**AHD – Endocarditis**

**Facilitator Guide**

**Agenda:**

1:05-1:20 PM Theory Burst

1:20-2:15 PM Small groups

2:15 -2:30 PM Questions for the Expert

2:30-2:40 PM Break

2:40-3:20 PM Small groups

3:20-3:30 PM Questions for the expert

**Learning objectives:**

* Identify at risk populations for endocarditis and explain why this risk is increased.
* Initiate appropriate work-up for suspected endocarditis based on history and physical examination.
* Recognize patients who require surgical intervention for infective endocarditis.
* Prescribe appropriate prophylaxis for medical procedures for patients at increased risk of infective endocarditis.

**Case 1:** Mr. Stephan Bovis is a 48-year-old male with h/o IVDU who presents with “passing out”. He was watching TV when he lost consciousness. No symptoms prior to this episode and this has never happened before. He has mild SOB for last week. SOB is present at all times but worse with exertion. He has also noticed 3 weeks of increased fatigue, intermittent fevers, and chills.

PMH: No known PMH

Medications: PRN tylenol

Social: Occasional alcohol consumption, smokes 1 ppd, uses IV heroin. Last use 2 days ago.

Recent injection sites: foot

Physical Exam:

Vitals: T 101, BP 95/45, HR 105, RR 20, 98% RA

Gen: Diaphoretic, mild discomfort

HEENT: PERRL, normal conjunctivae, MMM, multiple dental caries

CV: Tachycardic, regular rhythm, nl S1/S2, no murmur appreciated, no JVD, no edema

Resp: CTAB

Abd: Soft, NT/ND, +BS

Skin: Track marks present on bilateral forearms, no erythema or tenderness of feet at recent injection sites

**1. What is syncope and how might this patient have syncopized? What is your differential diagnosis?**

* **Syncope = transient global cerebral hypoperfusion**
	+ Types: reflex, orthostatic, cardiogenic
		- Reflex: no prodrome
		- Orthostats: orthostats negative in this patient
		- Cardiogenic: most concerning in this patient
	+ Cardiogenic
		- Structural:
			* Valvular
				+ Typically, AS if syncopal presentation

Valves with IE:

* + - * + AR or MR (usually doesn’t cause syncope)
				+ TR, associated with IVDU (usually doesn’t cause syncope)
		- Arrhythmia –
			* In IE, we worry about Heart block (intrinsic or as complication of endocarditis with myocardial abscess)
			* Most commonly associated with aortic valve. Perivalvular abscess can extend into the IV septum that contains the proximal conduction system – can lead to heart block.
	+ DDx: Other etiology of Transient Loss of Consciousness?
		- Neurogenic
			* TIA/Stroke (arterial occlusion) (septic emboli)
			* Intracranial hemorrhage (abscess, mycotic aneurysm)
			* Seizure (abscess as seizure focus)
		- Note: FYI cerebral complications are the most severe and most common extra-cardiac complications (17-20% of patients).
* **Shortness of breath** – possibly due to a complication of endocarditis
	+ Heart failure 2/2 valvulopathy
	+ Septic pulmonary emboli

**Why should we worry about IE in this patient?**

* Fevers (86%-96% of cases)
* Constitutional symptoms- chills, fatigue (non-specific but point towards systemic symptoms from his infection)
* At risk population (IVDU)

 Point: Worried about endocarditis with possible complications of endocarditis causing syncope. The presentation for acute IE is indistinguishable from general causes of sepsis, however; with the subacute illness and risk factors present, it must be considered.

**2. Why does IVDU create risk for endocarditis? What other patients are at risk for endocarditis?**

- **Point:** At risk when valve tissue is damage or replaced

With IVDU the risk for endocarditis is not just due to the potential bacteria being introduced from injecting (that’s the bacteremia risk), there is also damage to the valve from repeated IV injections of solid particles.

