Infective endocarditis

4th year medical lecture

Definition:

- is due to microbial infection of a heart valve (native or prosthetic), the lining of a cardiac chamber or blood vessel, or a congenital anomaly (e.g. septal defect).

- The causative organism is usually a bacterium, but may be a rickettsia, chlamydia or fungus.

- Both native and prosthetic valves can be affected.

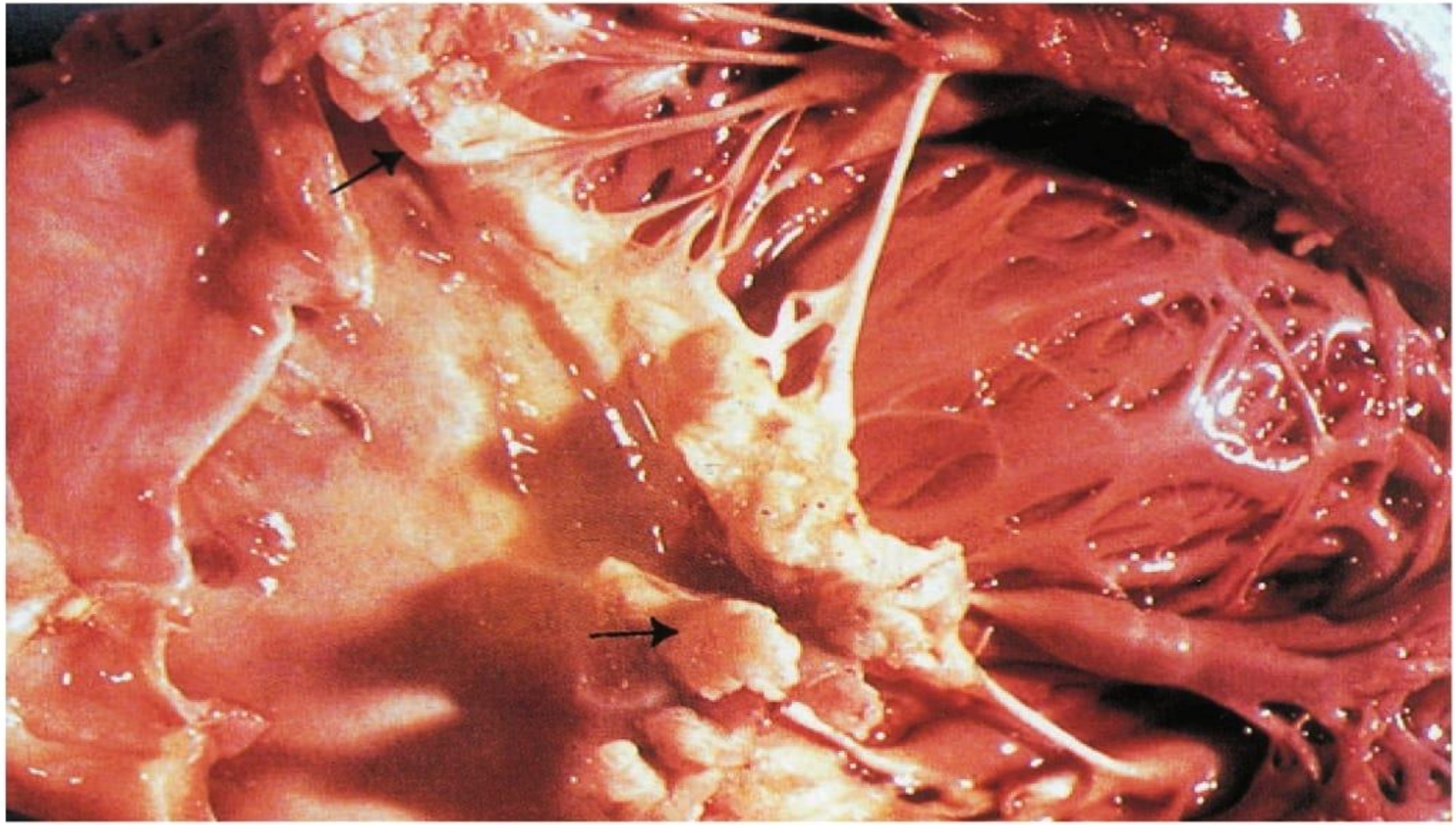
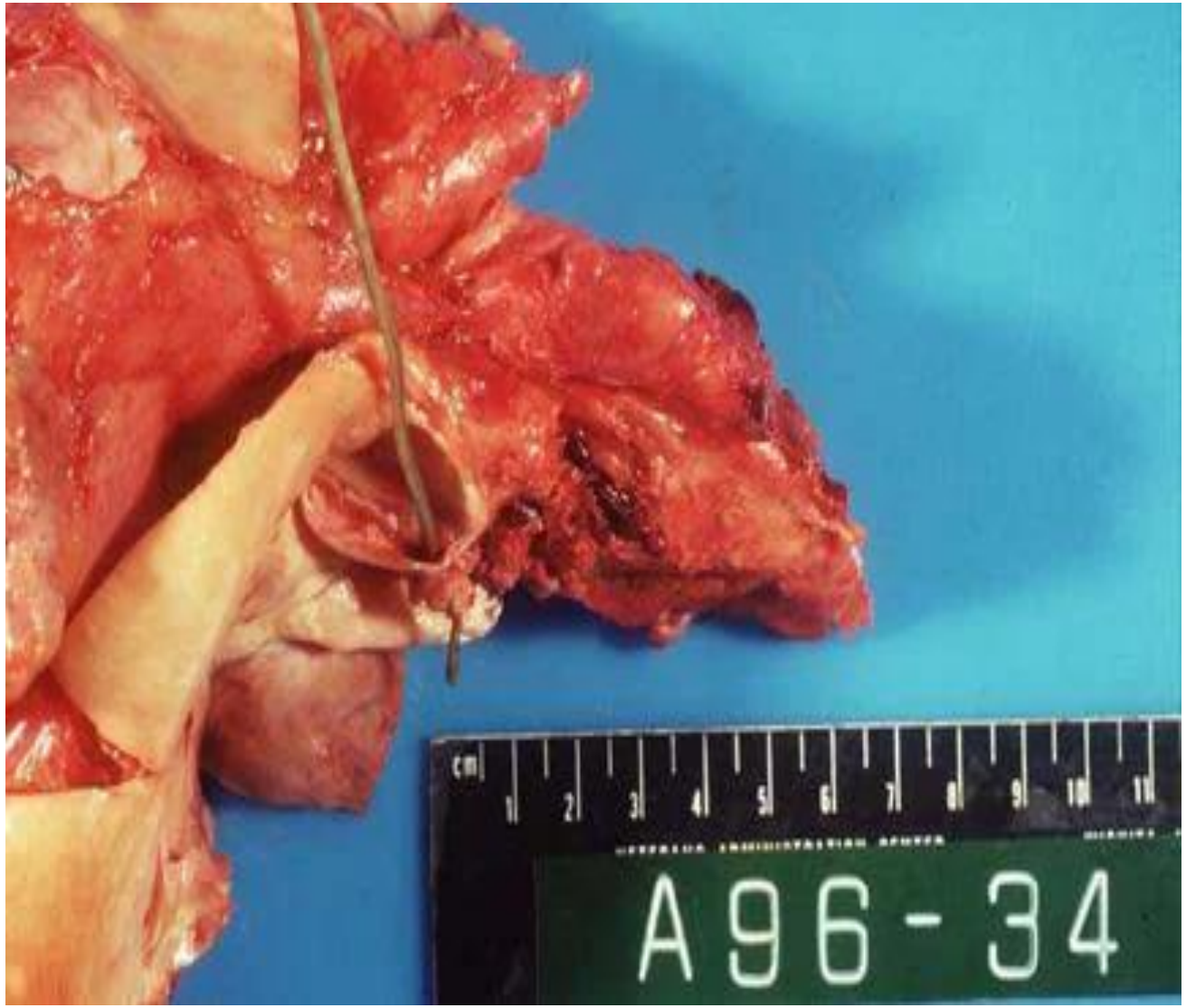


