UNIT 2 INFECTIVE ENDOCARDITIS (IE)

Structure

2.0 Objectives

2.1 Introduction

2.2 Definition

2.3 Epidemiology

2.4 Etiological Microorganisms

2.5 Pathogenesis

2.6 Clinical Features

2.7 Diagnosis

2.8 Treatment

2.9 Complications of Infective Endocarditis

2.10 Prevention

2.11 Let Us Sum Up

2.12 Answers to Check Your Progress

2.0 OBJECTIVES

After reading this unit, you should be able to:

- describe the epidemiology, pathophysiology and clinical presentation of infective endocarditis;
- know how to diagnose infective endocarditis by integrating clinical, microbiologic and echocardiographic data;
- recognition of complications of infective endocarditis; and
- describe the principles of management and prevention of infective endocarditis.

2.1 INTRODUCTION

Despite improvements in health care, the incidence of infective endocarditis has not decreased over the past decades. Infective endocarditis is lethal if not aggressively treated with antibiotics, combined or not with surgery. Developments in antibacterial therapy, clinical microbiology, cardiac imaging, and cardiac surgery have revolutionised its diagnosis and prognosis. In this section, we review and update the current literature with respect to pathophysiology, diagnostic challenges and strategies, and management choices in patients with IE.

2.2 DEFINITION

Infective endocarditis (IE) is a microbial infection of the endothelial surface of the heart. The characteristic lesion, the **vegetation**, is a variably sized amorphous mass of platelets and fibrin in which abundant microorganisms and scant inflammatory cells are enmeshed. Heart valves are most commonly involved. However, infection may occur at the site of a septal defect

or on chordae tendinae or mural endocardium. Both native valves and prosthetic valves can be involved.

The terms **acute** and **subacute** are often used to describe IE. **Acute IE** presents with marked toxicity and progresses to valvular destruction and metastatic infection and manifests within days to less than 2 weeks of onset of infection. In contrast, **subacute IE** evolves over weeks (> 2 weeks) to months with only modest toxicity and rarely causes metastatic infection. Acute IE is caused typically, although not exclusively, by staphylococcus aureus,and usually involves a normal heart valve whereas the subacute syndrome is more likely caused by viridans streptococci, enterococci, coagulase-negative staphylococci, or gram-negative coccobacilli.

2.3 EPIDEMIOLOGY

Endocarditis usually occurrs more frequently in men, gender derived ratios range from 1.6 to 2.5. The age specific incidence of endocarditis increased progressively after 30 years of age and exceed 15 to 30 cases per 100,000 person-years in the sixth through eighth decades of life. From 55 to 75 per cent of patients with native valve endocarditis (NVE) have predisposing conditions like rheumatic heart disease, congenital heart disease, mitral valve prolapse, degenerative heart disease, asymmetrical septal hypertrophy, or intravenous drug abuse. From 7 to 25 per cent of cases involve prosthetic valves. Predisposing conditions cannot be identified in 25 to 45 per cent of patients. The nature of predisposing conditions and in part the microbiology of IE correlate with the age of patients.

Rheumatic fever with subsequent rheumatic heart disease in children and young adults is still the most common predisposing cause for IE in developing countries. In recent decades, only the increasing role of intravenous (IV) drug abuse as predisposition for IE and the high IE risk in children and young adults surviving after correction of complex congenital heart disease favour the occurrence of infection in younger patients and the incidence has increased in the elderly because of the increased longeivity and the associated prevalence of degenerative valvular heart disease.

Table 2.1: Predisposing Conditions and Microbiology of Native Valve Endocarditis

Conditions	Neonates (%)	2 MO-15 YR (%)	15-16 YR (%)	> 60yr (%)
Predisposing conditions				
RHD		2-10	25-30	8
CHD	28	75-90	10-20	2
MVP		5-15	10-20	10
DHD			Rare	30
Parenteral dug abuse			15-35	10
Other			10-15	10
None	72		25-45	25-40
Microbiology				
Streptococci	15-20	40-50	45-65	30-45
Enterococci		4	5-8	15
S. aureus	40-50	25	30-40	25-30
Coagulase-negative staphylococci	10	5	3-5	5-8
GNB	10	5	4-8	5
Fungi	10	1	1	Rare

Polymicrobial	4		1	Rare
Other			1	2
Culture negative	4	0-5	3-10	5

Note: RHD = rheumatic heart disease;
CHD = congenital heart disease;
MVP = mitral valve prolapse;
DHD = degenerative heart disease;
GNB= gram-negative bacteria.

Children

Among neonates, IE typically involves the **tricuspid valve** of structurally normal hearts and is associated with very high mortality rates. It is likely that many of these episodes arise as a consequence of infected intra venous and right heart catheters as well as cardiac surgery.

The vast majority of children with IE occurring after the neonatal period have identifiable structural cardiac abnormalities. Rheumatic heart disease is the major predisposition for IE in developing countries. Congenital heart abnormalities, particularly those involving the aortic valve; ventricular septal defects; tetralogy of Fallot; and other complex structural anomalies associated with cyanosis (TGA, single ventricle) are found in remaining cases. Of children with IE on congenital defects, 50 per cent develop infection after cardiac surgery; in these children, infection frequently involves prosthetic valves, valved conduits, or synthetic patches. Mitral valve prolapse generally in association with a regurgitant murmur has been recognized to predispose to IE in children.

Endocarditis among neonates is caused primarily by **S.aureus, coagulase-negative staphylococci, and group B streptococci**. Occasionally infection is caused by gram- negative bacilli and candida species. Among older children, **streptococci**, the predominant cause account for at least 40 per cent of cases, and S. aureus occurring as a nosocomial or community acquired acute infection is the second most common cause of IE.

The clinical features and echocardiographic findings of IE in children are similar to those noted among adults with NVE or PVE, respectively. In contrast, IE among neonates is more cryptic; the clinical picture is dominated by bacteremia, and classical signs of IE are rare.

Adults

Mitral valve prolapse (MVP) has emerged as a prominent, predisposing structural cardiac abnormality and in adults accounts for 7 to 30 per cent of NVE in cases not related to drug abuse or nosocomial infection. This increased risk of endocarditis is largely confined to patients with both prolapse and a mitral regurgitation murmur. Risk is also increased among men and patients older than 45 years. Valve redundancy and thickened leaflets (> 5mm) by echocardiography also identify a population at increased risk for IE.

Rheumatic heart disease was the predisposing cardiac lesion for IE in 20 to 25 per cent. In patients with rheumatic heart disease, endocarditis occurs most frequently on the mitral valve, a site at which women are more commonly infected. The aortic valve is the next most common site for IE; infection in this setting occurs more commonly in men.

Congenital heart disease is the substrate for IE in 10 to 20 per cent of younger adults and 8 per cent of older adults. Among adults, the common predisposing lesions are patent ductus arteriosus, ventricular septal defect, and bicuspid aortic value, the latter particularly found among older men (> 60 years).

Intravenous Drug Abusers

The risk for IE among IV drug abusers, 2 to 5 per cent per patient- year, is estimated to be several fold greater than that of patients with rheumatic heart disease or prosthetic valves.

Endocarditis occurring in IV drug abusers has a unique propensity to infect right heart valves. In clinical series, distribution of valve involvement is tricuspid in 46 to 78 per cent, mitral in 32 to 24 per cent, and aortic in 8 to 19 per cent, (as many as 16 per cent of patients have infection at multiple sites). In IV drug abusers, the valves were normal before infection in 75 to 93 per cent of patients. In contrast to NVE among adults in general, **S aureus causes more than 50 per cent of these infections overall and 60 to 70 per cent of those involving the tricuspid valve**.

Prosthetic Valve Endocarditis

The risk of PVE is greatest during the initial 6 months after valve surgery (particularly during the initial 5 to 6 weeks) and thereafter declines to a lower but persistent risk (0.2 to 0.35 per cent per year)

PVE has been called "**early**" when symptoms begin within 60 days of valve surgery and "**late"** with onset thereafter. These terms were established to distinguish early PVE that arose as a complication of valve surgery from late infection that was more likely community acquired. In fact, many cases with onset between 60 days and 1 year after surgery are likely to be nosocomial and, despite their delayed presentation, derive from events during the surgical admission. Data suggest that during the initial months after valve implantation, mechanical prostheses are at greater risk of infection than bioprosthetic valves but that after 12 months the risk of infection of bioprostheses exceeds that of mechanical valves.

The intracardiac pathology of PVE differs notably from the largely leaflet-confined pathology of NVE. Infection on mechanical prostheses commonly extends beyond the valve ring into the annulus and periannular tissue as well as the mitral-aortic intravalvular fibrosa, resulting in ring abscesses, septal abscesses, fistulous tracts, and dehiscence of the prosthesis with hemodynamically significant paravalvular regurgitation.

Table 2.2: Microbiology of Prosthetic Valve Endocarditis

	NUMBER OF CASES (%)		
	Time of Onset After Valve Surgery		
	<2 mo	2-12 mo	>12 mo
	N-144	N=31	N=194
Streptococci+	2 (1)	3 (9)	61 (31)
Pneumococci	—	—	—
Enterococci	12 (8)	4 (12)	22 (11)
Staphylococcus auresu	32 (22)	4 (12)	22 (11)
Coagulase-negative staphylococci	47 (33)	11 (32)	22 (11)
Fastidious gram-negative Coccobacilli (HACEK group)	—	—	11 (6)
Gram-negative bacilli	19 (13)	1 (3)	11 (6)
Fungi, Candida species	12 (8)	4 (12)	3 (1)
Polymicrobial/ miscellaneous	4 (3)	2 (6)	9 (5)

Diphtheroids	9 (6)	—	5 (3)
Culture Negative	7 (5)	2 (6)	16 (8)

Note: + Includes viridans streptococci, Streptococcus bovis, other nongroup. A groupable streptococci, Abiotrophia Species (nutritionally variant streptococci).

2.4 ETIOLOGIAL MICROORGANISMS

Viridans Streptococci

These streptococci, which cause 30 to 65 per cent of NVE case unrelated to drug abuse, are normal inhabitants of the oropharynx, characteristically produce alpha-hemolysis when grown on sheep blood agar, and are usually nontypable using Lance-field's system. The species causing streptococcal NVE were distributed as follows: **Streptococcus mitior (31 per cent of cases). Streptococcus sanguis (24 per cent). S. bovis (27 per cent), Streptococcus faecalis (now Enterococcus faecalis (7 per cent) and streptococcus salivarius and other species (2 per cent).** S bovis NVE is frequently associated with coexistent colonic polyps or malignancy.

