

CARDIOVASCULAR PATHOLOGY

INFECTIVE ENDOCARDITIS

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Infective Endocarditis

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OUTLINE

- I) MAIN HEADING IN
- II) CONTENT FORMATTING
- III) APPENDIX

- IV) REVIEW QUESTIONS
- V) REFERENCES

I) CAUSES

(A) DEFINITION

- **Endocarditis:** inflammation of the endocardium
 - Inflammation, damage or destruction of the endocardium → forms microbial vegetations
- Recall: The **endocardium** lines the ventricles and more importantly, the valves of the heart

(B) TYPES OF INFECTIVE ENDOCARDITIS (IE)

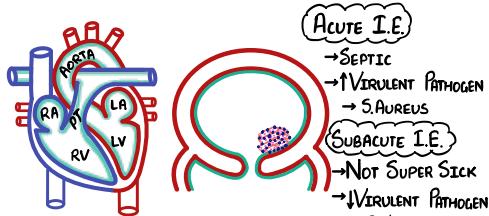


Figure 1. Types of infective endocarditis.

(1) Acute Infective Endocarditis

- Patients look really **septic** (really sick individuals)
 - Hypotensive, high fever, new heart failure symptoms and septic emboli
- Due to a highly virulent pathogen: **S. aureus**

(2) Subacute Infective Endocarditis

- Nonspecific symptoms: low-grade fever, dyspnea and fatigability
- More difficult to diagnose
- Usually due to a low virulent pathogen: **S. viridans**

Table 1. Acute vs subacute IE (Harrison's).

	Acute IE	Subacute IE
Usual Etiology	<i>S. aureus</i> B-hemolytic streptococci Pneumococci Aerobic gram-negative bacilli	<i>S. aureus</i> (sometimes) <i>S. viridans</i> Enterococci HACEK Coagulase-negative staph/strep (prosthetic valves)
Manifestations	High-grade fever (39.4-40°C) Acute/decompensated heart failure	Low-grade fever (rarely >39.4°C) Weight loss, abdominal symptoms, pleurisy
Course	Rapid Hematogenously seeded extracardiac sites Complications are common	Indolent, subtle, and non-specific symptom Rarely metastasizes
Prognosis	Poor (if untreated)	Better prognosis

(C) ABNORMAL VALVES

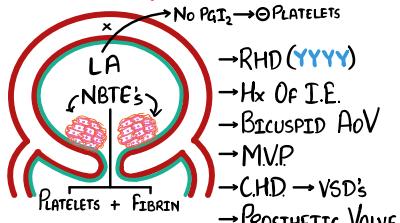


Figure 2. Causes of abnormal valves.

- Predisposes individuals to IE
- Endocardial cells release prostacyclins (PGI₂) and NO → inhibits platelet aggregation
 - Damage to endocardial cells results to inability to release PGI₂ and NO → cannot inhibit platelet aggregation → platelets attach to exposed collagen in damaged endocardium → **platelet plug** forms → **fibrin mesh** stabilizes the platelet plug

(1) Causes of Damaged Heart Valves

Table 2. Causes of abnormal heart valves.

Causes	Rationale
Rheumatic heart disease	Excessive amounts of antibodies that damage the endocardial lining
History of infective endocarditis	Pathogen damages the endocardium → fibrosis exposing the collagen, platelet plug forms, etc.
Bicuspid aortic valve	Patients with bicuspid aortic valve form calcifications and very susceptible to IE
Mitral valve prolapse	Damage to the valve leaflets causing MV degeneration
Congenital heart defects	VSD, truncus arteriosus, TOF, etc <ul style="list-style-type: none"> ● Underlying valvular damage increases the risk of IE
Prosthetic valves	Very high risk for binding of pathogens, platelets and thrombin

- **NBTEs:** non-bacterial thromboemboli

- Composed of platelets and fibrin
- Increases risk for bacterial infection



(D) BACTEREMIA

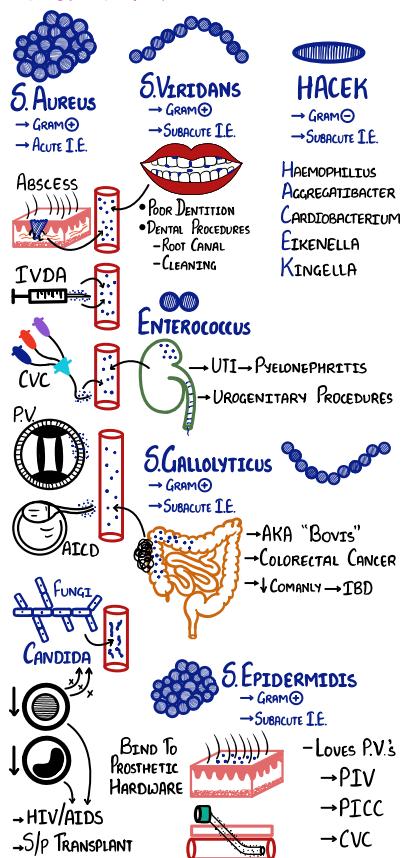


Figure 3. Bacterial and fungal organisms that can cause infective endocarditis.

- NBTEs increase the opportunity for bacterial infection, multiply and colonize → form microbial vegetations leading to damaged valves

(1) *S. aureus*

- Remember: most common cause of **acute IE**
- Gram-positive bacteria
- One of the few types of pathogens that can damage a healthy valve
 - Other bacteria commonly damage a compromised valve

Table 3. Common causes of *S. aureus* spread in the bloodstream.