FIGURE 24-1
Vegetations (arrows) due to viridans streptococcal endocarditis involving the mitral valve.



- Acute bacterial endocarditis caused by Staphylococcus aureus with perforation of the aortic valve and aortic valve vegetations. *Courtesy of Janet Jones, MD, Laboratory Service, Wichita Veterans Affairs Medical Center.*

Epidemiology

The incidence of infective endocarditis in community-based studies ranges from 5 to 15 cases per 100 000 per annum.

-More than 50% of patients are over 60 years of age.

-In a large British study, the underlying condition was:

✓ rheumatic heart disease in 24% of patients

✓ congenital heart disease in 19%,

✓and other cardiac abnormalities such as calcified aortic valve or floppy mitral valve in 25%.

✓The remaining 32% were not thought to have a pre-existing cardiac abnormality.

- The case fatality is approximately 20% even with treatment, and is even higher in those with prosthetic valve endocarditis and those infected with antibiotic-resistant organisms.

Pathophysiology

-Infective endocarditis typically occurs at sites of pre-existing endocardial damage.

-but infection with particularly virulent or aggressive organisms such as Staphylococcus aureus can cause endocarditis in a previously normal heart.

-Staphylococcal endocarditis of the tricuspid valve is a common complication of intravenous drug use.

- Many acquired and congenital cardiac lesions are vulnerable, particularly areas of endocardial damage caused by a high-pressure jet of blood, such as *ventricular septal defect, mitral regurgitation* and *aortic regurgitation*, many of which are haemodynamically insignificant.

-In contrast, the risk of endocarditis at the site of haemodynamically important low-pressure lesions, such as a large atrial septal defect, is minimal.

What is the process?

-Infection tends to occur at sites of endothelial damage because they attract deposits of platelets and fibrin that are vulnerable to colonization by blood-borne organisms.

- The avascular valve tissue with presence of fibrin and platelet aggregates help to protect proliferating organisms from host defence mechanisms.

-When the infection is established, vegetations composed of organisms, fibrin and platelets grow and may become large enough to cause obstruction or embolism.

-Adjacent tissues are destroyed and abscesses may form.

- Valve regurgitation may develop or increase if the affected valve is damaged by tissue distortion, cusp perforation or disruption of chordae.

- Extracardiac manifestations, such as vasculitis and skin lesions, may occur as the result of either emboli or immune complex deposition.

- Mycotic aneurysms may develop in arteries at the site of infected emboli.