Sreptococcus Pneumoniae

Although pneumococcal bacteremia occurs frequently, S. pneumoniae accounts for only 1 to 3 per cent of NVE cases. When causing IE, S. pneumoniae frequently involves a previously normal aortic valve and progresses rapidly with valve destruction, myocardial abscess formation and acute congestive heart failure (CHF).

Enterococci

E. Faecalis and Enterococcus faecium cause 85 per cent and 10 per cent of cases of enterococcal IE, respectively. Enterococci are part of the normal gastrointestinal flora and cause genitourinary tract infection. **Enterococci account for 5 to 15 per cent of cases of NVE and a similar percentage of PVE cases**. Cases occur in young women as a consequence of genitourinary tract manipulation or infection and in older predominantly male patients, who have the urinary tract as a likely portal of entry. Enterococci infect either normal or previously abnormal valves and present as either acute or subacute IE.

Staphylococci

The coagulase-positive staphylococci are a single species, **s. aureus**. Of the 13 species of coagulase-negative staphylococci that colonize humans, one **s. epidermidis** has emerged as an important pathogen in the setting of implanted devices and hospitalized patients.

S. aureus is a major cause of IE in all population groups. S. aureus IE is characterized by a highly toxic febrile illness, frequent focal metastatic infection and a 30 to 50 per cent rate of central nervous system complications. Among addicts, left-sided S. aureus IE resembles that in nonaddicts. In contrast, in patients with IE limited to the tricuspid valve, complications are rare and mortality rates are only 2 to 4 per cent.

Coagulase-Negative Staphylococci

These are a major cause of PVE, particularly during the initial year after valve surgery, an important cause of nosocomial IE, and the cause of 3 to 8 per cent of NVE cases, usually in the setting of prior valve abnormalities.

Gram-Negative Bacteria

Organisms of the so-called **HACEK group, (Haemophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella species, Kingella kingae**)

which are part of the upper respiratory tract and oropharyngeal flora, infect abnormal cardiac valves, causing subacute NVE and cause PVE that occurs a year or more after valve surgery. In NVE, the HACEK organisms have been associated with large vegetations and a high incidence of systemic emboli. These organisms are fastidious and slow growing; when they are suspected, blood cultures should be incubated for 3 weeks.

P. Aeruginosa is the gram-negative bacillus that most commonly causes endocarditis. Pseudomonal IE involves normal and abnormal valves on both sides of the heart and often causes valve destruction and heart failure.

The rickettsia C. burnetii infects humans after inhalation of desiccated materials from infected animals or contact with infected parturient animals. At variable intervals after acute infection by C. burnetii (Q. fever), persons with abnormal mitral or aortic valves who have not been able to eradicate the organism develop subacute IE with typical manifestations and often with valve dysfunction causing heart failure. The diagnosis is typically based on high IgG and IgA antibody titers to phase I C. burnetii antigens.

Fungi

Candida albicans, and Aspergillus species are the most common of the many fungal organisms identified as causing IE. Fungal endocarditis arises in specific settings. **Valve replacement cardiac surgery and IV drug abuse are major predispositions**. The most frequent fungi causing PVE are C. albicans, Aspergillus species, and nonalbicans Candida species, whereas addiction-associated fungal IE is most commonly caused by nonalbicans, Candida species, particularly C. parapsilosis. Bulky vegetations, which embolize frequently, are common in fungal IE. Removal and careful microbiological evaluation of an embolic vegetation may provide an etiological diagnosis in fungal IE.

Check Your Progress 1

1) What are the predisposing risk factors for endocarditis of native valves in adults?

.....

.....

.....

.....

.....

.....

2) Which congenital heart diseases are associated with IE?

.....

.....

.....

.....

.....

.....

3) List the organisms that are associated with IE of native valves in patients who are not intravenous drug users?

.....

.....

.....

.....

.....

.....

.....

4) What are HACEK group of organisms?

.....

.....

.....

.....

.....

2.5 PATHOGENESIS

The interactions between the human host and selected microorganisms that culminate in IE involve the vascular endothelium, hemostatic mechanisms, the host immune system, gross anatomic abnormalities in the heart, surface properties of microorganisms, and peripheral events that initiate bacteremia. Endothelial damage results in platelet-fibrin deposition, which in turn is more receptive to colonization by bacteria than is the intact endothelium. It is hypothesized that platelet-fibrin deposition occurs spontaneously in persons vulnerable to endocarditis and that these deposits, called **nonbacterial thrombotic endocarditis (NBTE)** are the sites at which micro organisms adhere during bacteremia to initiate IE. Bacteremia is the initiating event that ultimately converts NBTE to IE. Bacteremia rates are highest for events that traumatize the oral mucosa, particularly the gingiva, and progressively decrease with procedures involving the genitourinary tract and the gastrointestinal tract.

The platelet-thrombin deposits are found at the valve closure-contact line on the atrial surfaces of the mitral and tricuspid valves and on the ventricular surfaces of the aortic and pulmonic valves, the sites of infected vegetations in patients with IE.

Three hemodynamic circumstances may injure the endothelium, initiating NBTE: (1) a high velocity jet impacting endothelium (2) flow from a high to a low pressure chamber and (3) flow across a narrow orifice at high velocity. Flow through a narrowed orifice, as a consequence of venturi's effect, deposits bacteria maximally at the low-pressure sink immediately beyond an orifice or at the site where a jet stream impacts a surface.

To cause IE, the organism must be able to persist and propagate on the endothelium. This requires resistance to host defenses. The complement-mediated bactericidal activity of serum limits the ability of susceptible aerobic gram-negative bacilli to cause IE. Those organisms that most frequently cause endocarditis adhere more vigorously in vitro to cardiac valves than do organisms that rarely cause IE.

Adhere to damaged valves. Together, *Staph aureu*s, *Streptococcus* spp, and enterococci are responsible for more than 80 per cent of all instances of disease. These organisms have surface adhesins that mediate attachment to the vegetation. Fibronectin has been identified as an important factor in this process.

Pathophysiology

The clinical manifestations of IE result from

- the local destructive effects of intracardiac infection;
- the embolization of bland or septic fragments of vegetations to distant sites, resulting in infarction or infection;
- the hematogenous seeding of remote sites during continuous bacteremia; and
- an antibody response to the infecting organism with subsequent tissue injury due to deposition preformed immune complexes or antibody complement interaction with antigens deposited in tissues.

2.6 CLINICAL FEATURES

The interval between the presumed initiating bacteremia and the onset of symptoms of IE is estimated to be less than two weeks in more than 80 per cent of patients with NVE. Interestingly, in some patients with intraoperative or perioperative infection of prosthetic valves, the incubation period may be prolonged (2 to 5 or more months).

Table 2.3: Clinical Features of Infective Endocarditis

Symptoms	Per cent	Signs	Per cent
Fever	80-85	Fever	80-90
Chills	42-75	Murmur	80-85
Sweats	25	Changing/New murmur	10-40
Anorexia	25-55		
Weight loss	25-35	Neurological abnormalities	30-40
Malaise	25-40		
Dyspnea	20-40	Embolic event	20-40
Cough	25	Splenomegaly	15-50
Stroke	13-20	Clubbing	10-20
Headache	15-40	Peripheral manifestation	
Nausea/vomiting	15-20		
Myalgia/arthralgia	15-30	Osler's nodes	7-10

Chest pain	8-35	Splinter hemorrhage	5-15
Abdominal pain	5-15		
Back pain	7-10	Petechiae	10-40
Confusion	10-20	Janeway lesion	6-10
		Retinal lesion/ Roth's spots	4-10

Osler's nodes are small, tender subcutaneous nodules that develop in the pulp of the digits or occasionally more proximally in the fingers and persist for hours to several days. These too are not pathognomonic for IE.

Janeway lesions are small erythematous or hemorrhagic macular nontender lesions on the palms and soles and are the consequence of septic embolic events.

Roth spots, oval retinal hemorrhages with pale centers, are infrequent findings in patients with IE.

The **hallmarks of IE are fever and new murmur (over 85 per cent)**. However, fever may be absent in the elderly and the uremic or immunosuppressed population. Murmurs may be absent with right sided or mural infections or intracardiac device infection.

Systemic emboli are among the most common clinical sequelae of IE. Emboli often antedate diagnosis. Although embolic events may occur during or after antimicrobial therapy, the incidence decreases promptly during administration of effective antibiotic therapy. Embolic splenic infarction may cause left upper quadrant abdominal pain and left shoulder pain. Renal emboli may occur asymptomatically or with flank pain and may cause gross or microscopic hematuria. Embolic stroke syndromes, predominantly involving the middle cerebral artery territory, occur in 15 to 20 per cent of patients with NVE and PVE. Coronary artery emboli are common findings at autopsy but rarely result in transmural infarction. Emboli to the extremities may produce pain and overt ischaemia, and those to mesenteric arteries may cause abdominal pain, ileus, and guaiac positive stools.

Neurological symptoms and signs occur in 30 to 40 per cent of patients with IE, are more frequent when IE is caused by S. aureus, and are associated with increased mortality rates. Embolic stroke is the most common and clinically important of the neurological manifestations. Intra-cranial hemorrhage occurs in 5 per cent of patients with IE. Bleeding results from rupture of a mycotic aneurysm, rupture of an artery due to septic arteritis at the site of embolic occlusion, or hemorrhage into an infarct. Mycotic aneurysms, with or without rupture occur in 2 to 10 per cent of patients with IE: approximately half of these involve intracranial arteries. Cerebritis with microabscesses complicates IE caused by invasive, pathogens such as S. Aureus, but large brain abscesses are rare. Purulent meningitis complicates some episodes of IE caused by S. aureus or S. pneumoniae, but more typically the cerebrospinal fluid has an aseptic profile. Other neurological manifestations include severe headache (a potential clue to a mycotic aneurysm), seizure, and encephalopathy.

CHF complicating IE is primarily the result of valve destruction or distortion or rupture of chordae tendinae. Intracardiac fistulas, myocarditis, or coronary artery embolization may occasionally contribute to the genesis of CHF.