Causes	Rationale
Skin abscesses	Remember that <i>S. aureus</i> is part of the <u>skin flora</u> <ul style="list-style-type: none"> Skin abscesses form a break in the skin → allowing spread of the bacteria in the bloodstream
IV drug abuse	Using dirty needles that increases risk of injecting bacteria in the bloodstream
Catheters and prosthetic hardware introduction	Example: Central venous catheters <ul style="list-style-type: none"> Catheter is pushed through the skin allowing the bacteria to reach the bloodstream
Prosthetic heart valves, pacemakers, AICD	AICD: automated implanted cardioverter defibrillator

(2) *S. viridans*

- Remember: most common cause of **subacute IE**
- Gram positive bacteria
- Part of the oral flora
 - So any break in the normal barriers introduces the bacteria in the bloodstream
- Examples:
 - Poor dentition
 - Dental procedures (cleaning and root canal)

• Subtypes of *S. viridans*

- S. mitis*
- S. mutans*
- S. oralis*
- S. sanguinis*
- S. milleri*
- S. sobrinus*

(3) HACEK

- Stands for **Haemophilus spp**, **Aggregatibacter spp**, **Cardiobacterium spp**, **Eikenella carodens** and **Kingella spp**
- Gram negative rods
- Causes subacute IE
- Part of the oral flora
 - Has similar mechanism of introduction to *S. viridans*

(4) Enterococcus

- Part of the urogenital tract
- Causes of spread:
 - UTI, specially pyelonephritis**
 - Bacteria can enter the renal circulation
 - Catheter, urinary stent** and other urogenital procedures
 - Provides opportunity for the bacteria to enter through a break in the integrity of the walls

(5) *Streptococcus gallolyticus*

- AKA *Strep bovis*
- Associated with the following:
 - Colorectal cancer**
 - Inflammatory bowel disease** (ulcerative colitis or Crohn's disease)

(6) *Staphylococcus epidermidis*

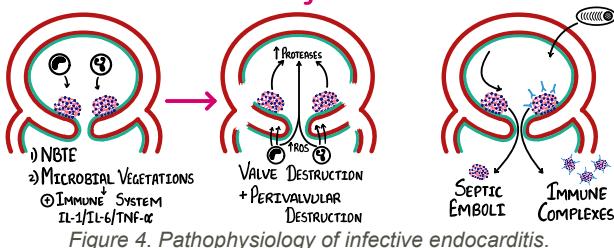
- Gram positive bacteria
- Loves prosthetic valves** and other prosthetic hardwares (AICD or pacemakers)
- Prominent in the skin
- Can travel the bloodstream through a break in the skin
 - PIV, PICC line, CVC

(7) *Candida*

- Fungi
- Not very common pathogen that can cause IE except for immunocompromised patients (e.g. HIV, s/p transplant)
 - In immunocompromised individuals, neutrophils and lymphocytes cannot clear *Candida* in the bloodstream



II) CLINICAL FEATURES AND PHYSICAL EXAMINATION



Recap:

- Inflammation of the endocardium from abnormal valve and bacteremia
 - Exposure of the underlying collagen and formation of platelet plug
 - Platelet plug stabilized by fibrin → NBTEs
 - Bacteremia → pathogen sticks to NBTE in the surface → infiltrates the NBTE → **microbial vegetation**
 - Vegetations stimulate the immune system bringing neutrophils, macrophages, etc. → increases production of cytokines (IL-1, IL-6, TNF- α)

Summary:

- 1) NBTE formation
- 2) Microbial vegetations
- 3) Immune response

(A) IMMUNE RESPONSE

- Immune cells (macrophages and neutrophils) attack the pathogens releasing ROS and proteases
 - Microbes release proteases as well
- Proteases and ROS start eroding both the valvular and perivalvular tissue causing **valve and perivalvular destruction**
 - One of the worst case scenarios
 - Creates an opportunity for abscess formation and prosthetic valve dysfunction
- Vegetations may flick off becoming **septic emboli**
 - Similar to clots in atrial fibrillation
 - May be right-sided or left-sided (*more common*)
- Plasma cells produce antibodies (Ab) against the microbes attacking bacterial antigens (Ag) → circulating Ab-Ag complexes (also called **immune complexes**) which deposit throughout the body

(B) ↑ CYTOKINES

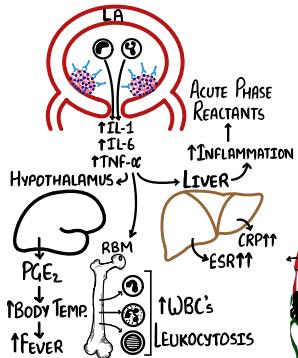


Figure 5. Clinical manifestations from increased cytokines. Take note that this can occur at any valve.

• IL-1, IL-6 and TNF- α

- Stimulates the hypothalamus to release PGE2 → increases the body temperature → **fever**
- Stimulates the bone marrow to produce white blood cells → **leukocytosis (CBC)**
 - "We need more help"
- Stimulates the liver to produce **acute phase reactants** ($\uparrow\uparrow$ **CRP** and $\uparrow\uparrow$ **ESR**)
 - Alerting the body of increased inflammation
 - Very non-specific

(C) ↑ VALVE DESTRUCTION

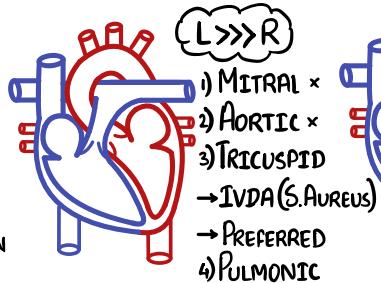


Figure 6. Preference of heart valves in infective endocarditis.