- In fatal cases, infarction of the spleen and kidneys and, sometimes, an immune glomerulonephritis may be found at postmortem.

Microbiology

-Over three-quarters of cases are caused by ***streptococci or staphylococci***.

-Viridans streptococci which are commensals in the oral cavity, can enter the blood stream on chewing or tooth-brushing, or at the time of dental treatment, and are common causes of subacute endocarditis.

-Other organisms, including Enterococcus faecalis, E. faecium and Strep. gallolyticus subsp. Gallolyticus (previously known as Strep. bovis), may enter the blood from the bowel or urinary tract.

-Patients who are found to have endocarditis caused by Strep. gallolyticus should undergo colonoscopy, since this organism is associated with large-bowel malignancy.

-Staph. aureus has now overtaken streptococci as the most common cause of acute endocarditis.

-It originates from skin infections, abscesses or vascular access sites such as intravenous and central lines, or from intravenous drug use.

-It is highly virulent and invasive, usually producing : vegetations, rapid valve destruction and abscess formation.

-Other causes of acute endocarditis include Strep. pneumoniae and Strep. pyogenes.

-history of contact with farm animals and clinical suspicion of Q fever endocarditis due to Coxiella burnetii, The aortic valve is usually affected and there may also be hepatitis, pneumonia and purpura.

HACEK:

-In about 3–4% of cases, endocarditis may be caused by Gram negative bacteria of the so-called HACEK group (Haemophilus aphrophilus (now known as Aggregatibacter aphrophilus) Aggregatibacter actinomycetemcomitans; Cardiobacterium hominis; Eikenella corrodens; and Kingella kingae).

-These are slow-growing, fastidious Gram-negative organisms that are oropharyngeal commensals.

-The diagnosis may be revealed only after prolonged culture and the organisms may be resistant to penicillin.

Others to be considered:

-Brucella endocarditis is associated with a history of contact with goats or cattle and often affects the aortic valve.

-Yeasts and fungi, such as Candida and Aspergillus, may attack previously normal or prosthetic valves, particularly in immunocompromised patients or those with in-dwelling intravenous catheters

Clinical features

- Endocarditis can take either an acute or a more insidious ‘subacute’ form.

- The subacute form may abruptly develop acute life-threatening complications, such as valve disruption or emboli.

*Subacute endocarditis:

a disease of low virulent organism (most commonly strep. Viridians) that seeds previously abnormal valve)left more than right).

-This should be suspected when a patient with congenital or valvular heart disease develops a persistent fever, complains of unusual tiredness, night sweats or weight loss, or develops new signs of valve dysfunction or heart failure.

-Less often, it presents as an embolic stroke or peripheral arterial embolism.

Other features include purpura and petechial haemorrhages in the skin and mucous membranes, and splinter haemorrhages under the fingernails or toenails.

-**Osler's nodes** are painful, tender swellings at the fingertips that are probably the product of vasculitis; they are rare.

- Digital clubbing is a late sign.

*Acute endocarditis:

-a disease of highly virulent organism (most commonly staph aureus) that seeds previously normal valve , rapidly damages cardiac structures.

- Usually occur in the right side of the heart in addicts.

This presents as a severe febrile illness with prominent and changing heart murmurs and petechiae.

-Clinical stigmata of chronic endocarditis are usually absent.

-Embolic events are common, and cardiac or renal failure may develop rapidly.

-Abscesses may be detected on echocardiography.

-Partially treated acute endocarditis behaves like subacute endocarditis.

*Post-operative endocarditis:

-This may present as an unexplained fever in a patient who has had heart valve surgery.

-The infection usually involves the valve ring and may resemble subacute or acute endocarditis, depending on the virulence of the organism.

-Morbidity and mortality are high and revision surgery is often required.

-The range of organisms is similar to that seen in native valve disease, but when endocarditis

occurs during the first few weeks after surgery it is usually due to infection with a coagulase-negative staphylococcus that was introduced during the perioperative period.

….Post op. endocarditis

-Post-operative endocarditis after cardiac surgery may affect native or prosthetic heart valves or other prosthetic materials.

-The most common organisms are coagulase-negative staphylococci such as Staph. epidermidis, which are part of the normal skin flora , frequently a history of wound infection with the same organism.

-Coagulase-negative staphylococci cause native valve endocarditis in approximately 5% of cases and this possibility should always be considered before they are dismissed as blood culture contaminants.

-causes a rapidly destructive acute endocarditis that is associated with previously normal valves and multiple emboli.

CLINICAL AND LABORATORY FEATURES OF INFECTIVE ENDOCARDITIS

FEATURE	FREQUENCY, %
Fever	80–90
Chills and sweats	40–75
Anorexia, weight loss, malaise	25–50
Myalgias, arthralgias	15–30
Back pain	7–15
Heart murmur	80–85
New/worsened regurgitant murmur	20–50
Arterial emboli	20–50
Splenomegaly	15–50
Clubbing	10–20
Neurologic manifestations	20–40
Peripheral manifestations (Osler's nodes, subungual hemorrhages, Janeway lesions, Roth's spots)	2–15
Petechiae	10–40
Laboratory manifestations	
Anemia	70–90
Leukocytosis	20–30
Microscopic hematuria	30–50
Elevated erythrocyte sedimentation rate	60–90
Elevated C-reactive protein level	>90
Rheumatoid factor	50
Circulating immune complexes	65–100
Decreased serum complement	5–40

