnetii, Erysipelothrix sp.</td>
</tr>
<tr>
<td>Homeless, body lice</td>
<td>Bartonella sp.</td>
</tr>
<tr>
<td>AIDS</td>
<td>Salmonella sp., Strep pneumonae, Staph aureus</td>
</tr>
<tr>
<td>Solid organ transplant</td>
<td>Staph aureus, Aspergillus fumigatus, Enterococcus sp., Candida sp.</td>
</tr>
<tr>
<td>GI lesions</td>
<td>Strep galolyticus (bovic), Enterococcus sp., Clostridium septicum</td>
</tr>
</tbody>
</table>

(AMA endocarditis guidelines 2015)

Below are potential empiric regimens for patients with suspected or definite endocarditis, to be used while blood cultures are pending. There is no prospective evidence regarding these regimens, nor is there consensus in the literature. These regimens are intended as general concepts, which may not work for every patient (depending on specific exposures as shown above). Antibiotic doses are listed in the table below.

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### native-valve endocarditis

- Endocarditis is nearly always due to gram-positive infections, so gram-negative coverage isn't necessary. Potential regimens are as follows
- [1] Vancomycin monotherapy
  - Widely used, but not terrific.
  - Main problem: vancomycin levels are often sub-therapeutic initially. Furthermore, vancomycin is a suboptimal antibiotic for the most common and virulent causes of endocarditis (e.g. MSSA, streptococcal species).
- [2] Acute endocarditis: **Vancomycin + cefazolin** (2 grams IV q8hr). For patients with cefazolin allergy, the combination of vancomycin + ceftriaxone may be used instead (noting that cefazolin and ceftriaxone are **not cross-allergic**).
Advantages of vancomycin+cefazolin compared to vancomycin monotherapy are as follows.3-7

(i) Cefazolin + Vancomycin may have improved efficacy against MRSA.8

(ii) Cefazolin + Vancomycin as initial therapy seems to have better efficacy for methicillin-sensitive Staph aureus (MSSA).3,9

(iii) Cefazolin and vancomycin act at different stages of cell wall synthesis, so they function in a synergistic fashion.10 This may partially explain the clinical evidence above.

(iv) If vancomycin levels are initially sub-therapeutic, the patient will still have therapeutic cefazolin levels (which will provide protection against most organisms).

(v) The combination of vancomycin plus either cefazolin or nafcillin is guideline-recommended therapy for Staph. aureus before sensitivities are available (Class IIb recommendation of the AHA/IDSA). Cefazolin is preferable to nafcillin unless there is possible brain embolization (cefazolin is easier to administer & better tolerated). Over time, Staph aureus is becoming an increasingly common cause of endocarditis (especially among acutely ill patients) – so it makes sense to start this regimen up-front.

Subacute endocarditis (gradually worsening illness over weeks): Vancomycin + ampicillin-sulbactam

Note: This doesn't usually cause critical illness (unless the endocarditis leads to some complication such as valvular dysfunction or embolic phenomena).

Ampicillin-sulbactam isn’t quite as good for Staph. aureus, but it provides better coverage for enterococcus and HACEK organisms (which typically cause subacute endocarditis). In ampicillin allergy, vancomycin plus ceftriaxone would be an alternative.

prosthetic valve endocarditis

American and European guidelines both recommend synergistic therapy with rifampin and gentamycin for prosthetic-valve endocarditis due to staphylococcus, streptococcus, and enterococcus. However, rifampin may be withheld until 3-5 days after initiation of treatment. Potential initial empiric regimens are as follows:

[1] Conventional regimen

- Vancomycin
- Gentamycin 3 mg/kg IV daily

[2a] Augmented regimen for acute bacterial endocarditis occurring within months of valve surgery (cefepime functions similarly to cefazolin, while also providing coverage for nosocomial gram-negative pathogens)