• Left-side is more commonly affected than right-side

- Recall: left side – mitral and aortic; right side – tricuspid and pulmonic valves
- Commonly affected valves arranged in order: (R) **mitral > aortic > (L) tricuspid > pulmonic**
 - EXCEPT for IV drug abusers with *S. aureus* in which the **tricuspid valve** is preferred
 - Mnemonic: TRI not doing drugs

(1) Mitral Valve Destruction

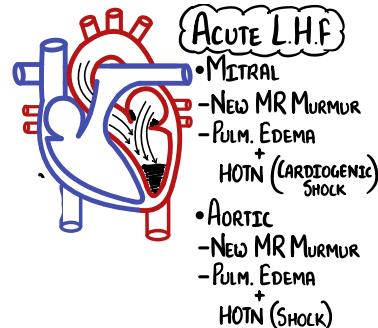


Figure 7. Acute left-sided heart failure symptoms from aortic and mitral valve destruction.

- MV is degenerated or chewed away → shortening of the MV → allows backflow of the blood → **new MV regurgitation murmur**
- Accumulated regurgitated blood flow back to the LV → overfilling of blood → blood accumulation in the left side of the heart → back up of blood in the lungs → **pulmonary edema**
- Every time the ventricle contracts, accumulated blood in the LV can be pushed to the left atrium → ↓stroke volume → ↓cardiac output → **hypotension** → **cardiogenic shock**
 - Example: normal SV is 70 mL; in mitral regurgitation, 50 mL is pushed to the aorta while 20 mL is pushed to the LA → decreased stroke volume

(2) Aortic Valve Destruction

- New aortic regurgitation
- Pulmonary edema
- Hypotension

(3) Acute Left-Sided Heart Failure

- Due to involvement of aortic and/or mitral valves
- Symptoms:
 - Shortness of breath due to pulmonary edema
 - Dyspnea on exertion
 - Paroxysmal nocturnal dyspnea
 - Hypoxemia
 - Hypotension
 - Cold extremities (ill-perfused extremities)
 - New aortic and/or mitral regurgitation



(D) PERIVALVULAR DESTRUCTION

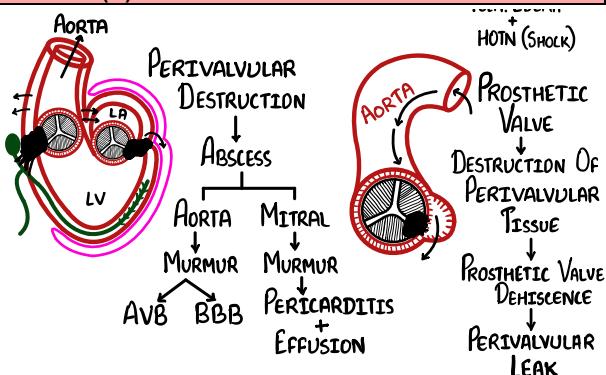


Figure 8. Perivalvular destruction in native and prosthetic valves.

- Vegetation on the valve eats away the perivalvular tissue leading to formation of annular abscess
 - Perivalvular destruction → abscess

(1) Aortic Valve

- Perivalvular destruction in the aortic valve produces **murmur** due to inflammation and dilatation of the aorta
 - Annular destruction may also involve the AV node and the bundle system leading to **AV blocks and bundle branch blocks**

(2) Mitral Valve

- Perivalvular vegetations in the mitral valve can infiltrate the pericardium → **pericarditis ± pericardial effusion**

(3) Prosthetic Valves

- Perivalvular tissues should anchor the prosthetic valve
 - Destruction of the perivalvular tissue separates it from the prosthetic valve leading to **prosthetic valve dehiscence**
- Prosthetic valve dehiscence produce a leak into the ventricle leading to perivalvular leak
 - Leads to **prosthetic valve dysfunction**

(E) SEPTIC EMBOLI

(1) Right-Sided Emboli

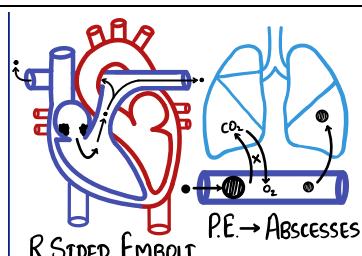


Figure 9. Right-sided emboli resulting to pulmonary embolism and lung abscesses.

- Flicking off pieces of the vegetations in the tricuspid valve → moves to the pulmonary circulation → occludes blood flow → **pulmonary embolism**
 - Symptoms:
 - Dyspnea
 - Increased sputum
- Smaller emboli can pass through the capillaries and infiltrate the lung tissue → **lung abscesses**
 - Small enough and can infiltrate to the lung tissue → **lung abscesses**

(2) Left-Sided Emboli

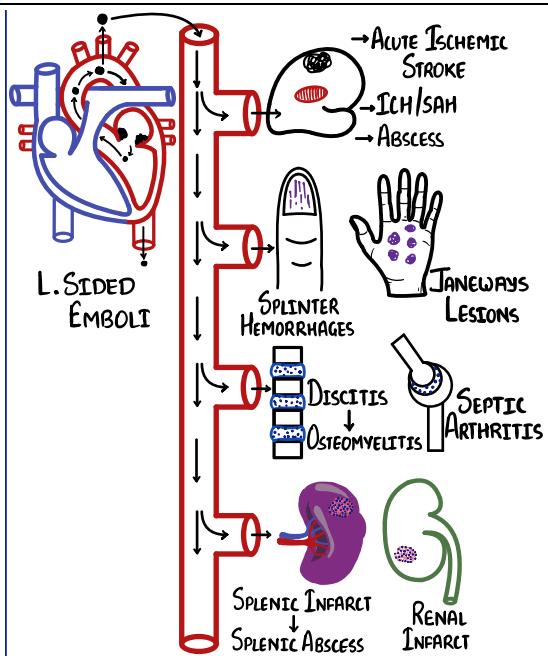


Figure 10. Left-sided emboli causing a variety of clinical manifestations.