Renal insufficiency as a result of immune complex-mediated glomerulonephritis occurs in less than 15 per cent of patients with IE. Azotemia as a result of this process may develop or progress during initial therapy. Renal dysfunction in patients with IE is most commonly a manifestation of

impaired hemodynamics or toxicities associated with antimicrobial therapy (interstitial nephritis or aminoglycoside-induced injury).

2.7 DIAGNOSIS

The symptoms and signs of endocarditis are often constitutional and, when localized, often result from a complication of IE rather than reflect the intracardiac infection itself. Consequently, inorder to avoid over looking the diagnosis of IE, a high index of suspicion must be maintained. **The diagnosis must be investigated when patients with fever present with one or more of the cardinal elements of IE: a predisposing cardiac lesion or behaviour pattern, bacteremia, embolic phenomenon, and evidence of the active endocardial process**. Because patients with prosthetic heart valves are always at risk for PVE, the presence of fever or new prosthesis dysfunction at any time warrants considering this diagnosis.

Even when the illness seems typical of endocarditis, the definitive diagnosis requires positive blood cultures or positive cultures (or histology or polymerase chain reaction recovery of a microorganism's DNA) from the vegetation or embolus.

Duke Criteria of Infective Endocarditis (Modified)

A) ***Definitive Infective Endocarditis***

1) *Pathological Criteria*

- Micro organism: demonstrated by culture or histology in a vegetation; or in a vegetation that has embolized, or in an intra cardiac abcess, or
- Pathological lesions: vegetation or intracardiac abscess present, confirmed by histology showing active endocarditis.

2) *Clinical Criteria,* using specific definitions listed below:

- Two major criteria, or
- One major and three minor criteria, or
- Five minor criteria.

B) ***Possible Infective Endocarditis***

- One major +1 minor or 3 minor.

C) ***Rejected***

- Firm alternative diagnosis for manifestations of endocarditis, or
- Sustained resolution of manifestations of endocarditis, with antibiotic therapy for 4 days or less, or
- No pathological evidence of infective endocarditis at surgery or autopsy, after antibiotic therapy for 4 days or less.

Clinical Criteria for Diagnosis of Infective Endocarditis

Major Criteria

1) *Positive blood culture*

- Typical microorganism for infective endocarditis from two separate blood cultures

  Viridans streptococci, Streptococcus bovis, HACEK group or Community-acquired Staphylococcus aureus or enterococci in the absence of a primary focus, or

- Persistently positive blood culture, defined as recovery of a microorganism consistent with infective endocarditis 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 1 hr apart Q fever serology

2) *Evidence of Endocardial Involvement*

- Positive echocardiogram

- Oscillating intracardiac mass, on valve or supporting structures, or in the path of regurgitant jets, or on implanted material, in the absence of an alternative anatomical explanation, or Abscess, or

- New partial dehiscence of prosthetic valve, or

- New valvular regurgitation (increase or change in preexisting murmur not sufficient)

Minor Criteria

- Predisposition: predisposing heart condition or intravenous drug use

- Fever $\geq$ 38.0 ^{o} C (100.4^{o} F)

- Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhage, Janeway lesions

- Immunological phenomena: glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor

- Microbiological evidence: positive blood culture but not meeting major criterion as noted previously (excluding single positive cultures for coagulase-negative staphylococci and organisms that do not cause endocarditis) or serologic evidence of active infection with organism consistent with infective endocarditis.

Adapted from Durack, D.T., Lukes, A.S., Bright, D.K., "New Criteria for Diagnosis of Infective Endocarditis: Utilization of Specific Echocardiographic Findings", *Am J Med 96:200*, 1994.

For the clinical diagnosis of infective endocarditis, the Duke criteria has an overall sensitivity of more than 80 per cent and a specificity of 99 per cent. To improve the diagnostic sensitivity for the clinical diagnosis of infective endocarditis certain modifications to the original Duke criteria have been suggested.

Proposed Modifications to the Duke Criteria for the Diagnosis of Infective Endocarditis (Li *et al.*, *Clin Infect Diseases*, 2000)

- The category "possible IE" should be defined as having at least 1 major criterion and 1 minor criterion or 3 minor criteria.
- The minor criterion "echocardiogram consistent with IE but not meeting major criterion" should be eliminated, given the widespread use of transesophageal echocardiography (TEE).
- Bacteremia due to *S. aureus* should be considered a major criterion, regardless of whether the infection is nosocomially acquired or whether a removable source of infection is present.
- Positive Q-fever serology should be changed to a major criterion.

Check Your Progress 2

1) Mention the valves affected and organisms involved in IE of drug addicts?

.....

.....

.....

.....

2) What are the most common organisms found in PVE?

.....

.....

.....

.....

.....

3) How common is splenomegaly and clubbing in IE?

.....

.....

.....

.....

4) Mention the characteristic peripheral manifestations of IE?

.....

.....

.....

.....

.....

.....

5) How do you diagnose IE based on DUKE criteria?

.....

.....

.....

.....

.....

.....

Obtaining Blood Cultures

- Blood cultures are critical in the diagnosis and management of IE.
- Obtain blood cultures before starting antimicrobial therapy whenever possible.
- Intravascular infection leads to constant bacteremia originating from vegetations. Therefore, it is unnecessary to await the arrival of a fever spike or chills to obtain blood cultures.
- There is no significant diagnostic benefit gained from using arterial versus venous blood for culture.
- Always use strict aseptic technique and optimal skin preparation when collecting blood for culture. The recommended antiseptic skin preparation is liberal swabbing with 70 per cent isopropyl alcohol applied in widening circles over a reasonably wide area of skin around the intended site for venepuncture and allowed to dry followed by similar application of an iodophore or tincture of iodine over the same area.
- Blood cultures should be obtained by way of fresh venepunctures and not through indwelling intravascular devices.
- For suspected cases of acute IE obtain atleast two, preferably three sets of blood cultures within 5 to 10 minutes of each other before starting empiric antibiotic therapy.
- For suspected cases of subacute IE draw three separate blood cultures, spaced 30 minutes to 1 hour apart. If these remain negative at 24 hours, draw two further separate cultures.
- The volume of each blood sample drawn should be 20 ml for adults, 1 to 2 ml for neonates, 2 to 3 ml for infants aged 1 month to 2 years, 3 to 5 ml for older children, and 10 to 20 ml for adolescents.
- Each separate blood culture should be divided for inoculation into two bottles. One anaerobic bottle should be included in the total of four bottles inoculated from the two samples to enhance the recovery of certain facultative anaerobes such as streptococci, especially nutritionally variant streptococci.
- If all blood cultures remain negative at 5 days but IE remains likely on clinical grounds, subculture bottles on to chocolate agar plates if the bottles are not held beyond 5 days.
- For optimal processing, the laboratory should be advised that endocarditis is a possible diagnosis and which, if any unusual bacteria are suspected (Legionella species, Bartonella species, HACEK organisms).

- If a clinically stable patient has received an antimicrobial agent during the past several weeks, it is prudent to delay therapy so that repeat cultures can be obtained on successive days.

- If fungal endocarditis is suspected, blood cultures should be obtained using the lysis centrifugation method.

- Always culture any embolus or vegetation that has been surgically removed from a patient with suspected IE for both bacteria and fungi.

- Serologic tests are occasionally used to make the presumptive etiological diagnosis of endocarditis caused by Brucella species, Legionella species, Bartonella species, C.burnetii or Chlamydia species.

Culture Negative Endocarditis

In patients who have not received prior antibiotics and who will ultimately have blood culture positive endocarditis, it is likely that 95 – 100 per cent of all cultures obtained will be positive and that one of the first two cultures will be positive in atleast 98 per cent of patients.

Blood cultures are negative in **5 – 25 per cent** of patients with IE diagnosed by strict diagnostic criteria.

Echocardiography

Echocardiographic evaluation should be performed in all patients with clinically suspected IE, including those with negative blood cultures. Not only is TEE the preferred approach in patients with clinically suspected IE in whom TTE is suboptimal it is also the procedure of choice for imaging the pulmonic valve, patients with PVE (especially at the mitral site) and patients who are at high risk for intracardiac complications or those with sign of persistent or invasive infection despite adequate antimicrobial therapy.

The sensitivity of TTE for the detection of vegetations in NVE is less than **65 per cent**, although its specificity is excellent. In contrast, in proven NVE the sensitivity for vegetation detection of TEE was **90 to 100 per cent**, and in clinically suspected NVE, it ranged from 82 to 94 per cent. In patients with PVE, TTE is limited by the shadowing effect of the mitral valve prosthesis. **The sensitivity of TEE for detecting vegetations in PVE, involving mechanical or bioprosthetic devices ranged from 80 to 96 per cent, whereas that of TTE was from 36 to 16 per cent.**

Despite the sensitivity of TEE in detecting vegetations in patients with proven IE, **echocardiography does not itself provide a definite diagnosis**. Vegetations and valve dysfunction may be demonstrated, but determination of causality requires clinical or direct anatomical and microbiological confirmation. Infectious vegetation cannot be distinguished from marantic lesions, nor can vegetations be distinguished from thrombus or pannus on prostheses. Further more, it is usually not possible to distinguish active from healed vegetations in NVE. Thickened valves, ruptured chordae or valve calcifications and nodules may be mistaken for vegetations, indicating the specificity limitations of echocardiography.

Myocardial abscesses are more readily detected by TEE than TTE in patients with NVE or PVE. **The sensitivity and specificity for abscess detection were 28 per cent and 98 per cent for TTE, compared with 87 per cent and 95 per cent for TEE**.