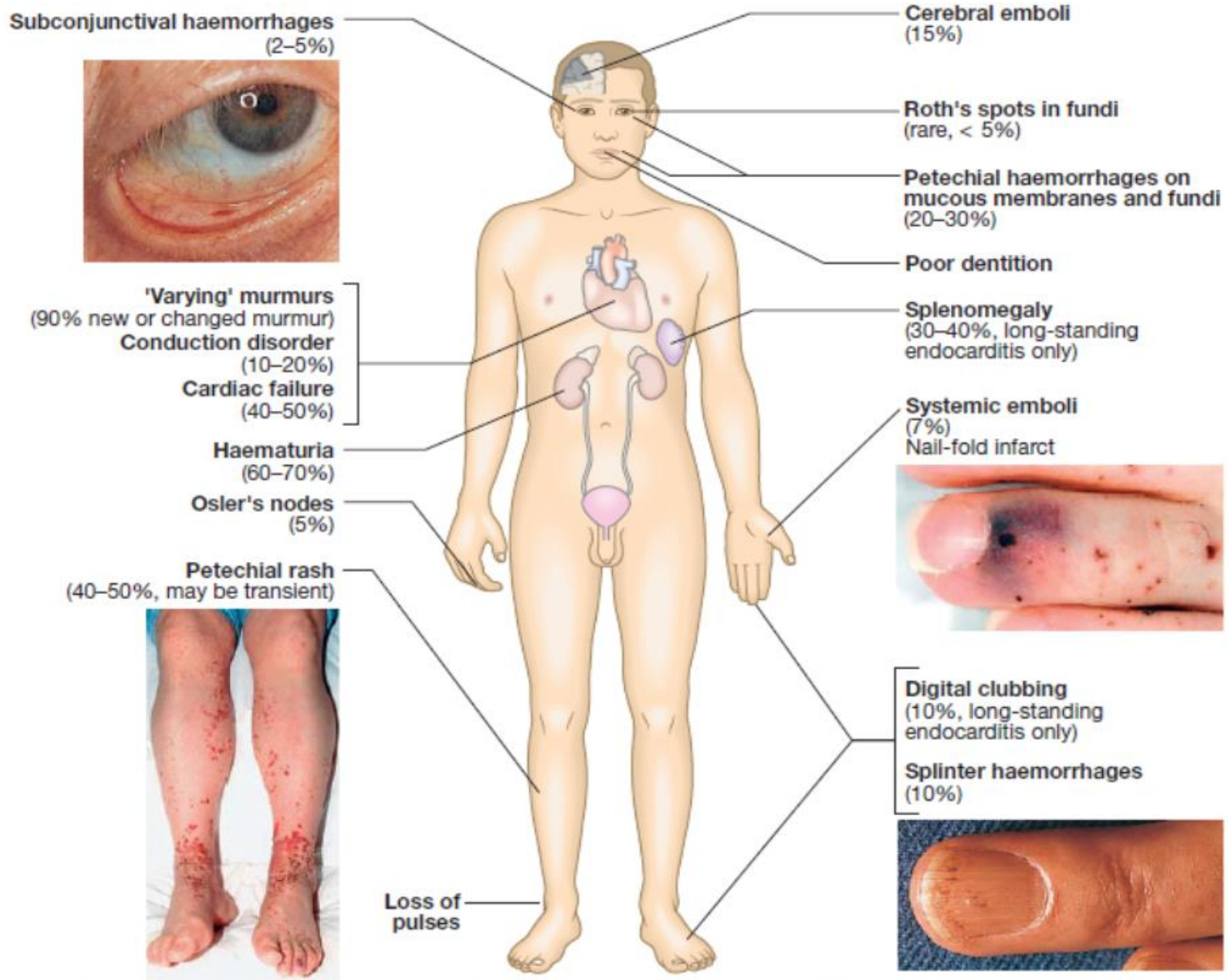


Fig. 16.89 Clinical features that may be present in endocarditis. *Insets (Petechial rash, nail-fold infarct) From Newby D, Grubb N. Cardiology: an illustrated colour text. Edinburgh: Churchill Livingstone, Elsevier Ltd; 2005.*

Pathophysiology of Osler’s and Janeway nodule

- Osler's nodes result from the **deposition of immune complexes**. The resulting inflammatory response leads to swelling, redness, and pain that characterize these lesions. The nodes are commonly indicative of subacute bacterial endocarditis.

- Janeway nodule : the lesion is a **microabscess** of the dermis with **thrombosis of small vessels** without vasculitis. They are caused by septic emboli that deposit bacteria leading to formation of microabscesses

Investigations

- Blood culture
- Echocardiography
- Lab tests

Blood culture:

-pivotal investigation to identify the organism and for planning treatment.

-Three to six sets of blood cultures should be taken prior to commencing therapy and should not wait for episodes of pyrexia.

- In patients with suspected NVE, PVE, or CIED endocarditis who have not received antibiotics during the prior 2 weeks, three 2-bottle blood culture sets, separated from one another by at least 2 h, should be obtained from different venipuncture sites over 24 h.

- If the cultures remain negative after 48–72 h, two or three additional blood culture sets should be obtained, and the laboratory should be consulted or advice regarding optimal culture techniques.