- Vancomycin
- Gentamycin 3 mg/kg IV daily
- Cefepime

[2b] Augmented regimen for acute bacterial endocarditis occurring >1 year after valve surgery (rationale for cefazolin same as above for native valve endocarditis)

- Vancomycin
- Gentamycin 3 mg/kg IV daily
• Cefazolin (2 grams IV q8hr)
• [3] Augmented regimen with ampicillin-sulbactam for subacute bacterial endocarditis (rationale for adding ampicillin-sulbactam explored above)
  • Vancomycin
  • Gentamicin 3 mg/kg IV daily
  • Ampicillin-sulbactam

**IV drug abuse**

• Patients at risk for broader spectrum of pathogens.
• [1] Vancomycin monotherapy
  • Still an OK regimen.
• [2] Vancomycin plus piperacillin-tazobactam
  • Improves coverage of enterococcus, MSSA, and gram-negatives compared to vancomycin monotherapy.
  • An alternative, similar regimen would be vancomycin plus ampicillin-sulbactam.

**CNS involvement due to mitral or aortic valve endocarditis**

• Background:
  • Ischemic strokes are common (~60% of endocarditis patients will have infarction detectable by MRI).
  • Intracranial hemorrhage can occur via various mechanisms:
    • i) Ischemic stroke which undergoes necrosis and develops small hemorrhage.
    • ii) Infection can cause an arterial aneurysm (mycotic aneurysm), with subsequently hemorrages.
  • Meningitis occurs in ~20% of patients with CNS complications. Brain abscess can also occur.
• Clinical implications:
  • Brain imaging should be used aggressively in patients with signs or symptoms of CNS involvement.
  • Patients with meningitis or abscesses may require antibiotics with good CNS penetration. Vancomycin doesn't penetrate the brain well, so it is reasonable to add meningeal doses of a beta-lactam (e.g. ceftriaxone 2 grams IV Q12hr).

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**definitive therapy**

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**antibiotics commonly used for endocarditis**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
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<tbody>
<tr>
<td>Ampicillin</td>
<td>12 grams/day in divided doses (e.g. 2 grams IV q6hr)</td>
</tr>
<tr>
<td>Ampicillin-Sulbactam</td>
<td>3 grams IV q8hrs</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>2 grams IV q12hr</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>Usually 2 grams IV q24 hours&lt;br&gt;High dose (2 grams IV q12) if: meningeval involvement, cephalosporin-resistant pneumococcus, enterococcus.</td>
</tr>
<tr>
<td>Ceftazidim</td>
<td>10 mg/kg IV daily for Staph; 10-12 mg/kg IV daily for enterococci</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>1 mg/kg q12hr (target 1-hour peak concentration 3 to 4 &lt;1 ug/ml) and trough &lt;1 ug/ml &lt;br&gt;3 mg/kg daily may be safer; adds possibility less effective (advocated in European guidelines) &lt;br&gt;Generally discontinued after two weeks of therapy (except with enterococcus)</td>
</tr>
<tr>
<td>Nafcillin</td>
<td>2 grams IV q12hr</td>
</tr>
<tr>
<td>Penicillin G</td>
<td>Beta-hemolytic streptococci: 24 Million Units daily, divided in 4-6 doses (e.g. 4 million units IV q4hr) &lt;br&gt;Enterococci: 18-10 million units, divided in six doses (e.g. 3 million units IV q4hr)</td>
</tr>
<tr>
<td>Rifampin</td>
<td>300 mg q12hr&lt;br&gt;Consider delaying initiation of rifampin until after 3-5 days of effective therapy (may avoid rifampin resistance)</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Use a loading dose, check levels early, aggressively dose-titrate to achieve an AUC of &gt;400 (see <a href="https://emcrit.org/eqpt/vancys/">https://emcrit.org/eqpt/vancys/</a>)</td>
</tr>
</tbody>
</table>

*Based on [9th Endocarditis Guidelines 2015 & European Society of Cardiology 2015 guidelines](https://emcrit.org/wp-content/uploads/2017/02/abxtable2.svg).* The following is based on a combination of the IDSA/AHA guidelines and the ESC guidelines. At a large center, infectious disease consultants will always be involved in these cases, but having a general understanding of this is still useful.