TEE is the method of choice in the diagnosis of IE in patients who are:

- Difficult to image,

- Possible prosthetic valve IE,

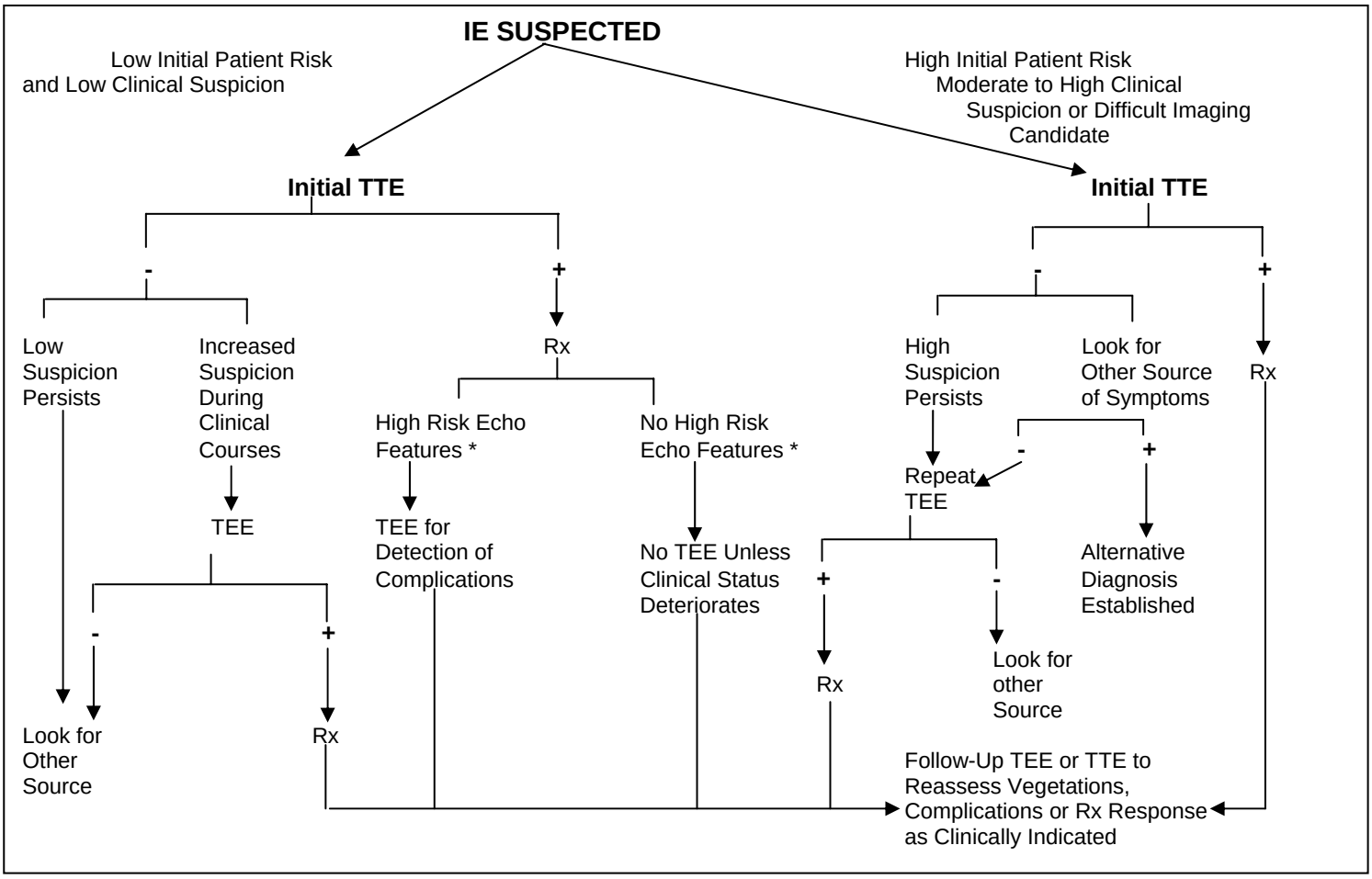

Fig. 2.1: An approach to the diagnostic use of echocardiography (echo)

* High-risk echocardiographic features include large and/or mobile vegetations, valvular insufficiency, suggestion of perivalvular extension,or secondary ventricular dysfunction (see text).

- For example, a patient with fever and a previously known heart murmur and no other stigmata of IE.

+ High initial patient risks include prosthetic heart values, many congenital heart diseases, previous endocarditis, new murmur, heart failure, or other stigmata of endocarditis.

Rx indicates antibiotic treatment for endocarditis.

Laboratory Examination

Blood tests often reflect nonspecific acute inflammatory responses manifest as a

- Modest leukocytosis
- Normochromic, normocytic anemia
- Slightly higher or lower platelet count
- Elevated ESR, Increased CRP

- Rheumatoid factor
- Hypergammaglobulinemia
- Decreased complement and elevated blood urea or creatinine may implicate renal dysfunction from an immuncomplex glomerulonephritis or drug toxicity.

Urine analysis – microhematuria with or without proteinuria may be seen.

ECG – All patients with suspected IE should have baseline and follow up ECG which may reveal conduction disturbances reflecting intramyocardial extension of infection, ranging from a prolonged PR interval to complete heart block (especially with PVE). A new atrioventricular block carries a 77 per cent positive predictive value for abscess formation with 42 per cent sensitivity. Myocardial infarction due to embolization of vegetations occur rarely.

Chest X-ray – may reveal congestive heart failure or pleural effusions. Right sided IE may cause nonspecific infiltrates due to multiple septic pulmonary emboli.

Culture negative mimics of IE – **atrial myxoma, a/c rheumatic fever/SLE, Antiphospholipid antibody syndrome, marantic endocarditis, carcinoid syndrome and Thrombotic thrombocytopenic purpura.**

Check Your Progress 3

1) What do you mean by continuous bacteremia or persistently positive blood culture?

.....

.....

2) What all things do you consider in collecting blood for culture for suspected IE?

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

.....

3) What is culture negative endocarditis (CNE)?

.....

.....

.....

.....

.....

4) List the Echocardiographic manifestations of IE?

.....

.....

.....

.....

.....

.....

.....

.....

5) What is the role of TEE in IE?

.....

.....

.....

.....

6) What is the significance of serial ECG monitoring in a patient with aortic valve IE?

.....

.....

.....

.....

7) What is the type of anemia in IE?

.....

.....

8) What do you mean by MIC and MBC and their significance?

.....

.....

.....

.....

2.8 TREATMENT

Two major objectives must be achieved to treat IE effectively. The infecting micro-organism in the vegetation must be eradicated. Also, invasive, destructive intracardiac and focal extracardiac complications of infection must be resolved if morbidity and mortality are to be minimized. The second objective often exceeds the capacity of effective antimicrobial therapy and requires cardiac or other surgical intervention.

Bacteria in vegetations multiply to population densities approaching 10^9 to 10^{10} organisms per gram of tissue, become metabolically dormant, and are difficult to eradicate. Optimal therapy should use **bactericidal antibiotics** or antibiotic combinations rather than bacteriostatic agents. Additionally, antibiotics reach the central area of avascular vegetations by passive diffusion. To reach effective antibiotic concentrations in vegetations, high serum concentration must be achieved, and penetration by some agents is limited even then. **Parenteral antimicrobial therapy** is used whenever feasible in order to achieve suitable serum antibiotic concentrations and to avoid the potentially erratic absorption or orally administered therapy. Treatment is continued for **prolonged period** to ensure eradication of dormant microorganisms.

In selecting antimicrobial therapy for patients with IE, one must consider the ability of potential agents to kill the causative organism as well as the MIC (minimum inhibitory concentration) and minimum bactericidal concentration (MBC) of these antibiotics for the organism. **The MIC is the lowest concentration that inhibits growth, and MBC is the lowest concentration that decreases a standard inoculum of organisms 99.9 per cent during 24 hours**. For the vast majority of streptococci and staphylococci, the MIC and MBC of penicillins, cephalosporins, or vancomycin are the same or differ by only a factor of two to four. Organisms for which the MBC for these antibiotics is 10 fold or greater than the MIC are occasionally encountered. This phenomenon has been termed tolerance. Most of the tolerant strains are simply killed more slowly than non tolerant strains and with prolonged incubation (48 hours) their MICs and MBCs are similar. Enterococci can be killed by the combined activity of selected penicillins or vancomycin and an aminoglycoside. This enhanced antibiotic activity of the combination against enterococci, if of sufficient magnitude, is called synergy or a synergistic bactericidal effect.A synergistic bactericidal effect is required for optimal therapy of enterococcal endocarditis and has been used to achieve more effective therapy or effective short-course therapy of IE caused by other organisms.

The regimens recommended for the treatment of IE caused by specific organisms are designed to provide high concentrations of antibiotics in serum, also deep in vegetations. Concentrations that exceed the organism's MIC throughout most, if not **routinely measured, but currently recommended antimicrobial regimens are based on these values for specific organisms.** With the exception of staphylococcal endocarditis, the antimicrobial regimens recommended for the treatment of NVE and PVE are similar, although more prolonged treatment is often advised for PVE.

Antimicrobial Therapy For Specific Organisms

1) Treatment for Native Valve Endocarditis Due to Penicillin-Susceptible Viridans Streptococci and Streptococcus Bovis (Minimum Inhibitory Concentration $\leq 0.1\mu g/ml$).

Antibiotic	Dosage and Route + (WK)	Duration
Aqueous penicillin G	12-18 million units/24 hr IV either continuously or every 4 hr in six equally divided doses	4
Ceftriaxone	2 gm. once daily IV or M	4
Aqueous Penicillin G	12-18 million units/24 hr IV either continuously or every 4 hr in six	2

	equally divided doses	
Plus Gentamicin	1mg/kg IM or IV every 8 hr	2
Vancomycin	30 mg/kg/24hr IV in two equally divided doses not to exceed 2 gm/24 hr	4

Dosage for Children - Penicillin: 200, 000U/kg/24hr, Ceftriaxone: 100mg/ kg/24hr, Gentamycin: 3mg/kg/24hr

2) Treatment for Native Valve Endocarditis Due to Strains of Viridans Streptococci and Streptococcus Bovis, Relatively Resistant to Penicillin G (Minimum Inhibitory Concentration >0.1μg/ml and <0.5μg/ml.

Antibiotic	**Dosage and Route**	**Duration (WK)**
Aqueous penicillin G plus	18 million units/24 hr IV either continuously or every 4 hr in 6 equally divided doses.	4
Gentamicin	1 mg/kg IM or IV every 8 hr	2
Vanocomycin	30 mg/kg/24 hr IV in two equally divided doses, not to exceed 2 gm/24 hr unless serum levels are monitored	4

For patients with PVE caused by penicillin susceptible streptococci, treatment with 6 weeks of penicillin is recommended, with gentamicin given during the initial 2 weeks.

Patients with endocarditis caused by streptococci that are highly resistant to penicillin (MIC > 0.5μg/ml) should be treated with one of the regimens recommended for enterococcal endocarditis.