- Flicking off pieces of the vegetations moving to the systemic circulation going to different organs of the body (Table 3)

Table 4. Effects of infiltration of vegetation to different organs and blood vessels.

Organ/Vessels	Complication	Symptoms or Clinical Signs
Carotid system	Acute ischemic stroke	Neural deficits, dysarthria, gait preferences, sensory deficits
Brain and its vessels	ICH, subarachnoid hemorrhage Brain abscesses	
Vessels of the nailbeds	Splinter hemorrhages (Figure 11)	
Vessels to the palms and soles	Janeway lesions (Figure 12) Painless lesions	
Vertebrae	Discitis or spondylitis → osteomyelitis Destruction of the discs and vertebrae	Back pain
Joint Tissue	Septic arthritis	Hot painful tender joints
Spleen and its vessels	Splenic infarct Splenic abscess	Significant amount of abdominal pain
Kidney vessels	Renal infarct	Flank pain ↓urine output ↑BUN or Cr





Figure 11. Splinter hemorrhages.



Figure 12. Janeway lesions on the hypothenar eminence [Arora et al., 2012].

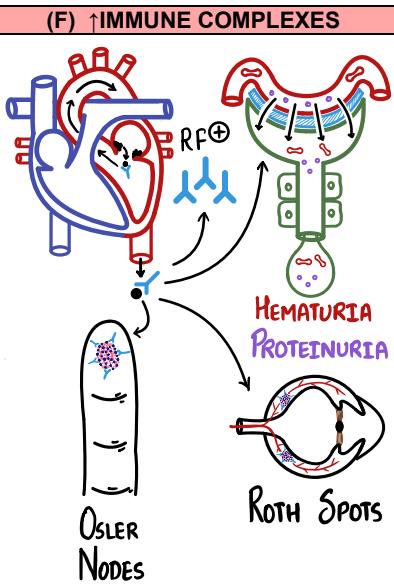


Figure 13. Increased immune complex deposition forming different clinical manifestations.

- Immune complexes can be distributed to the systemic circulation and can be deposited to the following:
 - Pulp of the digits producing painful lesions called **Osler's nodes** (Figure 15)
 - Mnemonic: Osler ouch!
 - Retina leading to hemorrhagic lesions called **Roth spots** (Figure 14)
 - Symptom: Visual changes
 - Glomerulus and glomerular tissue leading to their erosion once immune system attacks → leakage of blood (RBC) and plasma proteins (hematuria and proteinuria) → **glomerulonephritis**
- Specific antibodies for Ab-Ag deposition process: **rheumatoid factor (RF)**

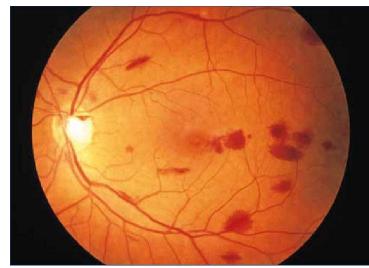


Figure 14. Roth spots [Arora et al., 2012].



Figure 15. Osler's nodes [Dermnet NZ].

Table 5. Summary of clinical findings in IE.

↑Cytokines	Fever Leukocytosis ↑Acute phase reactants (CRP and ESR)
↑Valve destruction	L >>> R <ul style="list-style-type: none"> ○ Mitral > Aortic > Tricuspid > Pulmonary MV or aortic valve regurgitation murmur Pulmonary edema Hypotension
↑Perivalvular destruction	Abscess Aortic valve: <ul style="list-style-type: none"> ○ Murmur ○ AV blocks and bundle branch blocks Mitral valve: <ul style="list-style-type: none"> ○ Pericarditis ± pericardial effusion Prosthetic valves: <ul style="list-style-type: none"> ○ Prosthetic valve dehiscence → prosthetic valve dysfunction
Septic emboli	Right-sided <ul style="list-style-type: none"> ○ Pulmonary embolism ○ Lung abscess Left-sided <ul style="list-style-type: none"> ○ Acute ischemic stroke ○ ICH, subarachnoid hemorrhage ○ Brain abscess ○ Splinter hemorrhage ○ Janeway lesions ○ Discitis or spondylitis → osteomyelitis ○ Septic arthritis ○ Splenic infarct, splenic abscess ○ Renal infarct
Immune complexes	Osler's nodes Roth spots Glomerulonephritis Specific antibodies: Rheumatoid factor



III) DIAGNOSIS

(A) ECHOCARDIOGRAPHY

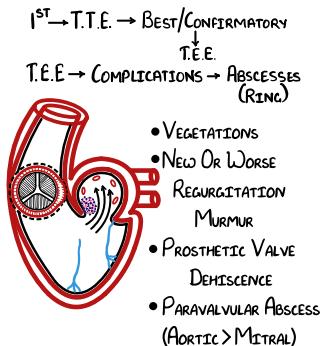


Figure 16. Diagnosis of IE with echocardiogram.