At risk:

Endothelial damage: repeated IV injections of solid particles, turbulent blood flow

Chronic inflammation: chronic rheumatic heart disease, degenerative valvular lesions, p rosthetic valves or materials

Other: Age >60, Male Sex, Chronic HD, IV catheter, indwelling cardiac device, oral hygiene or dental pathology, congenital heart disease

**3. What else would you look for on physical exam?**

*Please discuss this in general. Do not need to hit every single point. Percentages listed in case you get asked but do not worry about these details for learners otherwise.*

General: Presenting with syncope, may want to check orthostats (negative in this case)

HEENT:

- Dentition- poor dentition increases risk of endocarditis 2/2 oral flora, Some people who use IV drugs may lick needles which puts them at risk

- Conjunctival hemorrhage (5%)

- \*Roth’s spots (2%) – exudative, edematous hemorrhagic lesions of retina with pale centers. Usually related to subacute bacterial endocarditis, but also leukemia, DM, hypertensive retinopathy

CV:

- New regurgitant murmur (48%)

- Worsening of prior regurgitant murmur (20%)

- Bradycardia 2/2 heart block

Abd/Renal:

- \*Hematuria 2/2 glomerulonephritis (26%)

- Splenomegaly (11%)

MSK:

- Septic joints – warm, erythematous painful joints; effusions

- Signs of abscesses – pinpoint spinal tenderness, psoas sign

Skin:

- Janeway lesions (5%) – non-painful erythematous macular or nodular lesions on hands and feet (reflect microabscesses, vascular phenomena)

-\*Osler’s nodes (3%) – painful (**O**uch **O**sler), red, violaceous raised lesions on pads of fingers and toes (reflect vascular occlusion by microthrombi that cause immune-mediated vasculitis)

- Splinter hemorrhages (8%)

Neuro:

- Signs of abscesses/septic emboli – focal neurologic findings, mental status changes, seizure

\*Immunological phenomena uncommon in acute IE, more characteristic of the more insidious subacute form of untreated IE. Also, right-sided IE usually does not cause peripheral emboli and immunological phenomena.

**4. You are admitting this patient to general medicine service. What work-up do you do?**

*Ask the learners specifics about why and how they would order things. Ask to consider the close & distant anatomical complications!*

-EKG – evaluate for syncope (QT prolongation, LAD/LVH in HOCM, Brugada, WPW, MI, etc), heart block (perhaps from a septal muscle abscess; surgery indications later) & PR prolongation (suggests peri-valvular abscess)

-Blood Cultures

Guideline: Before starting abx at least 3 sets of BCx obtained from different venipuncture sites should be obtained, with the first and last samples drawn at least 1 hour apart. Class I, Level A.

Point: Multiple BCx across time, documents persistent bacteremia.

*Note: If learners bring it up you can look at modified Duke Criteria to see how this relates.*

-Echocardiogram – Transthoracic

Guideline: TTE should be performed in all cases of suspected IE. Class I, Level B.

*Not everyone needs a TEE as TTE may be positive. Some individuals are considered higher risk and will also need a TEE. Additionally, patients with high risk transthoracic echo features should also undergo TEE.* ***We will be discussing more details about high initial patient risk and high risk echo features later.***

Point: Start with TTE. If high initial patient risk, still get TTE but get TEE ASAP after.

 -Evaluate for other potential sources of infection and/or complications

 CXR, UA

**5. What organisms are you concerned about? What empiric antibiotics would you start?**

Organisms:

- IVDU: Staph aureus (MRSA or MSSA), Coag neg Staph, β-hemolytic Strep, Aerobic Gram Neg Bacilli (including Pseudomonas)

- Poor dentition: Viridian Group Strep, Streptococci, HACEK organisms

- Enterococcal

*Reminder*: HACEK organisms: Small fastidious gram negative bacilli. Haemophilus spp. Aggregatibacter spp, Cardiobacterium spp, Eikenella, Kingella spp

Antibiotics:

* Need to cover Staph/Strep including potential methicillin-resistance organisms -> Vancomycin
* Cover gram negative bacilli. Whether to empirically cover for PSA depends on the patient/clinical picture. For this patient would cover with cefepime or other anti-pseudomonal.