**streptococcus pneumoniae**

• Sensitivity unknown: ceftriaxone used initially for empiric therapy.
• Penicillin-sensitive: may treat with penicillin, cefazolin, or ceftriaxone.
• Penicillin-resistant, ceftriaxone sensitive: treat with ceftriaxone.
• Ceftriaxone-resistant (MIC >2 ug/mL): high-dose ceftriaxone seems to work regardless (e.g. 2 grams IV q12, as long as no meningeal involvement). For meningeal involvement, consider addition of vancomycin and rifampin (AHA guidelines).

**beta-hemolytic streptococci (Groups A, B, C, F, and G)**

• Group A streptococci: Penicillin G is the treatment of choice; ceftriaxone is a reasonable alternative.
• Groups B, C, F, G: May be slightly harder to kill than Group A streptococci. The cornerstone of therapy is still penicillin or ceftriaxone, but addition of gentamycin for the first two weeks may be considered (AHA guidelines) or recommended (ESC guidelines).

**coagulase-negative staphylococci**

• These are often methicillin-resistant. Methicillin-resistant strains are cross-resistant with cephalosporins and carbapenems (even though they may appear sensitive to these agents in vitro) (AHA guidelines).
• *Staph lugdunensis* ("slug")
  • More virulent, with a high rate of perivalvular extension and metastatic infection.
  • Should always be taken seriously (less likely to be a contaminant)
  • Uniformly susceptible to most antibiotics (including methicillin, which may be used for treatment) (AHA, ESC guidelines).
• Native valve endocarditis: Nafcillin or vancomycin monotherapy (depending on sensitivity)
• Prosthetic valve endocarditis:
  • Methicillin-resistant: Vancomycin + rifampin + gentamycin
  • Methicillin-sensitive: (Nafcillin or cefazolin) + rifampin + gentamycin

**methicillin-sensitive staphylococcus aureus (MSSA)**

• Native valve, right-sided (often in context of IVDU): may be treated with two-week course of nafcillin/oxacillin in straightforward cases (e.g. no renal failure, extrapulmonary metastatic infection, or meningitis).
• Native valve, left-sided:
  • Without brain involvement: cefazolin or nafcillin.
  • With brain emboli: cefazolin can't be used (doesn't penetrate brain). Nafcillin is the best agent. If nafcillin can't be tolerated, then vancomycin may be used instead.
• Prosthetic valve: Nafcillin + Rifampin + Gentamycin

**methicillin-resistant staphylococcus aureus (MRSA)**

• Native valve:
  • Vancomycin is 1st line (unless the vancomycin MIC is >1 mg/L, in which case daptomycin is probably superior)
  • Daptomycin is generally 2nd line. If daptomycin is used, combination of daptomycin plus a beta-lactam (e.g. ceftaroline) may enhance efficacy.
• Prosthetic valve:
  • Usually: Vancomycin + rifampin + gentamycin

**enterococcus**

• Third leading cause of endocarditis, accounting for ~10% of non-IVDU endocarditis. However, enterococcus tends to be indolent, so this may be somewhat less common (<10%) among critically ill patients. Unfortunately, enterococcus is rather difficult to kill (often requires synergistic combination of two drugs).
• Sensitive to both penicillin & gentamycin
  • i) (Ampicillin or Penicillin) + Gentamycin.
  • ii) Ampicillin + Ceftriaxone (2 grams IV q12hr)
  • Cannot tolerate ampicillin: (Vancomycin + Gentamycin)
• Sensitive to penicillin (but not gentamycin)
  • Ampicillin + Ceftriaxone (high-dose, 2 grams IV q12hr)
• Resistant to penicillin/ampicillin but not vancomycin
  • (Vancomycin + Gentamycin)
• Resistant to penicillin, aminoglycosides & vancomycin
  • Linezolid or daptomycin may be used.
Linezolid achieved cure in 17/22 patients with Enterococcus faecium.\textsuperscript{11} Daptomycin not supported by much evidence. If used, consider high doses and combination with a beta-lactam (either ampicillin or ceftaroline; AHA guidelines IIb recommendation).

