INFECTIVE ENDCARDITIS

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By

Objectives

- Definition
- Pathophysiology
- Microbiology
- Clinical features
- Investigations
- Treatment
- Prophylaxis



What is the endocardium?

The heart's endocardium is the innermost layer of tissue that lines the chambers of the heart. It covers the <u>left</u> <u>atrium</u>, the <u>right atrium</u>, the <u>left ventricle</u>, and the <u>right ventricle</u>. In addition, It covers and forms the surface of the four heart valves.



Infective endocarditis

Microbial infection of endocardium of any of the following:

- A heart valve (native or prosthetic valves)
- The lining of a cardiac chamber
- The lining of a blood vessel
- Congenital heart defects

Fatality is approximately 20% even with treatment

Pathophysiology

> Abnormal heart (sites of pre-existing endocardial damage) :

The most vulnerable areas of endocardial damage that are caused by a high-pressure jet of blood, such as VSD, AR, MR.

The risk is minimal at **low pressure lesions**, such as a large ASD

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

Vegetations



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



LV : left ventricle LA : left atrium RV : right ventricle RA : right atrium



Vegetations can :

- ➢ Become Large → Severe obstruction (uncommon; most with fungal infective endocarditis)
- ➤ Damage the value by (tissue distortion, cusp perforation or disruption of chordae) → severe regurgitation → heart failure
- \succ Destroy adjacent tissues \rightarrow abscess formation

Extra-cardiac manifestations :

• Immune phenomenon : Vasculitis , glomerulonephritis

• Embolic phenomenon :

Brain (CVA), limb (acute limb ischemia), kidney (AKI), spleen (Acute splenic infarction) Mycotic aneurysms may develop in arteries at the site of infected emboli (e.g cerebral mycotic aneurysm)

Microbiology

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

- 1- Staph. aureus
- The most common cause of IE
- Highly virulent and invasive, usually producing florid vegetations, rapid valve destruction and abscess formation.
- Origin : skin infections, abscesses or vascular access sites (IV or central lines) or from IV drug use.

2- Viridans streptococci

(such as Strep. mitis and Strep. sanguis)

- Oral cavity commensals
- Origin: chewing or tooth-brushing, or at the time of dental treatment

3- HACEK group (3-4%)

(Haemophilus aphrophilus , Aggregatibacter actinomycetemcomitans; Cardiobacterium hominis; Eikenella corrodens; and Kingella kingae)

- Orophayngeal commensals
- Origin : poor dental hygiene and recent dental procedures
- Prolonged culture is required The diagnosis may be revealed only after
- 4- Coagulase-negative staphylococci (CONS)
- 1. Staph. Epidermidis
- 2. Staph.lugdenensis: (rapidly destructive and associated with multiple emboli)
- They are part of the **normal skin flora**.
- **Origin :** Post-operative endocarditis after cardiac surgery.

They cause native valve endocarditis in approximately 5% of cases and **Should not be routinely dismissed** as blood culture contaminants.

5- Enterococcus faecalis, Enterococcus faecium and Strep. gallolyticus (previously known as Strep. bovis)

- **Origin:** bowel or urinary tract.
- Strep. gallolyticus associated with large bowel malignancy

6- Q fever endocarditis (Coxiella burnetii)

- Origin : farm animals(cattle , sheep, goats : urine, feces , milk)
- The aortic value is usually affected and there may also be hepatitis, pneumonia and purpura. Life-long antibiotic therapy may be required.

7- Brucella endocarditis

Origin: contact with goats or cattle.

8- Yeasts and fungi

- **Origin**: immunocompromised patients or those with in-dwelling intravenous catheters.
- Abscesses and emboli are common, mortality is high.
- Therapy is difficult, **surgery** is often required

			or prosu	ieuc vaive
Pathogen	Of native valve $(n = 280)$	In injection drug users (n = 87)	Early (n = 15)	Late (n = 72)
Staphylococci	124 (44%)	60 (69%)	10 (67%)	33 (46%)
<i>Staph. aureus</i> Coagulase-negative	106 (38%) 18 (6%)	60 (69%) 0	3 (20%) 7 (47%)	15 (21%) 18 (25%)
Streptococci	86 (31%)	7 (8%)	0	25 (35%)
Oral	59 (21%)	3 (3%)	0	19 (26%)
Others (non-enterococcal)	27 (10%)	4 (5%)	0	6 (8%)
Enterococcus spp.	21 (8%)	2 (2%)	1 (7%)	5 (7%)
HACEK	12 (4%)	0	0	1 (1%)
Polymicrobial	6 (2%)	8 (9%)	0	1 (1%)
Other bacteria	12 (4%)	4 (5%)	0	2 (3%)
Fungi	3 (1%)	2 (2%)	0	0
Negative blood culture	16 (6%)	4 (5%)	4 (27%)	5 (7%)