**Case Continued:**

CXR was normal. UA was negative for blood, RBCs, WBCs, LE and nitrites. ECG shows NSR. It’s the next morning and you are seeing your patient on pre-rounds. In the quiet of the 7NW bed you now notice a new 2/6 blowing diastolic decrescendo murmur at the 3rd left ICS which increases with isometric hand grip. The patient has just come back from TTE but the results aren’t back yet.

**6. How does this change your plan?**

The patient now should get a TEE regardless of the findings on TTE as they are considered high initial patient risk.

Follow-up question: Who is considered high initial patient risk?

Answer: prosthetic valves, many congenital heart conditions, prior endocarditis, new murmur, heart failure, and stigmata of endocarditis.

**7. What if instead of hearing a murmur, the TTE returns with findings of an 11 mm oscillating vegetation on the anterior leaflet of aortic valve? What is your next step?**

Obtain a TEE because the patient has high risk echo features.

 Follow-up question: What are the high risk echo features?

Answer: large vegetations (> 10 mm in diameter), severe valvular insufficiency, abscess cavities or pseudoaneurysms, valvular perforation or dehiscence, and evidence of decompensated heart failure.

Point: Patients with high risk echo features on TTE should also undergo TEE for detection of complications.

*Note: Below diagram is here for your reference.*



**Case Continued:**

Patient undergoes TEE for the new murmur. TEE shows a 7 mm vegetation on the aortic valve with moderate aortic regurgitation and EF of 55%. Then on hospital day 4 the team gets called for bradycardia on tele.

**8. What are your next steps? What do you think is going on?**

- Obtain a repeat TEE because the patient now has new findings consistent with intracardiac complications.

(Repeat TEE: shows vegetation that is 11 mm in size with abscess extending into interventricular septum.)

- Consult CT surgery

- Discuss moving patient to stepdown level of care

**9. Should this person have surgery? What are the indications for early surgery in left-sided endocarditis?**

Yes, indicated due to the heart block. Size of vegetation alone is not a definite indication for surgery, although still high risk echo feature.

Learners have a blank version of the following table. Work with your team to fill it in.



Levels of evidence

- Valve dysfunction with signs/sx of heart failure (Native Valve Endocarditis, Prosthetic VE). Class I, Level B.

- IE complicated by heart block, annular or aortic abscess, or destructive penetrating lesions (NVE, PVE). Class I, Level B.

- Evidence of persistent bacteremia (or fever) lasting > 5-7 days and other sources excluded (NVE, PVE). Class I, Level B.

- Early surgery considered when caused by fungi or resistant organisms (NVE, PVE). Class I, Level B.

- Early surgery reasonable for:

- Recurrent emboli despite appropriate antibiotic therapy >7 days (NVE, PVE). Class IIa, Level B.

- Mobile vegetation > 10 mm and severe valve regurg (NVE). Class IIa, Level B.

- Early surgery may be considered if mobile vegetation > 10 mm (PVE). Class IIb, Level C.

**Point:** There are some clear indications for surgery but often the decision is a balance of multiple factors and should be a multi-disciplinary decision. In all cases of left-sided, prosthetic valve or complicated endocarditis, consult to cardiac surgeon should be done.

Note: Early surgery is generally considered surgery done during initial hospitalization and before completion of a full course of antibiotics.

**10. What if instead the patient had right-sided endocarditis with septic pulmonary emboli? Is surgery indicated, why or why not?**

No, generally you would treat medically and not pursue surgery.

- Why not? Outcomes are better with right-sided endocarditis. Also, concern for reinfection of prosthetic valve.

Follow-up question: Do the emboli matter?

