

Infective endocarditis

Summary

Infective endocarditis (IE) is an infection of the endocardium that typically affects one or more heart valves. The condition is usually a result of bacteremia, which is most commonly caused by dental procedures, surgery, distant primary infections, and nonsterile injections. IE may be acute (developing over hours or days) or subacute (progressive over weeks to months). Acute bacterial endocarditis is usually caused by Staphylococcus aureus and leads to rapid destruction of endocardial tissue, while subacute bacterial endocarditis is most commonly caused by viridans streptococci and generally affects individuals with preexisting damage to the heart valves, structural heart defects, or prosthetic valves. Clinical features include constitutional symptoms (fatigue, fever/chills, malaise), signs of pathological cardiac changes (e.g., new or changed heart murmur, heart failure signs), and, in some cases, manifestations of subsequent damage to other organs (e.g., glomerulonephritis, septic embolic stroke). Management is complex and infectious disease specialists should be involved early. Diagnosis is made based on the Duke criteria, the main features of which are positive blood cultures and evidence of endocardial involvement on echocardiography. Initial treatment of IE consists of empiric IV antibiotics, which are then adapted according to blood culture results and continued for several weeks. Categorization into native valve endocarditis or prosthetic valve endocarditis helps to further tailor regimens. Surgery may be necessary in complex cases (e.g., valve perforation). IE prophylaxis is administered in specific circumstances, e.g., in patients with congenital heart disease having certain dental procedures. IE is typically fatal if left untreated.

FEEDBACK

Pathophysiology

• Pathogenesis [1]

1. Damaged valvular endothelium → exposure of the subendothelial layer → adherence of platelets and fibrin → sterile **vegetation** (microthrombus) 💬
2. Localized infection or contamination → bacteremia → **bacterial colonization** of vegetation → formation of fibrin clots encasing the vegetation → **valve destruction** with loss of function (valve regurgitation) 🗨️ [11]

• Valve involvement [10]

- Frequency of valve involvement: **mitral valve** > aortic valve > tricuspid valve > pulmonary valve
- The tricuspid valve is the most commonly affected valve in persons who inject drugs (associated with Pseudomonas, S. aureus, and Candida).

• Clinical consequences [11][1]

- Bacterial vegetation → **bacterial thromboemboli** → vessel occlusion → infarctions
- Emboli can lead to metastatic infections of other organs.
- Formation of immune complexes and antibodies against tissue antigens → glomerulonephritis, Osler nodes



"Don't **tri drugs** for the sake of your **tricuspid** valves."

• Etiology/epidemiology

- Most are *Streptococcus viridans* (alpha hemolytic) and *Staphylococcus aureus*
- Organism associations
 - *S. viridans*—after dental procedures
 - Group D streptococci—large bowel or genitourinary manipulation
 - *Pseudomonas aeruginosa* and *Serratia marcescens*—intravenous drug users
 - Fungi—after open heart surgery
 - Coagulase-negative *Staphylococcus*—indwelling intravenous catheters
- Highest risk with prosthetic valve and uncorrected cyanotic heart lesions

Note

Staphylococcal endocarditis is more common in those without underlying heart disease. *Strep viridians* is more common in patients with underlying heart disease or after dental procedures.

- Most cases occur after surgical or dental procedures (high risk with poor dental hygiene) are performed.