**surgery**

Involvement of cardiologists and cardiothoracic surgeons will help determine which patients may benefit from surgery. Potential indications for surgery are as follows:

**potential indications for surgery in left-sided endocarditis**

- Heart failure (due to valve dysfunction or fistulae).
- Failure to control infection with antibiotics.
  - Myocardial abscess
  - Vegetation enlargement despite antibiotics
  - Persistent fever and positive blood cultures for >7d, with exclusion of other foci of infection (e.g. splenic abscess)
- Prevention of embolism
  - Huge vegetation (>15 mm).
  - Large vegetation (>10 mm) with one or more embolic episodes despite antibiotic therapy.

**potential indications for surgery in right-sided endocarditis**

- Surgery plays smaller role:
  - (a) Better outcomes compared to left-sided endocarditis.
  - (b) Many patients have ongoing IV drug abuse, may infect prosthetic valve.
- Indications to consider surgery:
  - Right heart failure due to severe tricuspid regurgitation with poor response to medical therapy.
  - Failure of antibiotics to clear infection.
  - Tricuspid valve vegetation >20 mm and recurrent pulmonary embolism despite antibiotics.

**contraindications to surgery**

- Inability to tolerate anticoagulation during bypass (e.g. due to recent intracranial hemorrhage or large ischemic stroke).
  - In this situation, surgery may need to be delayed by four weeks (if possible).
- Refractory and ongoing IV drug abuse.
  - Enormous ethical issues regarding the role of surgery in patients with ongoing IV drug use.

**anticoagulation**

**controversial, particularly for prosthetic valve endocarditis:**

- Continuous anticoagulation is generally important for anyone with a mechanical prosthetic valve.
- Anticoagulation may increase the likelihood of hemorrhagic transformation following septic embolic stroke.
- Little high-quality evidence exists on this topic. In the absence of any solid evidence, be sure to discuss anticoagulation decisions with other specialists involved (e.g. cardiology and neurology).

**current recommendations in AHA 2015 guidelines**

- Patients with a mechanical valve who have experienced a CNS embolic event should stop all forms of anticoagulation for two weeks (Class IIa)(1).
- Initiation of aspirin or anti-platelet agents as adjunctive therapy in endocarditis is not recommended.
- Continuation of long-term anti-platelet therapy may be considered for patients without bleeding complications (Class IIb).
- (No recommendation is made regarding continuation of anticoagulation.)
Endocarditis may in some ways be viewed as a symptom of the larger disease of opioid use disorder.

- Patients with opioid use disorder are at enormous risk of endocarditis (e.g. 2-5% per year risk with active IV drug use).^{12}
- One episode of endocarditis is a risk factor for recurrence (due to damage to the heart valves). Therefore, if patients continue to use IV drugs then they are at astronomically high risk of recurrent endocarditis.
- Recurrent endocarditis is a common pathway whereby opioid use disorder leads to death.
- Medication-assisted therapy (MAT) is required for these patients. Simply telling them to stop using opioids won’t work (this is analogous to telling a depressed person to stop being depressed).
- Unfortunately, inpatient medical systems often fail miserably to deliver medication-assisted therapy. One study from a top teaching hospital in 2016 reported that merely 8% of patients admitted with endocarditis and IV drug use were discharged with a plan for medication-assisted therapy.^{13} This isn’t an anomaly – it’s an illustration of a huge gap in our treatment for these patients.
- For patients with endocarditis and opioid use disorder medication-assisted therapy is probably equally important as antibiotics.
  - Get help for these folks – consult addiction psychiatry and connect them with whatever services your hospital & healthcare system has to offer.
  - More on buprenorphine & medication-assisted therapy [here](https://emcrit.org/ibcc/buprenorphine/).