• Transthoracic Echocardiogram (TTE)

- Looking at different views: subxiphoid, parasternal long axis, short axis, apical, etc.
- Provides a global visualization of the heart
- However, it's difficult to have a good look at the AV and MV using this

• Transesophageal Echocardiogram (TEE)

- High specificity and sensitivity (>90%)
- Probe is swallowed allowing visualization of the posterior aspect of the heart
- Another advantage is the visualization of other complications such as ring abscesses

• Look for the following:

- Vegetations
- New or worse regurgitation murmur
 - Using Color Doppler
- Prosthetic valve dehiscence
 - Prosthetic valve rocking back and forth with perivalvular leak
- Perivalvular abscess (ring abscess)
 - More common in aortic than mitral valve

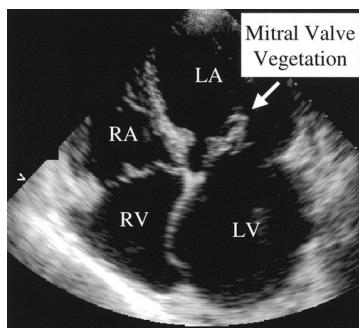


Figure 17. Mitral valve vegetation shown on echocardiogram

[Cabeil et al., 2003].

(B) BLOOD CULTURES

- FIND BACTEREMIA → TYPICAL PATHOGENS
- 3 SETS OF CULTURES

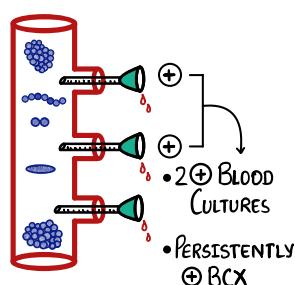


Figure 18. Diagnosis of IE with blood cultures.

• Purpose:

- To prove that bacteremia is present
 - Looking for typical pathogens + *Coxiella burnetii*
- To narrow the antibiotics for specific pathogens

• Three sets of blood culture is obtained

- Draw from different sites at different times
- Get a lot of blood to get a good number of potential bacteria
- Aerobic, anaerobic and fungal cultures
- Remember that IE is an endovascular infection meaning it's continuous

• Bacteremia is established when:

- ≥2 (+) blood cultures OR
- Persistently (+) blood cultures

(C) TESTS FOR SEPTIC EMBOLI

Table 6. Tests for septic emboli.

Brain MRI	<ul style="list-style-type: none"> • Assess for presence of infarct, abscess or bleeds <ul style="list-style-type: none"> ○ For patients with altered mental status
Spinal MRI	<ul style="list-style-type: none"> • Assess for discitis, osteomyelitis or spinal cord abscess
Splenic UTS or CT of abdomen and pelvis	<ul style="list-style-type: none"> • Assess for splenic infarcts or abscesses
Renal UTS	<ul style="list-style-type: none"> • Can show renal vascular emboli • Look for signs of AKI: <ul style="list-style-type: none"> ○ Basic metabolic panel (BMP) - ↑BUN, ↑Cr ○ ↓urine output
Physical Exam	<ul style="list-style-type: none"> • Splinter hemorrhages and Janeway lesions
Chest Xray or CT Scan	<ul style="list-style-type: none"> • CXR: opacities or abnormal nodular vision → proceed to CT scan • CT: look for pulmonary emboli or abscesses

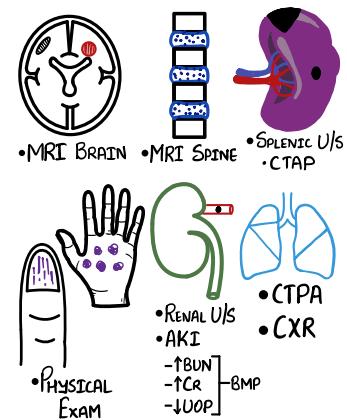


Figure 19. Diagnostic tests and imaging for septic emboli in IE.



(D) TESTS FOR IMMUNE COMPLEXES

Table 7. Tests for immune complexes.

Urinalysis with microscopy	<ul style="list-style-type: none"> • (+) RBC casts, protein • Look for signs of AKI: <ul style="list-style-type: none"> ◦ ↑BUN, ↑Cr, ↓urine output
Fundoscopy	<ul style="list-style-type: none"> • Check for presence of lesions (hemorrhages) on the retina
Physical Examination	<ul style="list-style-type: none"> • Osler's nodes
Rheumatoid Factor	<ul style="list-style-type: none"> • Positive RF

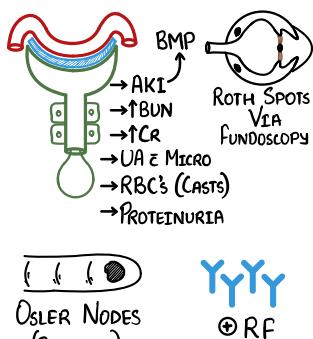


Figure 20. Diagnostic tests for immune complexes in IE.

(E) MODIFIED DUKE'S CRITERIA

- Establishes the diagnosis of infective endocarditis when the following conditions are met:
 - Two major criteria
 - One major criterium + three minor criteria
 - Five minor criteria

(1) Major Criteria

- (+) Echo findings
 - Vegetations, murmur, PV dehiscence, abscess
- (+) Blood culture
 - ≥2 (+) tests OR persistently (+) tests; AND
 - Typical pathogens
 - EXCEPT for *Coxiella burnetii*
 - Does not need to meet the aforementioned circumstances

(2) Minor Criteria

- (+) Fever ($\geq 38^{\circ}\text{C}$ or $\geq 100.4^{\circ}\text{F}$)
- (+) Predisposing factors:
 - Factors for abnormal valves and/or bacteremia
- (+) Septic emboli
- (+) Immune phenomenon
- (+) Blood cultures not meeting major criteria
 - <2 positive cultures or not persistently positive

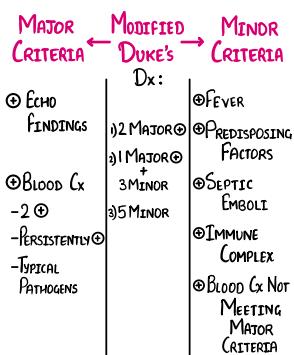


Figure 21. Modified Duke's criteria.