3) Standard Therapy for Endocarditis Due to Enterococci

Antibiotic	**Dosage and Route**	**Duration (WK)**
a) Aqueous penicillin G	18-30 million units/24 hr IV given continuously or every 4 hr in six equally divided doses	4-6
Plus Gentamicin	1mg/kg IM or IV every 8 hr	4-6
b) Ampicillin	12 gm/24 hr IV given continuously or every or ever 4 hr in six equally divided doses	4-6
Plus Gentamicin	1 mg/kg IM or IV every 8 hr	4-6
c) Vancomycin	30 mg/kg/24 hr IV in two equally divided doses	4-6

	not to exceed 2 mg/24 hr unless serum levels are moniotored	
Plus Gentamicin	1 mg/kg IM or IV every 8 hr	4-6

All enterococci causing endocarditis must be tested for antimicrobial susceptibility in order to select optimal therapy. These regimens are for treatment of endocarditis caused by enterococci that are susceptible to vancomycin or ampicillin and not highly resistant to gentamicin.

These may also be used for treatment of endocarditis caused by penicillin-resistant (MIC > 0.5) viridans streptococci and nutritionally variant spreptococci (S.defectivus, S. adjacens), or enterococcal PVE.

Cephalosporins are not alternatives to penicillin/ampicillin in penicillin-allergic patients.

4) Treatment for Staphylococcal Endocarditis in the Absence of Prosthetic Material

Antibiotic	**Dosage and Route**	**Duration (WK)**
Methicillin-Susceptible staphylococci		
Nafcillin or oxacillin	2 gm IV every 4 hr (200mg/kg/24hr in children)	4-6
With optional addition of gentamicin	1 mg/kg IM or IV every 8 hr	3-5 days
Cefazolin (or other first-generation cephalosporins in equivalent dosages)	2 gm IV every 8 hr	4-6
With optional addition of gentamicin	1 mg/kg/ IM or IV every 8 hr	3-5 days
Methicillin-Resistant Staphylococci		
Vancomycin	30 mg/kg/24 hr IV in two equally divided doses, not to exceed 2 gm/24 hr unless serum levels are monitored	4-6

Cefazolin, other first generation cephalosporins or vancomycin may be used in selected penicillin-allergic patients.

5) Treatment of Staphylococcal Endocarditis in the Presence of a Prosthetic Valve or other Prosthetic Material

Antibiotic	**Dosage and Route**	**Duration (WK)**
Regimen for Methicillin - Resistant Staphylococci		
Vancomycin Plus	30 mg/kg/24 hr IV in two equally divided doses, not to exceed 2 mg/24 hr unless serum levels are monitored	$\geq$6

Rifampicin and gentamicin	300 mg PO every 8 hr 1.0 mg/kg IM or IV every 8 hr		≥6
Regimen for Methicillin-susceptible staphylococci			
Nafcillin or oxacillin Plus	2gm IV every 4 hr	____	≥6
Rifampicin and gentamicin	300 mg PO every 8 hr 1.0 mg/kg IM or IV every 8 hr	____	≥6

6) Treatment for Endocarditis due to Hacek Microrganisms*

Antibiotic	**Dosage and Route**	**Duration (WK)**
Ceftriaxone	2 gm once daily IV or IM	4
Ampicillin	12 gm/24 hr IV given continuously or	4
	every 4 hr in six equally divided doses	
Plus Gentamicin	1 mg /kg IM or IV every 8 hr	4

ACEK imcroorganisma are haemophilus parainfluenzae, Haemophilus, aphrophilus, Actinobacillus actinomycetemcomitans, Cardio bacterium hominis, Eikenella corrodens, and Kingella kingae.

7) **Culture-Negative Endocarditis**

Special studies to diagnose IE caused by fastidious bacteria and other organisms must be performed (serological studies). Thereafter, unless clinical or epidemiologic clues suggest an etiological diagnosis, the recommended treatment for culture negative NVE is ampicillin plus gentamicin (standard regimen for enterococcal endocarditis, because in the absence of confounding antibiotic therapy enterococci and staphylococci are unlikely causes of culture-negative NVE, ceftriaxone could be used in this regimen instead of ampicillin. For patients with culture-negative PVE, vancomycin is added to this regimen.

Monitoring Therapy for Endocarditis

Within a week after initiation of effective antimicrobial therapy, almost **75 per cent** of patients with IE, including those with PVE, are afebrile and **90 per cent** have defervesced by the end of the second week of treatment. **Persistence or recurrence of fever more than 7 to 10 days after initiation of antibiotic therapy** identified patients with increased morality rate and with complications of infection or therapy.

Patients must be carefully monitored during therapy and for several months thereafter. **Failure of antimicrobial therapy, myocardial or metastatic abscess, emboli, hypersensitivity to antimicrobial agents, and other complications of therapy (catheter-related infection, thrombophlebitis) or intercurrent illness may be manifested by persistent or recurrent fever.** Drug reactions have accounted for fever in **17 to 28 per cent** of these patients. In **33 to 45 per cent of patients**, persistent fever was associated with significant intracardiac complications, many of which require surgical intervention.

Renal function should be monitored in patients receiving vancomycin or aminoglycosides, and the complete blood counts should be checked at least weekly in patients receiving high dose beta-lactam antibiotics or vancomycin.

Natural History of Vegetations

- On repeat echo, 3 weeks to 3 months after initiation of ultimately effective antibiotic therapy, 29 per cent disappear, 59 per cent were unchanged, 24 per cent were smaller, and 17 per cent were larger.

- In the absence of severe valvular regurgitation or ongoing clinical symptoms, such persistence does not correlate with late complications.

- In contrast, increase in vegetation size by echocardiography over the course of therapy may identify a subset of patients with a higher rate of complications, independently of the presence of persistent bacteremia or overt clinical stigmata of IE.

Check Your Progress 4

1) How do you treat enterococcal endocarditis?

.....

.....

.....

.....

.....

2) What is the difference between the treatment of staphylococcal endocarditis in a patient with a native valve and a prosthetic valve?

.....

.....

.....

.....

.....

.....

3) What should be the empiric therapy for NVE and PVE (i.e.; before obtaining blood culture result)?

.....

.....

.....

.....

.....

2.9 COMPLICATIONS OF INFECTIVE ENDOCARDITIS

- Congestive heart failure

- Embolic events – Coronary, Cerebral, renal, visceral, pulmonary
- Periannular extension of abscess
- Arrythmia development – New onset heart block
- Prosthetic valve dysfunction
- Metastatic infection
- Persistent bacteremia or Fungemia
- Mycotic aneurysms
- Renal failure

Congestive Heart Failure

In native-valve IE, acute CHF occurs more frequently in aortic-valve infections (29 per cent) than with mitral (20 per cent) or tricuspid disease (8 per cent). CHF may develop acutely from:

- Perforation of a native-or bioprosthetic-valve leaflet,
- Rupture of infected mitral chordae,
- Valve obstruction from bulky vegetations,
- Sudden intracardiac shunts from fistulous tracts or prosthetic dehiscence. CHF may also develop more insidiously, despite appropriate antibiotics, as a result of a progressive worsening of valvular insufficiency and ventricular dysfunction.
- CHF in IE, irrespective of the course or mechanism, signifies a grave prognosis with medical therapy alone and is also the most powerful predictor of poor outcome with surgical therapy.
- The decision to operate on the patient with IE is driven primarily by the severity of CHF. Medical and surgical management decisions can be guided by echocardiographic detection of abscesses, fistulae, prosthetic dehiscence, obstructive vegetations, or flail leaflets, none of which will resolve with medical therapy alone. Delaying surgery to the point of frank ventricular decompensation dramatically increases operative mortality, from 6 per cent to 11 per cent for patients without CHF and 17 per cent to 33 per cent for patients with CHF.

Poor surgical outcome is predicted by preoperative New York Heart Association class III or IV CHF, renal insufficiency, and advanced age. In any patient, a decision to delay surgery to extend pre-operative antibiotic treatment carries with it the risk of permanent ventricular dysfunction. The incidence of reinfection of newly implanted valves in patients with active IE has been estimated to be 2 per cent to 3 per cent, far less than the mortality rate for uncontrolled CHF.

Risk of Embolization

Systemic embolization occurs in 22 per cent to 50 per cent of cases of IE. Emboli often involve major arterial beds, including lungs, coronary arteries, spleen, bowel, and extremities. Up to 65 per cent of embolic events involve the central nervous system, and 90 per cent of central nervous system emboli lodge in the distribution of the middle cerebral artery. The highest incidence of embolic complications is seen with aortic- and mitral-valve infections and in IE due to *S aureus* and *Candida* species and HACEK and *Abiotrophia* organisms. Emboli can occur before diagnosis, during therapy, or after therapy is completed, although most emboli occur within the first 2 to 4 weeks of antimicrobial therapy. The rate of embolic events drops dramatically during the first 2 weeks of successful antibiotic therapy, from 13 to .2 embolic events per 1000 patient-

days. In general, mitral vegetations, regardless of size, are associated with higher rates of embolization (25 per cent) than aortic vegetations (10 per cent). The highest embolic rate (37 per cent) has been seen in the subset of patients with mitral vegetations attached to the anterior rather than the posterior mitral leaflet and with vegetation size > 1 cm in diameter. Staphylococcal or fungal IE appears to carry a high risk of embolization, i.e., independent of vegetation size. Large vegetations independently predict embolic events only in the setting of streptococcal IE. The embolic event rate among patients with IE and increasing vegetation size was twice that of patients with static or decreasing vegetation size over 4 to 8 weeks of therapy.

The indications for surgery for persistent vegetation after systemic embolization are:

1) Anterior mitral leaflet vegetation, particularly with size > 10 mm
2) One or more embolic events during first 2 weeks of antimicrobial therapy
3) Two or more embolic events during or after antimicrobial therapy
4) Increase in vegetation size after 4 weeks of antimicrobial therapy

Periannular Extension of Infection

Occur in 10 per cent to 40 per cent of all native-valve IE, and complicates aortic IE more commonly than mitral or tricuspid IE. Periannular infection is of even greater concern with prosthetic-valve IE, occurring in 56 per cent to 100 per cent of patients. Perivalvular abscesses are particularly common with prosthetic valves because the annulus, rather than the leaflet, is the usual primary site of infection. In native aortic-valve IE, this generally occurs through the weakest portion of the annulus, which is near the membranous septum and atrioventricular node.