Global epidemiology

Pathogens causing infective endocarditis (IE)	
Main pathogens	Characteristics
<u>Staphylococcus aureus</u>	• Approximately 35–40% of native valve IE cases ^[1] • Most common cause of acute IE, including persons who inject drugs and patients with prosthetic valves or pacemakers/ICDs ^{[2][3]} • Typically affects healthy valves. • Usually fatal within 6 weeks if left untreated
<u>Viridans streptococci</u>	• Approximately 20% of native valve IE cases ^[1] • Most common cause of subacute IE, especially in predamaged native valves (mainly the mitral valve) • Common cause of IE following dental procedures, respiratory tract incision and biopsy • Produce dextrans that facilitate binding of fibrin-platelet aggregates on heart valves
<u>Staphylococcus epidermidis</u>	• Less than 15% of native valve IE cases ^[1] • Bacteremia from infected peripheral venous catheters ^[4] • Common cause of subacute IE in patients with prosthetic heart valves, pacemakers, or ICDs ^[4]
<u>Enterococci (especially Enterococcus faecalis)</u>	• Approximately 10% of native valve IE cases ^[1] • Multiple drug resistance ^[5] • Common cause of IE following nosocomial UTIs ^[6] • Causes native and prosthetic valve IE • Following gastrointestinal or genitourinary procedures
<u>Streptococcus gallolyticus subsp. gallolyticus (Sgg)</u> ^[5]	• Less than 15% of native valve IE cases ^[1] • Associated with colorectal cancer ^[6] • If Sgg is detected, colonoscopy is indicated.
<u>Gram-negative HACEK group</u> ^[7]	• Less than 5% of native valve IE cases ^{[1][6]} • Physiological oral pharyngeal flora • In patients with poor dental hygiene and/or periodontal infection
<u>Fungal endocarditis (Candida, Aspergillus fumigatus)</u> ^{[7][8]}	• Less than 5% of native valve IE cases ^[1] • At risk groups ◦ Immunosuppressed patients (e.g., patients with HIV or organ transplantation) ◦ Persons who inject drugs ◦ Patients who have received cardiosurgical interventions ◦ Patients with long-term indwelling IV catheters ^[9]
<u>Coxiella burnetii</u> <u>Bartonella species</u>	• Less than 5% of native valve IE cases ^[1] • Gram-negative pathogens responsible for culture-negative endocarditis

Constitutional symptoms ^{[12][1]}

- Fever and chills (seen in ~ 90% of patients) ^[1]
- Tachycardia
- General malaise, weakness, weight loss, night sweats
- Dyspnea, cough, pleuritic chest pain
- Arthralgias, myalgias

! Patients with subacute IE often present with nonspecific flu-like symptoms, while patients with acute IE often present with signs of acute sepsis.

! A high index of suspicion is required in patients with risk factors for IE, as classic extracardiac manifestations (e.g., splinter hemorrhages, Janeway lesions) are absent in the majority of patients. ^{[13][6]}



Cardiac manifestations [12][1]

- Development of a new heart murmur or change in a preexisting murmur (seen in ~ 75% of patients) [1]
 - **Tricuspid valve** regurgitation
 - **Holosystolic** murmur that is loudest at the left sternal border [1]
 - Seen in **persons who inject drugs**, immunocompromised individuals, patients with congenital heart disease, and patients with instrumentation in the right heart (e.g., central venous catheters) [2]
 - **Aortic valve** regurgitation: **early diastolic** murmur that is loudest at the left 3rd and 4th intercostal spaces and along the left sternal border [4]
 - **Mitral valve** regurgitation: **holosystolic** murmur that is loudest at the heart's apex and radiates to the left axilla
- **Heart failure** (e.g., dyspnea, lower limb edema) due to valve insufficiency [1]
- **Arrhythmias**: Suspect a perivalvular abscess in patients with IE who develop a new conduction abnormality (e.g., heart block). [14]

Extracardiac manifestations of IE [12][1]

Extracardiac manifestations are typically caused by septic microemboli and/or immune complex precipitation and are more commonly seen in left-sided IE, with the exception of pulmonary embolic manifestations, which are more common in right-sided IE. [15][1]

- **Peripheral embolic and immunologic phenomena**: seen in only 5–10% of patients. [15][1]
 - **Petechiae**, especially **splinter hemorrhages** (hemorrhages underneath fingernails) [15][1]
 - **Janeway lesions**
 - Small, **nontender**, erythematous macules on palms and soles [15]
 - Microabscesses with neutrophilic capillary infiltration and areas of hemorrhage caused by septic microemboli from valve vegetations
 - **Osler nodes**: **painful** nodules on pads of the fingers and toes caused by immune complex deposition [15]
 - **Roth spots**: round retinal hemorrhages with pale centers [15]
- **Emboli to intraabdominal organs**
 - **Acute renal injury**
 - Including hematuria and anuria
 - Due to renal artery occlusion or glomerulonephritis
 - Splenomegaly and possible LUQ pain
 - Due to splenic artery occlusion or splenic abscess
 - May lead to splenic rupture [16]
- **Neurological manifestations** (e.g., seizures, paresis): due to septic embolic stroke, hemorrhage, meningitis, encephalitis, and/or abscess [17][18]
- **Pulmonary manifestations**: caused by septic emboli resulting from tricuspid valve involvement
 - Signs of pulmonary embolism (e.g., dyspnea)
 - Signs of pulmonary infection, e.g., multifocal pneumonia, lung abscess, and/or empyema. [19]
- **Others**: Arthritis [1]