-The first two specimens will detect bacteraemia in 90% of culture-positive cases.

- Taking discrete sets of blood cultures from peripheral sites at intervals of ≥ 6 hours reduces the risk of misdiagnosis due to contamination with skin commensals.

-Isolation of a typical organism in more than one culture provides strong evidence in favour of the diagnosis

-An in-dwelling line should not be used to take cultures.

- Both aerobic and anaerobic cultures are required.

Echocardiography

- is key for detecting and following the progress of vegetations, for assessing valve damage and for detecting abscess formation.
- detects intracardiac complications, and assesses cardiac function.

- Transthoracic or transesophageal

transthoracic echocardiography (TTE) is noninvasive and exceptionally specific ; however, it cannot image vegetations <2 mm in diameter, and in 20% of patients it is technically inadequate. because of emphysema or body habitus, *detects 65–80% of cases but is not optimal for evaluating prosthetic valves or detecting intracardiac complication.*

Transesophageal echocardiography (TEE) is safe and detects vegetations in >90% of patients with definite endocarditis.

**When endocarditis is likely, a negative TEE result does not exclude the diagnosis but rather warrants repetition of the study once or twice in 7–10 days.

- TEE is the optimal method or the diagnosis of PVE, the detection of myocardial abscess, valve perf oration, or intracardiac fistulae and for the detection of vegetations in patients with CIED.

Lab tests

-Elevation of the ESR, a normocytic normochromic anaemia, and leucocytosis are common but not invariable.

-Measurement of serum CRP is more reliable than the ESR in monitoring progress.

-Proteinuria may occur and non-visible haematuria is usually present.

*ECG ECG may show the development of AV block (due to aortic root abscess formation) and occasionally infarction due to emboli.

*CXR may show evidence of cardiac failure and cardiomegaly.

Modified Duke Criteria

- Patients with two major,
- Or one major and three minor,
- Or five minor

➔ *have definite endocarditis.*

- Patients with one major and one minor,
- Or three minor

➔ *have possible endocarditis.*

Major criteria

Positive blood culture:

- *Typical organism from two cultures*
- *Persistent positive blood cultures taken > 12 hrs apart*
- *Three or more positive cultures taken over > 1 hr*

Endocardial involvement:

- *Positive echocardiographic findings of vegetations*
- *New valvular regurgitation*

Minor criteria

- *Predisposing valvular or cardiac abnormality*
- *Intravenous drug misuse*
- *Pyrexia ≥ 38°C*
- *Embolic phenomenon*
- *Vasculitic phenomenon*
- *Blood cultures suggestive: organism grown but not achieving major criteria*
- *Suggestive echocardiographic findings*

Typical microorganisms consistent with IE from two separate blood cultures:

**Staphylococcus aureus*

*Viridans streptococci

**Streptococcus gallolyticus* (formerly *S. bovis*), including nutritional variant strains (*Granulicatella* spp and *Abiotrophia defectiva*)

*HACEK

group: *Haemophilus* spp, *Aggregatibacter* (formerly *Actinobacillus actinomycete comitants*), *Cardiobacterium hominis*, *Eikenella* spp, and *Kingella kingae)*

*Community-acquired enterococci, in the absence of a primary focus

Persistently positive blood culture:

- For organisms that are typical causes of IE: At least two positive blood cultures from blood samples drawn >12 hours apart.

- For organisms that are more commonly skin contaminants: Three or a majority of ≥4 separate blood cultures (with first and last drawn at least one hour apart).

* Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titer greater than 1:800.