Clinical parameters for the diagnosis of perivalvular extension in a patient with IE who is taking adequate antibiotics are:

- Persistent bacteremia or fever
- Recurrent emboli
- Heart block
- CHF
- New pathological murmur

Only aortic-valve involvement and recent IVDA have been prospectively identified as independent risk factors for perivalvular abscess. On ECG, new atrioventricular block has an 88 per cent positive predictive value for abscess formation but has a low sensitivity (45 per cent). The sensitivity of TTE to detect perivalvular abscess is low (18 per cent to 63 per cent in prospective and retrospective studies, respectively). TEE improves the sensitivity for defining periannular extension of IE (76 per cent to 100 per cent) while retaining excellent specificity (95 per cent) and positive and negative predictive values (87 per cent and 89 per cent, respectively). When it is combined with spectral and color Doppler techniques, TEE can demonstrate the distinctive flow patterns of fistulae and pseudoaneurysms and can rule out communications from unruptured abscess cavities. Surgery for patients with perivalvular extension of IE directed toward eradication of the infection as well correction of hemodynamic abnormalities. Drainage of abscess cavities, excision of necrotic tissue, and closure of fistulous tracts often accompanies valve-replacement surgery. Human aortic homografts, when available, can be used to replace the damaged aortic valve as well as to reconstruct the damaged aorta. Those pts who do not have heart block, echocardiographic evidence of progression of abscess during therapy, valvular dehiscence, or insufficiency can be managed with out surgical intervention. Such patients should

be monitored closely with serial TEE, and TEE should be repeated intervals of 2, 4, and 8 weeks after completion of antimicrobial therapy.

Splenic Abscess

Splenic infarction is a common complication of left-sided IE (40 per cent of cases). Only 5 per cent of patients with splenic infarction will develop splenic abscess. This infection develops via 1 of 2 mechanisms Bacteremic seeding of a bland infarction, created via splenic artery occlusion by embolized vegetations, or direct seeding of the spleen by an infected embolus also originating from an infected valvular vegetation. **Viridans streptococci** and ***S aureus*** each account for 40 per cent of cases in which splenic abscess cultures are positive, whereas the **enterococci** account for 15 per cent of cases. **Aerobic Gram-negative bacilli and fungi** are isolated in, 5 per cent of cases. Clinical splenomegaly, present in up to 30 per cent of cases of IE, is not a reliable sign of splenic infarction or abscess. Splenic infarction delineated by imaging techniques is often asymptomatic Back, left-flank, or left-upper-quadrant pain or abdominal tenderness, when present, may be associated with either splenic infarction or abscess. Splenic rupture with hemorrhage is a rare complication of infarction. Persistent or recurrent bacteremia, persistent fever, or other signs of sepsis are suggestive of splenic abscess, Abdominal CT or MRI appear to be the best tests for diagnosis of splenic abscess, with sensitivities and specificities of 90 per cent to 95 per cent. On ultrasonography, a sonolucent lesion suggests abscess. Infarcts are generally associated with clinical and radiographic improvement during appropriate antibiotic therapy. Ongoing sepsis, recurrent positive blood cultures, and persistence or enlargement of splenic defects CT or MRI suggest splenic abscess, which responds poorly to antibiotic therapy alone. Definitive treatment is splenectomy with appropriate antibiotics. Percutaneous drainage or aspiration of splenic abscess is an alternative to splenectomy for the patient who is a poor surgical candidate. Splenectomy should be performed before valve-replacement surgery because of the risk of infection of the valve prosthesis as a result of the bacteremia from abscess.

Mycotic Aneurysms

They result from septic embolization of vegetations to the arterial vasa vasorum or the intraluminal space, with subsequent spread of infection through the intima and outward through the vessel wall. Arterial branching points favour the impaction of emboli and are the most common sites of MA development. MAs due to IE occur most frequently in the intracranial arteries, followed by visceral arteries and arteries of the lower and upper extremities.

Intra Cranial Mycotic Aneurysms

The reported occurrence of ICMAs is 1.2 per cent to 5 per cent of cases. **Streptococci and S.aureus** account for 50 per cent and 10 per cent of cases, respectively, and are seen with increased frequency among IVDA patients with IE. The **distal middle cerebral artery branches** are most often involved, especially the bifurcations. ICMAs are multiple in 20 per cent of cases.

Mortality rates are similar for multiple or single distal ICMAs. The overall mortality rate among IE patients with ICMAs is 60 per cent. Among those without rupture, the mortality rate is 30 per cent; this approaches 80 per cent if rupture occurs. Clinical presentation is variable Headache, altered sensorium, FND, SAH or IVH. CSF is sterile and contains erythrocytes, leucocytes and elevated protein. Imaging procedures to detect ICMAs are indicated in IE patients with localized or severe headaches, “sterile” meningitis, or focal neurological signs. Contrast-enhanced CT may provide useful initial information. This technique has a 90 per cent to 95 per cent sensitivity for intracerebral bleed and may thus indirectly identify the location of the MA. Magnetic resonance angiography is a promising new technique for the detection of ICMAs, although its sensitivity for

aneurysms smaller than 5 mm is inferior to conventional 4-vessel cerebral angiography. Conventional angiography remains the diagnostic imaging of choice. ICMAs may heal with medical therapy: ICMAs resolved between an initial and follow-up angiogram in 52 per cent of patients treated with effective antibiotic therapy. A decrease in ICMA size was seen in an additional 29 per cent. In 19 per cent of patients, however, the ICMA increased in size by the time of the second angiogram, and a new ICMA was discovered in 10 per cent. Currently, there are no data that precisely identify at risk for imminent rupture, and decisions concerning medical versus surgical therapy must be individualized. It is generally felt that a Single ICMA distal to the first bifurcation of a major artery (e.g., middle cerebral artery) and Multiple ICMAs should be monitored with frequent serial angiograms and excised promptly if the aneurysm enlarges or bleeds.

Extra Cranial MAs

Intrathoracic or intra-abdominal MAs are often asymptomatic until leakage or rupture occurs. Most extracranial MAs (ECMAs) will rupture if not excised. The appearance of a tender, pulsatile mass in a patient with IE should suggest an ECMA. Hematemesis, hematobilia, and jaundice suggest rupture of a hepatic artery MA; Arterial hypertension and hematuria suggest rupture of a renal MA; Massive bloody diarrhea suggests the rupture of an ECMA into the small or large bowel. Proximal and distal ligation with excision of all infected material and revascularisation with interposed vascular grafts or autologous venous grafts is ideal.Mortality among patients with IE and ECMA is high, which is attributable to suture line infection with vessel or graft rupture.

Anticoagulation Issues

Anticoagulation is contraindicated in native-valve endocarditis because of the risk of intracerebral hemorrhage. Patients with prosthetic valve endocarditis who normally take maintenance anticoagulation, however, are usually maintained on anticoagulant therapy during treatment of IE, provided there is no evidence of cerebral events.

Surgical Treatment of Infective Endocarditis

Cardiac surgical intervention has an increasingly important role in the treatment of intracardiac complications of endocarditis. Retrospective data suggest that mortality is unacceptably high when these complications are treated with antibiotics alone, whereas mortality is reduced when treatment combines antibiotics and surgical intervention.

It encompasses both radical valve replacement and more conservative vegetectomy and valve repairs. Surgery is necessary in 25–30 per cent of cases during acute infection, and in 20–40 per cent in later phases. The final outcome has little relation to the duration of previous antibiotic therapy. Results of studies on surgery for active infective endocarditis indicate mortality rates of 8–16 per cent, with actuarial survival at 5 years of 75–76 per cent and at 10 years of 61 per cent.

Cardiac Surgery in Patients with Infective Endocarditis

Absolute Indications

1) Moderate to severe congesive heart failure due to valve dysfunction.
2) Unstable prosthesis.

3) Unconrolled infection despite optimal antimicrobial therapy.

4) Unavailable effective antimicrobial therapy; endocarditis due to fungi, Brucellae, pseudomonas aeruginosa (aortic or mitral valves).

5) Staphylococcus aureus PVE with an intracardiac complication.

6) Relapse of PVE after optimal therapy.

Relative Indications (Surgery commonly required for optimal outcome)

- Perivalvular extension of infection, intracardiac fistula
- Poorly responsive S. aureus NVE (aortic or mitral valves)
- Relapse of NVE after optimal antimicrobial therapy
- Culture-negative NVE or PVE with persistent fever (≥ 10 d)
- Large (> 10 mm diameter) hypermobile vegetation (with or without prior arterial embolus)
- Endocarditis due to highly antibiotic resistant enterococci.

Mortality Rates

- NVE – 16 –27 per cent
- PVE - Early - 50-60 per cent

  Late - 33 – 45 per cent
- Treated NVE – survival is 88 per cent at 5 years and 81 per cent at 10 yrs
- Treated PVE – 50 –80 per cent at 4 – 6 years.

Mortality rates associated with various organisms are:

- Viridans streptococci – 4-16 per cent
- Enterococci - 15-25 per cent
- S.aureus – 25-47 per cent
- C.burnetti- 5-37 per cent
- P.aeruginosa and Fungi - > 50 per cent

Death due to IE has been a/w:

- Old age > 65 yrs
- CHF

- Aortic valve infection
- Renal failure
- Neurological complications

Relapse and Recurrence

Relapse of infective endocarditis usually occurs within **two months** of the discontinuation of antimicrobial therapy. The relapse rate for patients with native-valve endocarditis caused by penicillin-susceptible viridans streptococcus who have been treated with one of the recommended courses of therapy is generally less than 2 per cent.

The relapse rate for patients with enterococcal native-valve endocarditis after standard therapy is 8 to 20 per cent. Among patients with infective endocarditis caused by *Staph.aureus,* Enterobacteriaceae, or fungi, treatment failure often occurs during the primary course of therapy. Positive culture at the time of valve-replacement surgery, particularly in patients with staphylococcal endocarditis, is a risk factor for subsequent relapse. The relapse rate in prosthetic-valve endocarditis is approximately 10 to 15 per cent, and relapse of infection may be an indication for combined medical and surgical therapy. Recurrence rate of NVE and PVE is around 4.5 – 7 per cent. In IVDA recurrent IE is around 43 per cent.