(F) NON-INFECTIVE ENDOCARDITIS

→ NONINFECTIVE ENDOCARDITIS??

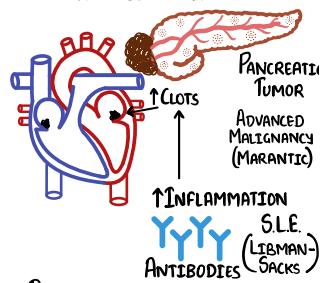


Figure 22. Non-infective endocarditis.

(1) Marantic Endocarditis

- Pancreatic carcinoma
 - Tumor produce cytokines that stimulate clot formation → microclots spread to the valves
 - Microclots are non-septic emboli

(2) Libman-Sacks Endocarditis

- Endocarditis from **SLE (systemic lupus erythematosus)**
 - Body produces a lot of auto-Abs that increase inflammation → increases activity of microthrombi that form on the heart valves

(3) Diagnosis

- Manifestations:
 - Low-grade fevers
 - Little vegetations on the valves (on Echo)
 - Valve dysfunction leading to heart murmurs
 - (-) blood cultures
 - Does not improve on antibiotics
 - It does not always mean non-infective endocarditis; it may also mean IE that needs surgery

(i) Biopsy

- For confirmation

(ii) Look for underlying condition

- More important
- CT of the abdomen or MRCP = pancreatic tumors
- (+) SLE antibodies

IV) TREATMENT

(A) ANTIBIOTICS

- To clear the infection that causes problems such as septic emboli, vegetations, etc.
- Patients are sometimes hemodynamically unstable, especially patients with **acute IE**, where cardiogenic shock can occur
 - Immediately start on empiric antibiotics after taking the blood cultures
 - On **subacute IE**, it's possible to hold off the antibiotics after taking the blood cultures unless they are not as hemodynamically stable as possible



(1) Empiric Antibiotics

- Depends upon the valve affected
- When blood cultures come back positive, narrow the types of antibiotics depending the type of pathogens

(i) Native Valve IE

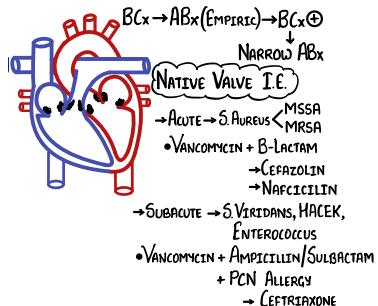


Figure 23. Antibiotics used in native valve IE.

- Vegetations on the mitral, aortic, tricuspid or pulmonary valves
- Establish whether acute or subacute

• Acute IE

- S. aureus*: either MSSA or MRSA
 - Vancomycin + Cefazolin/Nafcillin (β -lactam)**
 - Vancomycin: for MRSA
 - Cefazolin/Nafcillin: augments effect of vancomycin covering MISA

MSSA: Methicillin-susceptible *S. aureus*

MRSA: Methicillin-resistant *S. aureus*

• Subacute IE

- S. viridans, HACEK, Enterococcus*
 - Vancomycin + Ampicillin-Sulbactam (or Ceftriaxone)**
 - Vancomycin: for gram-positive bacteria
 - Ampicillin-Sulbactam: covers HACEK and Enterococci
 - Ceftriaxone** to replace Ampicillin-Sulbactam if there is penicillin allergy

(ii) Prosthetic Valve IE

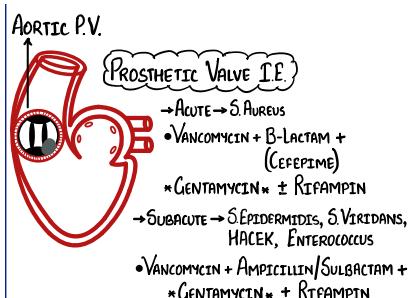


Figure 24. Antibiotics used in prosthetic valve IE.

• Acute IE

- S. aureus*: either MSSA or MRSA
 - Vancomycin + Cefepime (β -lactam) + Gentamicin \pm Rifampin**
 - Cefepime is much more superior than cefazolin/nafcillin in prosthetic valve IE
 - Gentamicin is IMPORTANT for prosthetic valve IE
 - Covers *Staph* species
 - Rifampin can cause bacterial resistance to other Abx so this should be added later on (after 1 week)

• Subacute IE

- S. epidermidis, S. viridans, HACEK, Enterococcus*
 - Recall that *S. epidermidis* love prosthetic hardware
 - Vancomycin + Ampicillin-Sulbactam (or Ceftriaxone) + Gentamicin \pm Rifampin**

Table 8. Summary of empiric Abx used in native and prosthetic valve IE.

		Native Valve IE	Prosthetic Valve IE
Pathogens	Acute	<i>S. aureus</i> (MSSA or MRSA)	
	Sub-acute	<i>S. viridans, HACEK, Enterococci</i>	<i>S. epidermidis, S. viridans, HACEK, Enterococci</i>
Abx	Acute	Vancomycin + Cefazolin/ Nafcillin	Vancomycin + Cefepime + Gentamicin \pm Rifampin
	Sub-acute	Vancomycin + Ampicillin-Sulbactam (or Ceftriaxone) + Gentamicin \pm Rifampin	Vancomycin + Ampicillin-Sulbactam (or Ceftriaxone) + Gentamicin \pm Rifampin

(B) SURGERY

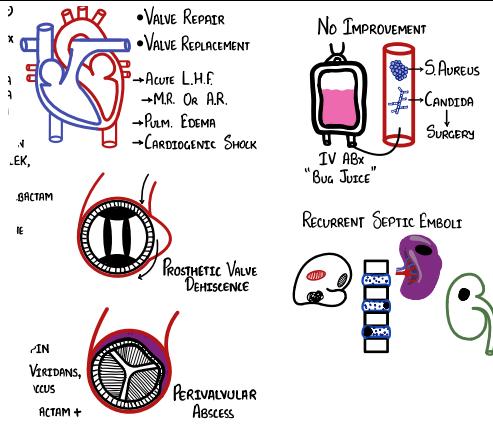


Figure 25. Indications for surgery in IE.