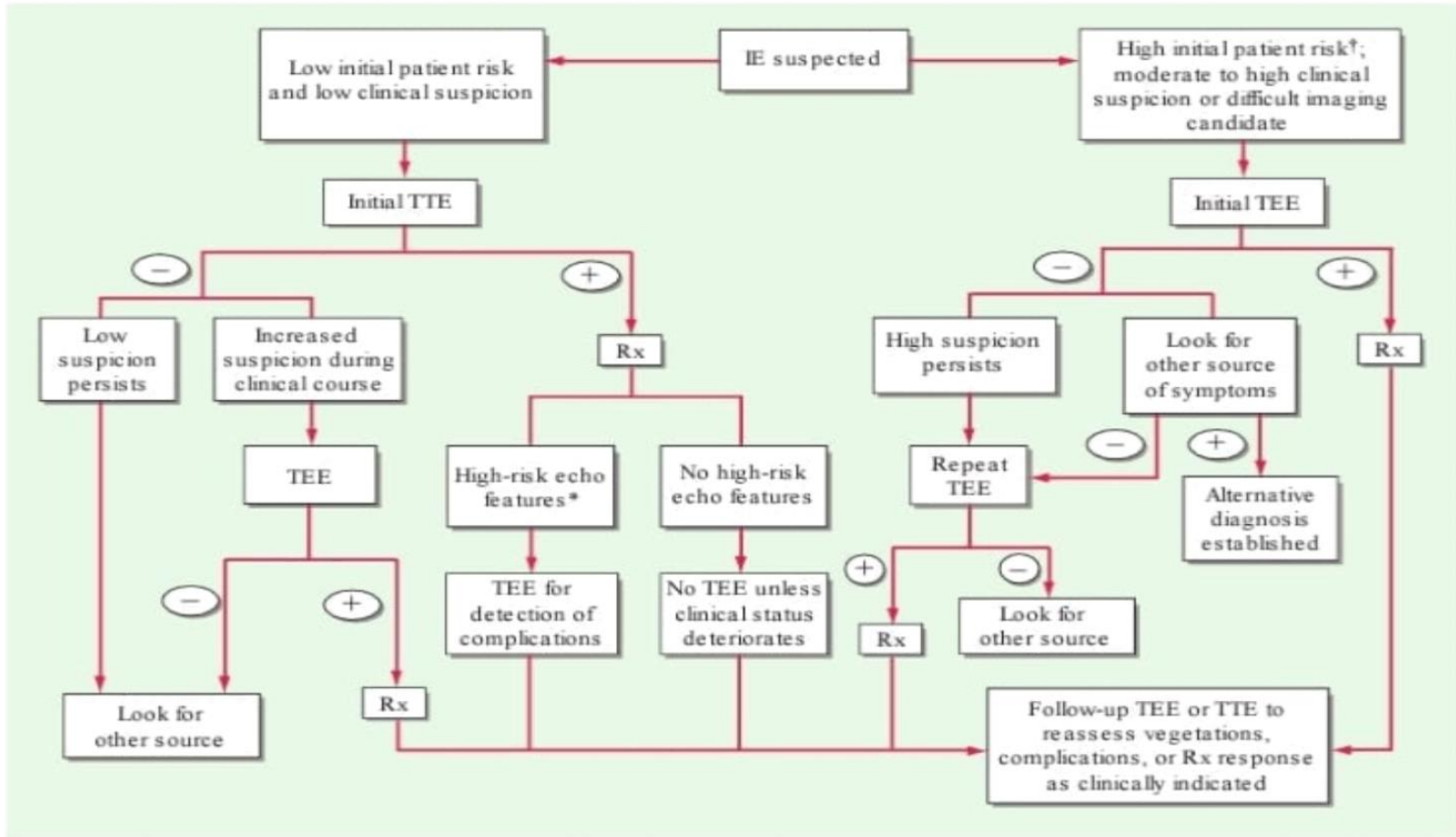


FIGURE 24-4

The diagnostic use of transesophageal and transtracheal echocardiography (TEE and TTE, respectively). †High initial patient risk for infective endocarditis (IE), as listed in Table 24-8, or evidence of intracardiac complications (new regurgitant murmur, new electrocardiographic conduction changes, or congestive heart failure). *High-risk echocardiographic features include large vegetations, valve insufficiency, paravalvular infection, or ventricular dysfunction. Rx indicates initiation of antibiotic therapy. (Reproduced with permission from Diagnosis and Management of Infective Endocarditis and Its Complications. Circulation 98:2936, 1998. ©1998 American Heart Association.)

LEFT sided IE and RIGHT sided IE

- Infective endocarditis occurs most often on the left side (eg, mitral or aortic valve). About 10 to 20% of cases are right-sided (tricuspid or pulmonic valve)

- Right-sided endocarditis: Septic pulmonary emboli may cause cough, pleuritic chest pain, and sometimes hemoptysis. A murmur of tricuspid regurgitation is typical.

Management

-A multidisciplinary approach.

-Any source of infection should be removed as soon as possible; for example, a tooth with an

apical abscess should be extracted.

-Empirical treatment depends on the mode of presentation, the suspected organism and the presence of a prosthetic valve or penicillin allergy.

-If the presentation is subacute, and the culture results are pending, empirical antimicrobial therapy should be withheld initially from hemodynamically stable patients especially those who have received antibiotics within the preceding 2 weeks. Thus, if necessary, additional blood culture sets can be obtained without the confounding effect of empirical treatment.

- Patients with acute endocarditis or with deteriorating hemodynamics who may require urgent surgery should receive empirical treatment immediately after three sets of blood cultures are obtained over several hours.

- if empirical antibiotic treatment is considered necessary, amoxicillin (2 g 6 times daily IV) should be considered (with or without gentamicin).

-If the presentation is acute, empirical therapy should be started with vancomycin (1 g twice daily IV) and gentamicin (1 mg/kg twice daily IV), with dose adjustment based on antibiotic levels.

-Patients with suspected prosthetic valve endocarditis should be treated with vancomycin and gentamicin at the above-mentioned doses, plus rifampicin orally in a dose of 300–600 mg twice daily.

-Following identification of the causal organism, determination of the minimum inhibitory concentration (MIC) for the organism helps guide antibiotic therapy.

- A 2-week treatment regimen may be sufficient for fully sensitive strains of streptococci, provided specific conditions are met.

- Cardiac surgery with débridement of infected material and valve replacement may be required in a substantial proportion of patients, particularly those with Staph. aureus and fungal infections.