2.10 PREVENTION

Prevention of endocardial infection by the use of antimicrobial agents, although desirable, is not always possible. By identifying the patients at risk, the causative bacteria and the events that induce bacteremia, strategies for prevention of some episodes of IE have been formulated and are routinely recommended even in the absence of supporting clinical trials. Rates of bacteremia are highest for events that traumatize the oral mucosa followed by those that traumatize the genitourinary tract.The frequency of bacteremia is relatively low for gastrointestinal diagnostic procedures.

Procedures for which Prophylaxis Against Endocarditis is Considered

PROPHYLAXIS RECOMMENDED	PROPHYLAXIS NOT RECOMMENDED
• Dental procedures known to induce gingival or mucosal bleeding, including professional cleaning and scaling	• Dental procedures not likely to cause bleeding, such as adjustment of orthodontic appliances and simple fillings above the gum line
• Tonsillectomy or adenoidectomy	• Intraoral Injection or local anesthetic (non intraligamentary)
• Surgery involving gastro intestinal or upper respiratory mucosa	• Shedding of primary teeth
• Bronchoscopy with rigid bronchoscope	• Tympanostomy tube insertion
• Sclerotherapy for esophageal varices	• Endotracheal tube insertion
• Esophageal dilation	• Bronchoscopy with flexible bronchoscope, with or without biopsy
• Endoscopic retrograde cholangiography with biliary obstruction	• Transesophageal echocardiography
• Gallbladder surgery	• Cardiac catheterization, coronary angioplasty

• Cystoscopy, urethral dilation • Urethral catheterization if urinary infection is present • Urinary tract surgery, including prostate surgery • Incision and drainage of infected tissue	• Pacemaker implantation • Gastrointestinal endoscopy, with or without biopsy. • Incision or biopsy of scrubbed skin • Cesarean section • Vaginal hysterectomy • Circumcision • In the absence of the infection: urethral catheterization, dilatation and curettage, uncomplicated vaginal delivery, therapeutic abortion, insertion or removal of intrauterine device, sterilization procedures, laparoscopy.

Relative Risk of Infective Endocarditis Associated with Preexisting Cardiac Disorders

RELATIVELY HIGH RISK	***INTERMEDIATE RISK***	**VERY LOW OR NEGLIGIBLE RISK**
• Prosthetic heart valves • Previous infective endocarditis • Cyanotic congenital heart disease (TOF, TGA) • Patent ductus arteriosus • Aortic regurgitation • Aortic stenosis • Mitral regurgitation • Ventricular septal defect • Coarctation of the aorta • Surgically repaired intracardiac lesion with residual hemodynamic abnormality or prosthetic device • Surgically constructed systemic- pulmonary shunts	• Mitral valve prolapse with regurgitation (murmur) or thickened valve leaflets • Pure mitral stenosis • Tricuspid valve disease • Pulmonary stenosis • Asymmetrical septal hypertrophy • Bicuspid aortic valve or calcific aortic sclerosis with minimal hemodynamic abnormality • Degenerative valvular disease in elderly patients • Surgically repaired intracardiac lesions with minimal or no hemodynamic abnormality, less than 6 month after operation	• Mitral valve prolapse without • Regurgitation (murmur) or thickened valve leaflets • Trivial valvular regurgitation on • Echocardiography without structural abnormality • Isolated atrial septal defect (secundum) • Arteriosclerotic plaques • Coronary artery disease • Cardiac pacemaker, implanted • defibrillators • Surgically repaired intracardiac lesions, with minimal or no hemodynamic abnormality more than 6 month after operation (atrial septal defect, ventricular septal defect, patent ductus arteriosus, pulmonary stenosis

Regimens for Prophylaxis Against Endocarditis: Use with Genitourinary and Gastrointestinal (Except Esophageal) Procedures

SETTING	ANTIBIOTIC	REGIMEN
High-risk patients	Ampicillin plus gentamicin	Ampicillin 2.0 gm IV/IM plus gentamicin 1.5 mg/kg within 30 min of procedure, repeat ampicillin 1.0 gm IV/IM or give amoxicillin 1.0 gm PO 6 hr later
High- risk, penicillin-allergic patients	Vancomycin plus gentamicin	Vancomycin 1.0 gm IV over 1-2 hr plus gentamicin
Moderate-risk patients	Amoxicillin or ampicillin	1.5 mg/kg IM/IV infused or injected 30 min before procedure. No second dose recommended. Amoxicillin 2.0 gm PO 1 hr before procedure or ampicillin 2.0 gm IM/IV 30 min before procedure
Moderate-risk, penicillin-allergic patients	Vancomycin	Vancomycin 1.0 gm IV infused over 1-2 hr and completed within 30 min of procedure
*Dosing for children: ampicillin 50 mg/kg IV/IM, vancomycin 20 mg/kg IV, gentamicin 1.5 mg/kg IV/IM (children's doses should not exceed adult doses)		

Regimens for Prophylaxis Prior to Dental, Oral, Respiratory Tract and Esophageal Procedures

SETTING	ANTIBIOTIC	REGIMEN
Standard	Amoxicillin	2.0 gm PO 1 hr before procedure
Unable to take oral medication	Ampicillin	2.0 gm IM/IV within 30 mts of procedure
Penicillin allergic	Clindamycin	600 mg PO 1 hr before Or IV 30 mts before procedure
	Clarithromycin Cephalexin Cephadroxil	500 mg PO 1 hr before procedure 2.0 gm PO 1 hr before procedure 2.0 gm PO 1 hr before procedure
(Dosing for children – Amoxicillin, ampicillin, Cephalexin, cephadroxil – 50 mg/kg PO Clindamycin – 20 mg/kg PO/ IV, Clarithromycin – 15 mg/kg PO)		

Check Your Progress 5

1) List the common complications of IE.

.....

.....

.....

.....

.....

.....

.....

2) What do you mean by mycotic aneurysms and their significance?

.....

.....

.....

.....

3) Mention the organisms that are frequently associated with embolic complications?

.....

.....

.....

.....

4) Mention the role of anticoagulation in IE?

.....

.....

.....

.....

.....

5) What are the definite indications of surgery in IE?

.....

.....

.....

.....

.....

6) List the adverse prognostic features in IE?

.....

.....

.....

.....

7) Mention the high-risk cardiac conditions that require antibiotic prophylaxis?

.....

.....

.....

.....

8) List the antibiotics that can be used for prophylaxis in patients with penicillin allergy?

.....

.....

.....

.....

.....

.....

.....

2.11 LET US SUM UP

Infective endocarditis is clinical syndrome associated with significant morbidity and mortality. Therefore, its early recognition and treatment should impact favourably on patient outcome. Endocarditis is typically characterized by fever and a heart murmur. It is confirmed by positive blood cultures or Echocardiographic or pathologic evidence of valvular or paravalvular infection. Effective therapy requires identification of the microbial cause, determination of a bactericidal regimen of proven efficacy, an understanding of the intracardiac pathology of infective endocarditis and its implications for surgery and effective management of extracardiac complications. Antibiotic prophylaxis is advised whenever the combination of the underlying cardiac condition and the procedure seems to pose substantial risk of IE.

2.12 ANSWERS TO CHECK YOUR PROGRESS

Check Your Progress 1

1) Mitral valve prolapse (MVP) mitral regurgitation murmur has emerged as a prominent, predisposing structural cardiac abnormality and in adults accounts for 7 to 30 per cent of NVE in cases not related to drug abuse or nosocomial infection.

Rheumatic heart disease is the predisposing cardiac lesion for IE in 20 to 25 per cent.

Congenital heart disease is the substrate for IE in 10 to 20 per cent of younger adults and 8 per cent of older adults.

2) Congenital heart abnormalities, particularly patent ductus arteriosus, ventricular septal defect, and bicuspid aortic valve, the latter particularly found among older men (>60 years); Tetralogy of Fallot; and other complex structural anomalies associated with cyanosis (TGA, single ventricle) are found in remaining cases. Of children with IE on congenital defects, 50 per cent develop infection after cardiac surgery; in these children, infection frequently involves prosthetic valves, valved conduits, or synthetic patches. Mitral valve prolapse generally in association with a regurgitant murmur has been recognized to predispose to IE in children.

3) Streptococcus viridans

   Enterococci

   S Aureus

4) Organisms of the so-called **HACEK group, (Haemophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella species, Kingella kingae**) are part of the upper respiratory tract and oropharyngeal flora, infect abnormal cardiac valves, causing subacute NVE and cause PVE that occurs a year or more after valve surgery. In NVE, the HACEK organisms have been associated with large vegetations and a high incidence of systemic emboli. These organisms are fastidious and slow growing; when they are suspected, blood cultures should be incubated for 3 weeks.

Check Your Progress 2

1) Endocarditis occurring in IV drug abusers has a unique propensity to infect right heart valves. In clinical series, distribution of valve involvement is tricuspid in 46 to 78 per cent, mitral in 32 to 24 per cent, and aortic in 8 to 19 per cent, (as many as 16 per cent of patients have infection at multiple sites).

   In IV drug abusers, the valves were normal before infection in 75 to 93 per cent of patients. In contrast to NVE among adults in general, S aureus causes more than 50 per cent of these infections overall and 60 to 70 per cent of those involving the tricuspid valve.

2) Coagulase negative staphylococci

   Staphylococcus aureus

   Gram-negative bacilli

   Enterococci

   Fungi

3) Splenomegaly around 15-50 per cent. Clubbing 10-20 per cent.

4) Osler nodes

   Splinter haemorrhages

   Petechiae

Janeway lesion

Retinal lesion/Roth spots

Check Your Progress 3

1) Intravascular infection leads to constant bacteremia originating from vegetations. Therefore it is unnecessary to await the arrival of a fever spike or chills to obtain blood cultures.