• Valve repair or valve replacement

Depending on the cardiothoracic surgeon's opinion

(1) Indications

- (+) Acute left-sided heart failure**
 - Mitral regurgitation or aortic regurgitation
 - Pulmonary edema
 - Cardiogenic shock
- (+) Prosthetic valve dehiscence**
 - Can lead to acute LHF
- (+) Perivalvular abscess**
 - Abx cannot adequately clear the infections
- (-) Improvement on IV Abx**
- (+) Pathogens that cannot be cleared with antibiotics**
 - Candida* species
 - Need IV antifungals (amphotericin B and/or caspofungin)
 - S. aureus*
- Recurrent septic emboli**
 - Resistant to antibiotics
 - Led to brain abscesses, hemorrhages, mycotic aneurysms, splenic abscess, renal infarcts, discitis



V) ENDOCARDITIS PROPHYLAXIS

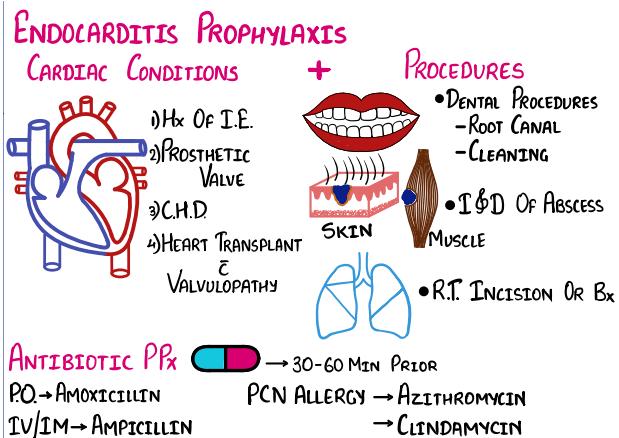


Figure 26. Endocarditis prophylaxis.

- For people who are high-risk (cardiac conditions) and are undergoing specific procedures

(1) Indications

(i) Cardiac Conditions

- History of IE
- Prosthetic valve
- Congenital heart defects
- s/p Heart transplant with associated valvulopathy

(ii) Procedures

- Any simple dental procedure
 - Cleaning
 - Root canal
- Incision and drainage (I&D) of skin or musculoskeletal abscess
- Respiratory tract incision or biopsy
- Insertion of cardiac prosthetic hardware (AICD, pacemakers, etc)

(2) Antibiotic Prophylaxis

- PO (per orem): **amoxicillin**
 - Most common
 - 30-60 mins prior the procedure
- IV or IM: **ampicillin**
- Penicillin allergy: **azithromycin** or **clindamycin**



VI) APPENDIX

Table 23-9 Summary

	Acute Infective Endocarditis	Subacute Infective Endocarditis
Definition	<ul style="list-style-type: none"> Patients are really septic (hypotensive, high fever, new heart failure symptoms, septic emboli) Due to S. aureus 	<ul style="list-style-type: none"> Non-specific symptoms: low-grade fever, dyspnea, fatigability Due to S. viridans (most common), HACEK, Enterococci, S. gallolyticus, S. epidermidis, Candida
Causes	<ul style="list-style-type: none"> Abnormal Valves <ul style="list-style-type: none"> Rheumatic heart disease Hx of IE Bicuspid aortic valve Mitral valve prolapse Congenital heart defects Prosthetic valves 	<ul style="list-style-type: none"> Bacteremia <ul style="list-style-type: none"> S. aureus <ul style="list-style-type: none"> Skin abscesses, IV drug abuse, prosthetic hardwires S. viridans <ul style="list-style-type: none"> Dental procedures, poor dentition HACEK <ul style="list-style-type: none"> Dental procedures, poor dentition Enterococci <ul style="list-style-type: none"> UTI (pyelonephritis), catheters and other urogenital procedures S. gallolyticus <ul style="list-style-type: none"> Colorectal cancers, IBD S. epidermidis <ul style="list-style-type: none"> Loves prosthetic hardwares; skin flora Candida <ul style="list-style-type: none"> Immunocompromised patients
Clinical Manifestations and PE	<ul style="list-style-type: none"> ↑Cytokines <ul style="list-style-type: none"> Fever Leukocytosis Acute Heart Failure Symptoms <ul style="list-style-type: none"> Shortness of breath due to pulmonary edema Dyspnea on exertion Paroxysmal nocturnal dyspnea Orthopnea Hypoxemia Hypotension Cold extremities New aortic and/or mitral regurgitation Left side >>> Right side ↑Perivalvular Destruction <ul style="list-style-type: none"> Murmur AV blocks and BBB Pericarditis +/- pericardial effusion Perivalvular dehiscence → perivalvular dysfunction 	<ul style="list-style-type: none"> Septic Emboli <ul style="list-style-type: none"> Pulmonary embolism (right-sided) Lung abscess (right-sided) Acute ischemic stroke ICH/SAH Abscess Splinter hemorrhages Janeway's lesions Discitis → Osteomyelitis Septic arthritis Splenic infarct → splenic abscess Renal infarct ↑Immune Complexes <ul style="list-style-type: none"> Glomerulonephritis = hematuria and proteinuria Osler nodes Roth spots (+) Rheumatoid factor
Diagnosis	<ul style="list-style-type: none"> Echocardiogram <ul style="list-style-type: none"> Vegetations New or worse regurgitation murmur Prosthetic valve dehiscence Perivalvular abscesses Blood Cultures <ul style="list-style-type: none"> Two positive cultures Persistently positive BCx Tests for Septic Emboli <ul style="list-style-type: none"> Brain MRI Spinal MRI Splenic UTS or CTAP Renal UTS PE CXR or CT scan 	<ul style="list-style-type: none"> Tests for Immune Complexes <ul style="list-style-type: none"> Urinalysis with microscopy Fundoscopy PE Rheumatoid factor Modified Duke's Criteria <ul style="list-style-type: none"> Two major criteria One major criterium + three minor criteria Five minor criteria <u>Major criteria</u> <ul style="list-style-type: none"> (+) Echo findings (+) Blood culture <u>Minor criteria</u> <ul style="list-style-type: none"> (+) Fever (+) Predisposing factors (abnormal valves and/or bacteremia) (+) Septic emboli (+) Immune phenomenon (+) Blood cultures not meeting the major criteria