Of prosthetic valve

(HACEK = <u>*Haemophilus aphrophilus – now known as Aggregatibacter aphrophilus*–<u>*Aggregatibacter actinomycetemcomitans;*</u> <u>*Cardiobacterium hominis;*</u> <u>*Eikenella corrodens;*</u></u> and <u>*K</u>ingella kingae*)</u>

Adapted from Moreillon P, Que YA. Infective endocarditis. Lancet 2004; 363:139–149.

Clinical features

- Acute
- Subacute

There is considerable overlap because :

1- The clinical pattern is influenced by the

- Microorganism
- Site of infection
- Prior antibiotic therapy
- Presence of a valve or shunt prosthesis

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

IE should be suspected when a patient with congenital or valvular heart disease develops

- Persistent fever, unusual tiredness, night sweats or weight loss (constitutional symptoms)
- New signs of valve dysfunction or heart failure.
- Less often the patient can present with complications:



Fig. 16.89 Clinical features that may be present in endocarditis Insets (Petechial rash nail-fold infarct) From Newby D. Grubb N. Cardiology: an



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Embolic phenomenon

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Vasculitic

(immune

phenomenon)

henomenon

Fig. 16.89 Clinical features that may be present in endocarditis. Insets (Petechial rash nail-fold infarct) From Newby D. Gruhb N. Cardiology: an





16.95 Diagnosis of infective endocarditis

Major criteria

Positive blood culture

- <u>Typical</u> 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

*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.

- Staphylococcus aureus
- Viridans streptococci
- Streptococcus gallolyticus
- Enterococci (in the absence of a primary focus)
- HACEK group

UPDATES IN MAJOR CHROTERIA OF IE

- 2. Imaging positive for IE
- a. Echocardiogram positive for IE:
 - Vegetation
 - Abscess, pseudoaneurysm, intracardiac fistula
 - Valvular perforation or aneurysm
 - New partial dehiscence of prosthetic valve
- b. Abnormal activity around the site of prosthetic valve implantation detected by ¹⁸F-FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabelled leukocytes SPECT/CT.
- c. Definite paravalvular lesions by cardiac CT.

i	16.95	Diagnosis	of infect	ive endo	ocarditis	
Major ci	riteria					
<pre>Positive • _ Typica</pre>		culture nism from tw	o cultures	}		
• Pt	<u> </u>					-

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- Pi
- Intravenous drug misuse
- Pyrexia ≥38°C
- Embolic phenomenon
- Vasculitic phenomenon
- Blood cultures suggestive: organism grown but criteria
- Suggestive echocardiographic findings

*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.

Indications for echocardiography



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

*The chest X-ray may show evidence of cardiac failure and cardiomegaly.

*Blood tests : Positive Rheumatoid factor (immune phenomenon), elevation of the ESR, CRP, a normocytic normochromic anaemia, and leucocytosis are common but not invariable.

*General urine examination: Proteinuria and non-visible haematuria (Glomerulonephritis)

Rejected IE

- Firm alternate diagnosis; or
- Resolution of symptoms suggesting IE with antibiotic therapy for
 4 days; or
- No pathological evidence of IE at surgery or autopsy, with antibiotic therapy for ≤4 days; or
- Does not meet criteria for possible IE, as above

Accessory Pathway Locations Anterior Trigone/aortic valve + Right Left + Posterior VOFT **Right anterior** ~ Left anterolateral LCG RCC Anteroseptal /NCC **Right anterolateral** Mitral Tricuspid vallve AVN Valive Left lateral Right lateral Midseptal Left posterolateral **Right posterolateral** Coronary sinus @ MAYO 2009 Left posterior **Right posterior** Posteroseptal



Empirical treatment

Subacute presentation :

Antibiotic treatment should ideally be withheld until the results of blood cultures are available.

Acute presentation :

Intially, empirical therapy should be started, after blood samples for blood culture are drawn, with:

- Native valve endocarditis : vancomycin IV + gentamicin IV
- Prosthetic valve endocarditis : vancomycin IV + gentamicin IV + rifampicin orally.