! Up to one-third of patients with left-sided IE present with symptoms of stroke. [18]

! IE should always be considered as a cause of fever of unknown origin (FUO), especially in the presence of a new heart murmur.

🧠 **"FROM JANE:"** Features of IE include **F**ever, **R**oth spots, **O**sler nodes, **M**urmur, **J**aneway lesions, **A**nemia, **N**ail bed hemorrhage, and **E**mboli.



Splinter hemorrhages in endocarditis

The vertical hemorrhages (arrowheads) underneath this patient's fingernails are most commonly caused by trauma but can also occur as a result of immune complex deposition or microthrombosis in subacute, infective endocarditis, SLE, or rheumatoid arthritis.



Janeway lesions

Multiple erythematous macules are visible on the thenar eminence and the base of the thumb. These Janeway lesions are typically caused by septic microembolisms secondary to infective endocarditis.



Osler nodes

There are multiple raised nodular lesions on the palm and palmar aspects of the first and second digits. The lesions appear dark brown, indicating subcutaneous hemorrhages. This is the typical appearance of Osler nodes.



Roth spots

Fundus photography of a left eye. There are multiple red, white-centered lesions, which reflect small retinal hemorrhages with central accumulation of leukocytes or fibrin thrombocyte emboli (examples indicated by arrowheads). Although these findings were formerly considered to be associated almost exclusively with infective endocarditis, they may actually occur in a variety of conditions, including hypertensive, diabetic, and HIV-related retinopathy; leukemia; and intracranial hemorrhage. Circle: optic disc; M= macula

Table 13-3. Duke Criteria

Major Criteria	Minor Criteria
• Positive blood culture (two separate for usual pathogens; at least two for less common) • Evidence on echocardiogram (intracardiac or valve lesion, prosthetic regurgitant flow, abscess, partial dehiscence of prosthetic valve, new valvular regurgitant flow)	• Predisposing conditions • Fever • Emboli or vascular signs • Immune complex disease (glomerulonephritis, arthritis, positive rheumatoid factor, Osler node, Roth spots [retinal hemorrhages with white centers]) • Single positive blood culture • Echocardiographic signs not meeting criteria

- Complications
 - **Most common—heart failure from aortic or mitral lesions**
 - Others—systemic or pulmonary emboli, myocardial abscess, myocarditis, valve obstruction, heart block, meningitis, osteomyelitis, arthritis, renal abscess, immune complex-mediated glomerulonephritis
- Treatment
 - Organism specific for 4–6 weeks (*S. viridans*, Enterococci, *S. aureus*, MRSA, *S. epidermidis*, HACEK)
 - Heart failure—digitalis, diuretic, salt restriction
 - Surgery—severe aortic or mitral involvement with intractable failure, failure of blood culture to clear, abscess, recurrent emboli, increasing size of vegetations with worsening regurgitation
 - Prophylaxis (AHA, 2007) for:
- Artificial valves
 - Previous history of infective endocarditis
 - Unrepaired or incompletely repaired cyanotic disease, including those with palliative shunts and conduits
 - A completely repaired defect with prosthetic material or device for first 6 months
 - Any residual defect at site of any repair
 - Cardiac transplant which develops a problem in a valve
 - Given ONLY for dental procedures with manipulation of gingival tissue or periapical area or perforation of oral mucosa; incision or biopsy of respiratory tract mucosa and surgery on infected skin or musculoskeletal structures
 - Drug of choice is amoxicillin