2)
- Blood cultures should be obtained by way of fresh venepunctures and not through indwelling intravascular devices.
- For suspected cases of acute IE obtain at least two, preferably three sets of blood cultures within 5 to 10 minutes of each other before starting empiric antibiotic therapy.
- For suspected cases of subacute IE draw three separate blood cultures, spaced 30 minutes to 1 hour apart. If these remain negative at 24 hours, draw two further separate cultures.
- The volume of each blood sample drawn should be 20 ml for adults , 1 to 2 ml for neonates, 2 to 3 ml for infants aged 1 month to 2 years, 3 to 5 ml for older children, and 10 to 20 ml for adolescents.
- Each separate blood culture should be divided for inoculation into two bottles. One anaerobic bottle should be included in the total of four bottles inoculated from the two samples to enhance the recovery of certain facultative anaerobes such as streptococci, especially nutritionally variant streptococci.
- If all blood cultures remain negative at 5 days but IE remains likely on clinical grounds, subculture bottles on to chocolate agar plates if the bottles are not held beyond 5 days.
- For optimal processing, the laboratory should be advised that endocarditis is a possible diagnosis and which, if any unusual bacteria are suspected (Legionella species, Bartonella species, HACEK organisms).
- If a clinically stable patient has received an antimicrobial agent during the past several weeks, it is prudent to delay therapy so that repeat cultures can be obtained on successive days.
- If fungal endocarditis is suspected, blood cultures should be obtained using the lysis centrifugation method.
- Always culture any embolus or vegetation that has been surgically removed from a patient with suspected IE for both bacteria and fungi.
- Serologic tests are occasionally used to make the presumptive etiological diagnosis of endocarditis caused by Brucella species, Legionella species, Bartonella species, C.burnetii or Chlamydia species.

3) Blood cultures are negative in **5 – 25 per cent** of patients with IE diagnosed by strict diagnostic criteria.

In patients who have not received prior antibiotics and who will ultimately have blood culture positive endocarditis, it is likely that 95 – 100 per cent of all cultures obtained will

be positive and that one of the first two cultures will be positive in atleast 98 per cent of patients.

4) The sensitivity of TTE for the detection of vegetations in NVE is less than 65 per cent, although its specificity is excellent. In contrast, in proven NVE the sensitivity for vegetation detection of TEE was 90 to 100 per cent, and in clinically suspected NVE, it ranged from 82 to 94 per cent. In patients with PVE, TTE is limited by the shadowing effect of the mitral valve prosthesis. The sensitivity of TEE for detecting vegetations in PVE, involving mechanical or bioprosthetic devices ranged from 80 to 96 per cent, whereas that of TTE was from 36 to 16 per cent.

   Despite the sensitivity of TEE in detecting vegetations in patients with proven IE, echocardiography does not itself provide a definite diagnosis. Vegetations and valve dysfunction may be demonstrated, but determination of causality requires clinical or direct anatomical and microbiological confirmation.

   Infectious vegetation cannot be distinguished from marantic lesions, nor can vegetations be distinguished from thrombus or pannus on prostheses. Furthermore, it is usually not possible to distinguish active from healed vegetations in NVE. Thickened valves, ruptured chordae or valve calcifications and nodules may be mistaken for vegetations, indicating the specificity limitations of echocardiography. High-risk echocardiographic features include large and/or mobile vegetations, valvular insufficiency, suggestion of perivalvular extension,or secondary ventricular dysfunction .

   Myocardial abscesses are more readily detected by TEE than TTE in patients with NVE or PVE. The sensitivity and specificity for abscess detection were 28 per cent and 98 per cent for TTE, compared with 87 per cent and 95 per cent for TEE.

5) TEE is the method of choice in the diagnosis of IE in patients who are:

   - Difficult to image,
   - Possible prosthetic valve IE,
   - Patients with intermediate or high clinical suspicion of IE,
   - Patients with a high risk for IE-related complications.

   An approach to the diagnostic use of echocardiography is shown below.

6) All patients with suspected IE should have baseline and follow up ECG which may reveal conduction disturbances reflecting intramyocardial extension of infection, ranging from a prolonged PR interval to complete heart block (especially with PVE). A new atrioventricular block carries a 77 per cent positive predictive value for abscess formation with 42 per cent sensitivity. Myocardial infarction due to embolization of vegetations occur rarely.

7) Normochromic, normocytic anemia.

8) The MIC is the lowest concentration that inhibits growth, and MBC is the lowest concentration that decreases a standard inoculum of organisms 99.9 per cent during 24 hours.

Check Your Progress 4

1)

Antibiotic	Dosage and Route (WK)	Duration

a) Aqueous penicillin G	18-30 million units/24 hr IV given continuously or every 4 hr in six equally divided doses	4-6
Plus Gentamicin	1mg/kg IM or IV every 8 hr	4-6
b) Ampicillin	12 gm/24 hr IV given continuously or every or ever 4 hr in six equally divided doses	4-6
Plus Gentamicin	1 mg/kg IM or IV every 8 hr	4-6
c) Vancomycin not to exceed 2 mg/24 hr unless serum levels are moniotored	30 mg/kg/24 hr IV in two equally divided doses	4-6
Plus Gentamicin	1 mg/kg IM or IV every 8 hr	4-6

2)

Antibiotic	**Dosage and Route (WK)**	**Duration**
Methicillin-Susceptible staphylococci		
Nafcillin or oxacillin (200mg/kg/24hr in children)	2 gm IV every 4 hr	4-6
With optional addition of gentamicin	1 mg/kg IM or IV every 8 hr	3-5 days
Cefazolin (or other first-generation cephalosporins in equivalent dosages)	2 gm IV every 8 hr	4-6
With optional addition of gentamicin	1 mg/kg/ IM or IV every 8 hr	3-5 days
Methicillin-Resistant Staphylococci		
Vancomycin equally divided doses, not to exceed 2 gm/24 hr unless serum levels are monitored	30 mg/kg/24 hr IV in two	4-6

Cefazolin, other first generation cephalosporins or vancomycin may be used in selected penicillin-allergic patients.

Treatment of Staphylococcal Endocarditis in the Presence of a Prosthetic Valve or other Prosthetic Meterial

Antibiotic	**Dosage and Route**	**Duration (WK)**
Regimen for Methicillin - Resistant Staphylococci		
Vancomycin Plus	30 mg/kg/24 hr IV in two equally divided doses, not to exceed 2 mg/24 hr unless serum levels are monitored	≥6
Rifampicin and gentamicin	300 mg PO every 8 hr 1.0 mg/kg IM or IV every 8 hr	≥6
Regimen for Methicillin-susceptible staphylococci		
Nafcillin or oxacillin Plus	2gm IV every 4 hr	≥6

Rifampicin and gentamicin	300 mg PO every 8 hr 1.0 mg/kg IM or IV every 8 hr	____	≥6

3) **NVE**

Antibiotic	Dosage and Route +	Duration (WK)
Aqueous penicillin G	12-18 million units/24 hr IV either continuously or every 4 hr in six equally divided doses	4
Ceftriaxone	2 gm. once daily IV or M	4
Aqueous Penicillin G	12-18 million units/24 hr IV either continuously or every 4 hr in six equally divided doses	2
Plus Gentamicin	1mg/kg IM or IV every 8 hr	2
Vancomycin	30 mg/kg/24hr IV in two equally divided doses not to exceed 2 gm/24 hr	4

Dosage for Children - Penicillin: 200, 000U/kg/24hr, Ceftriaxone: 100mg/kg/24hr, Gentamycin: 3mg/kg/24hr

PVE

Antibiotic	Dosage and Route	Duration (WK)
Regimen for Methicillin - Resistant Staphylococci		
Vancomycin Plus	30 mg/kg/24 hr IV in two equally divided doses, not to exceed 2 mg/24 hr unless serum levels are monitored	≥6
Rifampicin and gentamicin	300 mg PO every 8 hr 1.0 mg/kg IM or IV every 8 hr	≥6
Regimen for Methicillin-susceptible staphylococci		
Nafcillin or oxacillin Plus	2gm IV every 4 hr ____	≥6
Rifampicin and gentamicin	300 mg PO every 8 hr 1.0 mg/kg IM or IV every 8 hr ____	≥6

Check Your Progress 5

1)
- Congestive heart failure
- Embolic events – Coronary, Cerebral, renal, visceral, pulmonary

- Periannular extension of abscess
- Arrythmia development – New onset heart block
- Prosthetic valve dysfunction
- Metastatic infection
- Persistent bacteremia or Fungemia
- Mycotic aneurysms
- Renal failure

2) Mycotic aneurysms.They result from septic embolization of vegetations to the arterial vasa vasorum or the intraluminal space, with subsequent spread of infection through the intima and outward through the vessel wall. Arterial branching points favour the impaction of emboli and are the most common sites of MA development. MAs due to IE occur most frequently in the intracranial arteries, followed by visceral arteries and arteries of the lower and upper extremities.

3) The highest incidence of embolic complications is seen with aortic- and mitral-valve infections and in IE due to *S aureus* and *Candida* species and HACEK and *Abiotrophia* organisms.

4) Anticoagulation is contraindicated in native-valve endocarditis because of the risk of intracerebral hemorrhage. Patients with prosthetic valve endocarditis who normally take maintenance anticoagulation, however, are usually maintained on anticoagulant therapy during treatment of IE, provided there is no evidence of cerebral events.

5) Cardiac Surgery in Patients with Infective Endocarditis

Absolute Indications

1) Moderate to severe congesive heart failure due to valve dysfunction.
2) Unstable prosthesis.
3) Unconrolled infection despite optimal antimicrobial therapy.
4) Unavailable effective antimicrobial therapy; endocarditis due to fungi, Brucellae, pseudomonas aeruginosa (aortic or mitral valves).
5) Staphylococcus aureus PVE with an intracardiac complication.
6) Relapse of PVE after optimal therapy.

6)
- Old age > 65 yrs
- CHF
- Aortic valve infection
- Renal failure

- Neurological complications

7)
- Prosthetic heart valves
- Previous infective endocarditis
- Cyanotic congenital heart disease (TOF, TGA)
- Patent ductus arteriosus
- Aortic regurgitation
- Aortic stenosis
- Mitral regurgitation
- Ventricular septal defect
- Coarctation of the aorta
- Surgically repaired intracardiac lesion
- with residual hemodynamic abnormality or prosthetic device
- Surgically constructed systemic-pulmonary shunts

8) Vancomycin 1.0 gm IV over 1-2 hr plus gentamicin 1.5 mg/kg IM/IV infused or injected 30 min before procedure. No second dose recommended.

Clindamycin	600 mg PO 1 hr before or IV 30 mts before procedure
Clarithromycin	500 mg PO 1 hr before procedure
Cephalexin	2.0 gm PO 1 hr before procedure
Cephadroxil	2.0 gm PO 1 hr before procedure