ORGANISM	DRUG (DOSE, DURATION)	COMMENTS
Streptococci		
Penicillin-susceptible[b] streptococci, S. gallolyticus	• Penicillin G (2–3 mU IV q4h for 4 weeks)	—
	• Ceftriaxone (2 g/d IV as a single dose for 4 weeks)	Can use ceftriaxone in patients with nonimmediate penicillin allergy.
	• Vancomycin[c] (15 mg/kg IV q12h for 4 weeks)	Use vancomycin in patients with severe or immediate β-lactam allergy.
	• Penicillin G (2–3 mU IV q4h) or ceftriaxone (2 g IV qd) for 2 weeks plus Gentamicin[d] (3 mg/kg qd IV or IM, as a single dose[e] or divided into equal doses q8h for 2 weeks)	Avoid 2-week regimen when risk of aminoglycoside toxicity is increased and in prosthetic valve or complicated endocarditis.
Relatively penicillin-resistant[f]	• Penicillin G (4 mU IV q4h) or ceftriaxone (2 g IV qd) for 4 weeks plus Gentamicin[d] (3 mg/kg qd IV or IM, as a single dose[e] or divided into equal doses q8h for 2 weeks)	Penicillin alone at this dose for 6 weeks or with gentamicin during the initial 2 weeks is preferred for prosthetic valve endocarditis caused by streptococci with penicillin MICs of ≤0.1 μg/mL.
	• Vancomycin[c] as noted above for 4 weeks	—
Moderately penicillin-resistant[g] streptococci, nutritionally variant organisms, or Gemella species	• Penicillin G (4–5 mU IV q4h) or ceftriaxone (2 g IV qd) for 6 weeks plus Gentamicin[d] (3 mg/kg qd IV or IM as a single dose[e] or divided into equal doses q8h for 6 weeks)	Preferred for prosthetic valve endocarditis caused by streptococci with penicillin MICs of >0.1 μg/mL.
	• Vancomycin[c] as noted above for 4 weeks	Regimen is preferred by some.
Enterococci[h]		
	• Penicillin G (4–5 mU IV q4h) plus gentamicin[d] (1 mg/kg IV q8h), both for 4–6 weeks	Can use streptomycin (7.5 mg/kg q12h) in lieu of gentamicin if there is not high-level resistance to streptomycin.
	• Ampicillin (2 g IV q4h) plus gentamicin[d] (1 mg/kg IV q8h), both for 4–6 weeks	—
	• Vancomycin[c] (15 mg/kg IV q12h) plus gentamicin[d] (1 mg/kg IV q8h), both for 4–6 weeks	Use vancomycin plus gentamicin for penicillin-allergic patients (or desensitize to penicillin) and for isolates resistant to penicillin/ampicillin.
	• Ampicillin (2 g IV q4h) plus ceftriaxone (2 g IV q12h), both for 6 weeks	Use for E. faecalis isolates with high-level resistance to gentamicin and streptomycin or for patients at high risk for aminoglycoside

or Gemella species	divided into equal doses q8h for 6 weeks) • Vancomycin[c] as noted above for 4 weeks	Regimen is preferred by some.
Enterococci[h]		
	• Penicillin G (4–5 mU IVq4h) plus gentamicin[d] (1 mg/kg IVq8h), both for 4–6 weeks	Can use streptomycin (7.5 mg/kg q12h) in lieu of gentamicin if there is not high-level resistance to streptomycin.
	• Ampicillin (2 g IVq4h) plus gentamicin[d] (1 mg/kg IVq8h), both for 4–6 weeks	—
	• Vancomycin[c] (15 mg/kg IVq12h) plus gentamicin[d] (1 mg/kg IVq8h), both for 4–6 weeks	Use vancomycin plus gentamicin for penicillin-allergic patients (or desensitize to penicillin) and for isolates resistant to penicillin/ampicillin.
	• Ampicillin (2 g IVq4h) plus ceftriaxone (2 g IVq12h), both for 6 weeks	Use for E faecalis isolates with high-level resistance to gentamicin and streptomycin or for patients at high risk for aminoglycoside nephrotoxicity (see text).
Staphylococci		
MSSA infecting native valves (no foreign devices)	• Nafcillin, oxacillin, or flucloxacillin (2 g IVq4h for 4–6 weeks)	Can use penicillin (4 mU q4h) if isolate is penicillin-susceptible (does not produce β-lactamase).
	• Cefazolin (2 g IVq8h for 4–6 weeks)	Can use cefazolin regimen for patients with nonimmediate penicillin allergy.
	• Vancomycin[c] (15 mg/kg IVq12h for 4–6 weeks)	Use vancomycin for patients with immediate (urticarial) or severe penicillin allergy; see text regarding addition of gentamicin, fusidic acid, or rifampin.
MRSA infecting native valves (no foreign devices)	• Vancomycin[c] (15 mg/kg IVq8–12h for 4–6 weeks)	No role for routine use of rifampin (see text). Consider alternative treatment (see text) for MRSA with vancomycin MIC >1.0 or persistent bacteremia during vancomycin therapy.
MSSA infecting prosthetic valves	• Nafcillin, oxacillin, or flucloxacillin (2 g IVq4h for 6–8 weeks) plus Gentamicin[d] (1 mg/kg IM or IVq8h for 2 weeks) plus • Rifampin[i] (300 mg PO q8h for 6–8 weeks)	Use gentamicin during initial 2 weeks; determine susceptibility to gentamicin before initiating rifampin (see text); if patient is highly allergic to penicillin, use regimen for MRSA; if β-lactam allergy is of the minor nonimmediate type, cefazolin can be substituted for oxacillin/nafcillin.
MRSA infecting prosthetic valves	• Vancomycin[c] (15 mg/kg IVq12h for 6–8 weeks) plus Gentamicin[d] (1 mg/kg IM or IVq8h for 2 weeks) plus Rifampin[i] (300 mg PO q8h for 6–8 weeks)	Use gentamicin during initial 2 weeks; determine gentamicin susceptibility before initiating rifampin (see text).
HACEK Organisms		
	• Ceftriaxone (2 g/d IV as a single dose for 4 weeks)	Can use another third-generation cephalosporin at comparable dosage.
	• Ampicillin/sulbactam (3 g IVq6h for 4 weeks)	—