### Endocarditis checklist

- **Initial evaluation**
  - Peripheral blood cultures (three sets at three different sites)
  - Additional culture of any indwelling line in place >48 hours
  - Echocardiography (TTE +/- TEE)
  - Chest CT, if suspect right-sided endocarditis w/ septic pulmonary embolization
  - Evaluate for metastatic infection, if suspected (e.g., spine, joints, spleen, brain)

- **Empiric therapy**
  - Acute bacterial endocarditis: May consider vancomycin* plus cefazolin
  - Subacute bacterial endocarditis: May consider vancomycin* plus ampicillin/sulbactam
  - Prosthetic valve, acute-onset, <1 yr after surgery: May consider vancomycin*, gentamicin, and cefepime
  - Prosthetic valve, acute-onset, >1 yr after surgery: May consider vancomycin*, gentamicin, and cefazolin
  - Prosthetic valve, subacute onset: May consider vancomycin*, gentamicin, ampicillin/sulbactam
  - *Dose vancomycin like you mean it – obtain labs early & consider pharmacokinetic modeling

- **Indications for surgical consultation**
  - Valve regurgitation or fistula causing heart failure
  - Myocardial abscess
  - Vegetation enlargement despite ABX
  - Persistent fever, positive cultures
  - Large vegetation with multiple embolic phenomena

- **Follow course**
  - Adjust antibiotics depending on speciation & sensitivities
  - Obtain single blood culture daily (until blood sterilizes)
  - Monitor on telemetry for heart block (+/- daily EKG)
  - Consider repeat echo (to r/o vegetation growth or worsening valve function)
  - Aggressive management of any metastatic foci of infection (e.g. septic arthritis, splenic abscess)

- **Address opioid use disorder if present**
  - Untreated opioid use disorder is likely to persist and lead to recurrent endocarditis & death.
  - Consider initiation of buprenorphine and close follow-up care.

[The Internet Book of Critical Care, by @PulmCrit](https://emcrit.org/wp-content/uploads/2017/02/endoappr.pdf)

[The Podcast Episode](https://emcrit.org/ibcc/endo/)
Staph lugdunensis ("slug") is a type of coagulase-negative staph which tends to cause invasive infections (more than other types of coagulase-negative Staph). Be careful about writing this off as a contaminant.

Exactly which patients need surgery can be confusing. Infectious disease should always be consulted in these cases. If there is any consideration for possible surgery, then cardiology and cardiothoracic surgery should be involved as well.

Thrombolytic therapy for ischemic stroke is contraindicated in the context of infectious endocarditis.

Do not fail to provide aggressive medication-assisted therapy for associated opioid use disorder.

Be careful about the use of vancomycin mono-therapy for empiric treatment of endocarditis. If you are going to pursue this, check levels early (ideally two levels following the initial dose) and make absolutely sure that the vancomycin is dosed properly.

Direct PDF links to key guidelines referenced in this chapter

- 2015 American Heart Association (AHA) endocarditis guidelines
- 2015 European Society of Cardiology (ESC) endocarditis guidelines

Going further:

- Related chapters in the IBCC:
  - Antibiotics
  - Penicillin allergies don't exist
  - Buprenorphine
- Related FOAMed
  - EMCrit Podcast: Endocarditis with David Carr
  - Best Cases: Endocarditis (David Carr, Anton Helman)
  - Endocarditis (Jacob Avila, RebelEM)
  - Endocarditis (LITFL, Chris Nickson)

References


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The Internet Book of Critical Care is an online textbook written by Josh Farkas (@PulmCrit), an associate professor of Pulmonary and Critical Care Medicine at the University of Vermont.