Differentials	<ul style="list-style-type: none"> Marantic Endocarditis <ul style="list-style-type: none"> (+) Advanced malignancy such as pancreatic carcinoma Clinical Features <ul style="list-style-type: none"> Low grade fevers Little vegetations Heart murmurs (-) Blood cultures Does not improve on Abx Diagnosis <ul style="list-style-type: none"> Biopsy Look for underlying condition 	<ul style="list-style-type: none"> Libmann-Sacks Endocarditis <ul style="list-style-type: none"> (+) SLE
Treatment	<ul style="list-style-type: none"> Empiric Antibiotics <ul style="list-style-type: none"> Native valve IE <ul style="list-style-type: none"> Vancomycin + cefazolin/nafcillin Prosthetic valve IE <ul style="list-style-type: none"> Vancomycin + ceftazidime + gentamicin +/- rifampin 	<ul style="list-style-type: none"> Native valve IE <ul style="list-style-type: none"> Vancomycin + ampicillin-sulbactam (or ceftazidime) Prosthetic valve IE <ul style="list-style-type: none"> Vancomycin + ampicillin-sulbactam (or ceftazidime) + gentamicin +/- rifampin
	<ul style="list-style-type: none"> Surgery <ul style="list-style-type: none"> Valve repair or valve replacement Indications: <ul style="list-style-type: none"> (+) Acute LHF (+) PV dehiscence (+) PV abscess (-) Improvement on IV Abx (+) Pathogens that cannot be cleared with Abx Recurrent septic emboli 	
Prophylaxis	<ul style="list-style-type: none"> Cardiac Conditions <ul style="list-style-type: none"> History of IE PV Congenital heart defects s/p Heart transplant with assoc. valvulopathy Procedures <ul style="list-style-type: none"> Dental procedures I&D Respiratory tract incision or biopsy Insertion of cardiac prosthetic hardware Abx Prophylaxis <ul style="list-style-type: none"> PO: amoxicillin IV: ampicillin Penicillin allergy: azithromycin/clindamycin 	



VII) REVIEW QUESTIONS

- 1) Which of the following is NOT a pathogen for subacute endocarditis?
- S. aureus*
 - S. viridans*
 - Klebsiella*
 - Haemophilus*
- 2) The following are causes of damaged heart valves EXCEPT:
- Infective endocarditis three years ago
 - Mitral valve regurgitation
 - Tetralogy of Fallot
 - Prosthetic valves
- 3) The following can cause spread of *S. aureus* into the bloodstream which may cause IE?
- Dental cleaning
 - IV drug abuse
 - Colorectal cancer
 - Pyelonephritis
- 4) Which of the following is TRUE about *S. aureus*?
- One of the pathogens that can damage healthy valves
 - Gram-positive
 - Most common bacteria causing IE on IV drug abusers
 - All of the above
- 5) Which is a clinical manifestation caused by increased immune complexes?
- Janeway lesions
 - Roth spots
 - Regurgitation murmur
 - Shortness of breath
- 6) What diagnostic tests should you order if a patient with IE presented with altered mental status?
- MRI of the brain
 - CT scan
 - Physical exam is okay
 - None of the above
- 7) A 58/F patient with history of IE, presented with fever. Her spinal MRI revealed abscesses on the vertebral discs. Upon fundoscopy, you observed small hemorrhages in the retina. You ordered blood cultures but only one of the cultures are positive. Her echo findings showed vegetations and perivalvular abscesses. Will you establish IE as diagnosis?
- Yes, it met the Duke's criteria.
 - No, I will order more tests.
- 8) Aside from vancomycin, what antibiotics will you prescribe for a septic IE patient with prosthetic valves?
- Cefazolin
 - Ampicillin-Sulbactam
 - Gentamicin
 - B and C
- 9) What antibiotic prophylaxis is prescribed PO if the patient has no allergies?
- Ampicillin
 - Amoxicillin
 - Clindamycin

VIII) REFERENCES

- Jameson, J. L., & Loscalzo, J. (2015). Harrison's principles of internal medicine (19th edition.). New York: McGraw Hill Education.
- Le T. First Aid for the USMLE Step 1 2020. 30th anniversary edition: McGraw Hill; 2020.
- Papadakis MA, McPhee SJ, Rabow MW. Current Medical Diagnosis & Treatment 2018. New York: McGraw-Hill Education; 2017.
- Sabatine MS. Pocket Medicine: the Massachusetts General Hospital Handbook of Internal Medicine. Philadelphia: Wolters Kluwer; 2020.
- Williams DA. Pance Prep Pearls. Middletown, DE: Kindle Direct Publishing Platform; 2020.