INDICATIONS FOR CARDIAC SURGICAL INTERVENTION IN PATIENTS WITH ENDOCARDITIS

Surgery Required for Optimal Outcome
Moderate to severe congestive heart failure due to valve dysfunction
Partially dehisced unstable prosthetic valve
Persistent bacteremia despite optimal antimicrobial therapy
Lack of effective microbicidal therapy (e.g., fungal or Brucella endocarditis)
S. aureus prosthetic valve endocarditis with an intracardiac complication
Relapse of prosthetic valve endocarditis after optimal antimicrobial therapy
Surgery to Be Strongly Considered for Improved Outcome[a]
Perivalvular extension of infection
Poorly responsive S. aureus endocarditis involving the aortic or

therapy
Surgery to Be Strongly Considered for Improved Outcome[a]
Perivalvular extension of infection
Poorly responsive S. aureus endocarditis involving the aortic or mitral valve
Large (>10 mm in diameter) hypermobile vegetations with increased risk of embolism, particularly with prior embolic event or with significant valve dysfunction
Persistent unexplained fever (≥10 days) in culture-negative native valve endocarditis
Poorly responsive or relapsed endocarditis due to highly antibiotic-resistant enterococci or gram-negative bacilli

[a]Surgery must be carefully considered; findings are often combined with other indications to prompt surgery.

Antithrombotic therapy in patients with infective endocarditis

- Management of antithrombotic therapy (anticoagulant and antiplatelet agents) in patients with infective endocarditis (IE) is challenging given the competing risks of embolism and intracerebral hemorrhage in this condition and limited evidence on the effects of therapy.

- Anticoagulant and antiplatelet therapy have not been shown to reduce the risk of embolism in IE. Therefore, they are not indicated to reduce the risk of thromboembolic complications of IE.
- However, many patients with IE have indications for antithrombotic therapy, particularly patients with mechanical prosthetic valves.
- In such patients, the potential risks and benefits of antithrombotic therapy must be carefully weighed.
- It is reasonable to discontinue all forms of anticoagulation for 2 weeks in patients with a mechanical valve and IE in whom a CNS embolic event has occurred.
- Antiplatelet therapy should not be initiated as adjunctive therapy upon a diagnosis of IE, although established antiplatelet therapy may be continued in patients with IE who have no bleeding complications

- Failure to sterilize the bloodstream, despite adequate serum levels of appropriate antibiotics, should prompt a search for metastatic infection (eg, abscesses, especially splenic, or mycotic aneurysm).

- Fever lasting longer than 10 days into therapy with an indicated antibiotic regimen should be of concern and should prompt a search for suppurative complications.
- Approximately 30% of patients have a return of fever after the initial response.
- This is usually caused by an intracardiac abscess or metastatic infection.
- Causes of unresponsive fever include myocardial or septal abscesses, large vegetations that resist sterilization, and metastatic infection. Occasionally, fever in patients with uncomplicated IE may take as long as 3 weeks to abate.

Consider prophylaxis against IE in patients at higher risk, including those with the following conditions:

- Presence of prosthetic heart valve
- History of endocarditis
- Cardiac transplant recipients who develop cardiac valvulopathy
- Congenital heart disease with a high-pressure gradient lesion
- Completely repaired congenital heart defect during the 6 month after repair

➢ The presence of a coronary artery stent is <u>not considered</u> to place the patient at high risk for endocarditis.

Prophylaxis must be considered before procedures that may cause transient bacteremia, such as the following:

- Prophylaxis is recommended only when there is manipulation of gingival tissue or the periapical region of the teeth or perforation of the oral mucosa.
- Any procedure involving incision in the respiratory mucosa.
- Procedures on infected skin or musculoskeletal tissue including incision and drainage of an abscess

- Prophylaxis is no longer routinely recommended for gastrointestinal or genitourinary procedures.

- However high-risk patients should be treated before or when they undergo procedures on an infected genitourinary tract or on infected skin and soft tissue.

American Heart Association guidelines for prophylaxis

- The AHA periodically compiles recommendations for IE prophylaxis.
- The guidelines remain unproven by randomized controlled clinical trials; indeed, many examples of failure of these recommendations h
- The 3 major steps in the pathogenesis of IE that are vulnerable to antibiotic prophylaxis are the following:

1. Killing of the pathogen in the bloodstream before it can adhere to the valve

2. Preventing adherence to the valve/fibrin-platelet thrombus

3. Eradicating any organisms that have attached to the thrombus

ave been noted, even when they are applied appropriately.

- The United Kingdom's NICE guidelines on prophylaxis against IE differ from the AHA recommendations. The NICE guidelines do not recommend antibiotic prophylaxis for IE in patients undergoing dental procedures; however, they agree with the AHA guidelines in not recommending prophylaxis for those undergoing procedures in the upper and lower gastrointestinal tracts, the genitourinary tract, or the upper and lower respiratory tracts.

The End