Answer: Emboli get tricky with left-sided or right-sided IE. Generally, do not pursue surgery for presence of emboli alone. However, recurrent emboli despite appropriate antibiotic therapy would be a reason to consider surgical intervention.

- If do intervene surgically, then *valve repair* rather than replacement should be performed when feasible. Class I, Level C.

 Follow-up question: When else would you consider surgical intervention?

Answer: right heart failure 2/2 severe tricuspid regurgitation with poor response to medical therapy, sustained infection caused by difficult-to-treat organisms (i.e. fungi, MDRO) or lack of response to appropriate antimicrobial therapy, and tricuspid valve vegetations that are ≥20 mm in diameter and recurrent pulmonary emboli despite antimicrobial therapy.

**11. What if instead the patient already had a prior history of endocarditis with a mechanical AVR on warfarin and he presented with recurrent endocarditis with the emboli to brain as above? What would you do with his anticoagulation?**

*Discuss risk vs benefit of clotting valve vs bleeding around brain emboli*

Guideline: Discontinuation of all forms of anticoagulation in patients with mechanical valve IE who have experienced a CNS embolic event for at least 2 weeks is reasonable. Class IIa, Level C (only expert opinion).

**Case Continued:**

Patient undergoes AVR and does well post-operatively. His cultures grew MSSA.

**12. If the patient had prosthetic valve would this change your antibiotics?**

Point: Staph aureus- infected prosthetic valves need combination therapy:

antistaphylococcal beta-lactam OR vancomycin for 6 weeks PLUS rifampin for 6 weeks PLUS an aminoglycoside for 2 weeks

**He completes a 6 week course of nafcillin. He is then seen in the IM Hoxworth clinic to establish care with a new PCP. He hasn’t seen a dentist in years so you refer him to a dentist who recommends deep cleaning and tooth extraction.**

**13. Does the patient need antibiotic prophylaxis? If so, why and with what antibiotic? What are the indications for antibiotic prophylaxis prior to dental procedures?**

Yes, due to prior history of endocarditis.

Prophylaxis with amoxicillin 2 gm 30-60 min prior to procedure

(alternative if allergic: clindamycin, erythromycin, or clarithromycin; cephalexin if rash only)

Indications for antibiotic prophylaxis:

* Prosthetic cardiac valve or prosthetic material used for valve repair
* Previous infective endocarditis
* Cardiac transplantation recipients who develop cardiac valvulopathy
* Some congenital heart disease
	+ Unrepaired cyanotic CHD
	+ Completely repaired CHD with prosthetic material/device during first 6 months after procedure or lifelong if there is residual shunt or valvular regurgitation

**Quick Cases: Which antibiotic would you choose in the following cases?**

|  |  |
| --- | --- |
| 25 yo with history of IVDU with tricuspid valve endocarditis and right leg weakness. MRI shows small abscess. Blood culture with MSSA.  | Nafcillin or Cefazolin x 6 weeks |
| 68 yo M presenting with 4-6 weeks of fevers and weight loss. Blood cultures + for *Strep gallolyticus* | Aqueous penicillin OR ceftriaxone x 4 weeks Note: Could also treat with PCN or CTX PLUS gent for 2 weeks \* Patient also needs a colonoscopy ASAP |
| 40 yo F with history of fistulizing Crohn’s on TPN. Blood cultures with Candida albicans.  | Amphotericin B + flucytosine or Micafungin CT surgery consultLikely will require lifelong suppression with an azole |

 **Supplemental Questions**

**What is your differential diagnosis for culture negative endocarditis?**

Antibiotics administered before cultures drawn (Most common cause)

Brucella

Bartonella

Coxiella burnetti (Q fever)

Chlamydia

Legionella

Mycoplasma

Whipples disease (T whipplei)

Libman Sacks/other autoimmune (rheumatoid, Behcets, etc)

Malignancy (myxoma, etc)

**If you end early – great time to sneak in a generalized antibiotic review for coverage and common adverse effects!**

MRSA Coverage: Ceftaroline, Doxycycline, Daptomycin, Vancomycin, Telavancin, Bactrim, Linezolid, Clindamycin (can be variable), Delafloxacin

PSA Coverage: Piperacillin-Tazobactam, Carbapenems (except ertapenem!), Aztreonam, Cipro/Levofloxacin, Ceftolozane/Tazobactam, Ceftazidime, Cefepime, Ceftazidime/Avibactam, Aminoglycosides, Polymyxin B, Colistin

**Appendix**

**High Risk Echocardiogram features:**

* Large (>10mm in diameter) or mobile vegetations
* Severe valvular insufficiency
* Abscess cavities or pseudoaneurysms
* Valvular perforation or dehiscence
* Evidence of decompensated heart failure

**Modified Duke Criteria for Endocarditis**

|  |
| --- |
| **Definite IE** |
| **Pathologic criteria** |
| Microorganism: demonstrated by culture or histological examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen **OR** |
| Pathologic lesions: vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis. |
| **Clinical criteria** |
| Using specific definitions listed in Table 2: |
| 2 major criteria **OR** |
| 1 major and 3 minor criteria **OR** |
| 5 minor criteria |
| **Possible IE** |
| 1 major criterion and 1 minor criterion **OR** |
| 3 minor criteria |
| Rejected IE |
| Firm alternate diagnosis for manifestations of endocarditis **OR** |
| Resolution of manifestations of endocarditis, with antibiotic therapy for four days or less **OR** |
| No pathologic evidence of infective endocarditis at surgery or autopsy after antibiotic therapy for four days or less |
| Does not meet criteria for possible infective endocarditis, as above |

**Definition of Terms Used in the Modified Duke Criteria for the Diagnosis of IE**

|  |
| --- |
| **Major Criteria** |
| **Blood culture positive for IE** |
| **Typical microorganisms consistent with IE from 2 separate blood cultures** |
| Viridans streptococci |
| *Streptococcus gallolyticus* (formerly *S. bovis*), including nutritional variant strains (*Granulicatella* spp and *Abiotrophia defectiva*) |
| HACEK group: *Haemophilus* spp, *Aggregatibacter* (formally *Actinobacillus actinomycete comitants*), *Cardiobacterium hominis*, *Eikenella* spp, and *Kingella kingae* |
| *Staphylococcus aureus* |
| Community-acquired enterococci, in the absence of a primary focus; **OR** |
| **Persistently positive blood culture, defined as recovery of a microorganism consistent with IE from:** |
| Blood cultures drawn more than 12 hours apart **OR** |
| All of three or a majority of four or more separate blood cultures, with first and last drawn at least one hour apart |
| **Single positive blood culture for *Coxiella burnetii* or antiphase I IgG antibody titer >1:800** |
| **Evidence of endocardial involvement** |
| **Positive echocardiogram for IE** |
| TEE recommended in patients with prosthetic valves, rated at least “possible IE” by clinical criteria, or complicated IE (paravalvular abscess) |
| Definition on positive echocardiogram |
| Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or an implanted material in the absence of an alternative anatomic explanation **OR** |
| Abscess **OR** |
| New partial dehiscence of prosthetic valve |
| **New valvular regurgitation** |
| Increase in or change in preexisting murmur not sufficient |
| **Minor criteria** |
| Predisposition: predisposing heart condition or intravenous drug use |
| Fever: 38.0°C (100.4°F) |
| Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway lesions |
| Immunological phenomena: glomerulonephritis, Osler nodes, Roth spots, and rheumatoid factor |
| Microbiological evidence: positive blood culture but does not meet a major criterion as noted above (excludes single positive cultures for coagulase-negative staphylococci and organisms that do not cause endocarditis) **OR** serological evidence of active infection with organism consistent with IE |
| Echocardiographic minor criteria eliminated |