Then, Specific treatment : Results of blood culture and sensitivity (MIC = minimum inhibitory concentration of drugs) help to guide antibiotic therapy

16.96 Antimicrobial treatment of common causative organisms in infective endocarditis				
			Duration	
Antimicrobial susceptibility	Antimicrobial	Dose	Native valve	Prosthetic valve
Streptococci Penicillin MIC \leq 0.125 mg/L Penicillin MIC $>$ 0.125, \leq 0.5 mg/L Penicillin MIC $>$ 0.5 mg/L	Benzylpenicillin IV Benzylpenicillin IV and gentamicin IV Vancomycin IV and gentamicin IV	 1.2g 6 times daily 2.4g 6 times daily 1 mg/kg twice daily² 1 g twice daily³ 1 mg/kg twice daily² 	4 weeks ¹ 4 weeks 2 weeks 4 weeks 4 weeks	6 weeks 6 weeks 2 weeks 6 weeks 6 weeks
Enterococci Amoxicillin MIC \leq 4 mg/L and gentamicin MIC \leq 128 mg/L Amoxicillin MIC $>$ 4 mg/L and gentamicin MIC \leq 128 mg/L	Amoxicillin IV and gentamicin IV ² Vancomycin IV and gentamicin IV ²	2 g 6 times daily 1 mg/kg twice daily ² 1 g twice daily ³ 1 mg/kg twice daily ²	4 weeks 4 weeks 4 weeks 4 weeks	6 weeks 6 weeks 6 weeks 6 weeks
Staphylococci – native valve Meticillin-sensitive Meticillin-resistant, vancomycin MIC ≤2 mg/L, rifampicin-sensitive	Flucloxacillin IV Vancomycin IV Rifampicin orally	2g 4–6 times daily ⁴ 1g twice daily ³ 300–600 mg twice daily	4 weeks 4 weeks 4 weeks	_ _ _
Staphylococci – prosthetic valve Meticillin-sensitive Meticillin-resistant, vancomycin MIC ≤2 mg/L, rifampicin-sensitive	Flucloxacillin IV and gentamicin IV and rifampicin orally Vancomycin IV and rifampicin orally	2 g 4–6 times daily 1 mg/kg twice daily ² 300–600 mg twice daily 1 g twice daily ³ 300–600 mg twice daily		6 weeks 6 weeks 6 weeks 6 weeks 6 weeks

¹When conditions in Box 16.97 are met, 2 weeks of benzylpenicillin and gentamicin (1 mg/kg twice daily) may be sufficient. Ceftriaxone 2 g once daily IV/IM can be used instead of benzylpenicillin for those with non-severe penicillin allergy. ²Pre-dose gentamicin level should be $\leq 1 \text{ mg/L}$, post-dose 3–5 mg/L. Adjust dose according to levels and renal function. ³Pre-dose vancomycin level should be 15–20 mg/L. Adjust dose according to levels and renal function. ⁴Use 6 times daily if weight >85 kg. (IV = intravenous; MIC = minimum inhibitory concentration)

Adapted from Gould FK, Denning DW, Elliott TS, et al. Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the working party of the British Society for Antimicrobial Chemotherapy. J Antimicrob Chemother 2012; 67:269–289.

16.96 Antimicrobial treatme	ent of common causative o	rganisms in infective endoca	rditis	
			Di	uration
Antimicrobial susceptibility	Antimicrobial	Dose	Native valve	Prosthetic valve
Streptococci				
Penicillin MIC \leq 0.125 mg/L	Benzylpenicillin IV	1.2g 6 times daily	4 weeks ¹	6 weeks
Penicillin MIC >0.125,	Benzylpenicillin IV and	2.4g 6 times daily	4 weeks	6 weeks
$\leq 0.5 \text{mg/L}$	gentamicin IV	1 mg/kg twice daily ²	2 weeks	2 weeks
Penicillin MIC > 0.5 mg/L	Vancomycin IV and	1 g twice daily ³	4 weeks	6 weeks
	gentamicin IV	1 mg/kg twice daily ²	4 weeks	6 weeks
Enterococci				
Amoxicillin MIC \leq 4 mg/L and	Amoxicillin IV and	2g 6 times daily	4 weeks	6 weeks
gentamicin MIC \leq 128 mg/L	gentamicin IV ²	1 mg/kg twice daily ²	4 weeks	6 weeks
Amoxicillin MIC > 4 mg/L and	Vancomycin IV and	1 g twice daily ³	4 weeks	6 weeks
gentamicin MIC ≤128 mg/L	gentamicin IV ²	1 mg/kg twice daily ²	4 weeks	6 weeks
Staphylococci – native valve				
Meticillin-sensitive	Flucloxacillin IV	2g 4–6 times daily ⁴	4 weeks	—
Meticillin-resistant, vancomycin MIC	Vancomycin IV	1 g twice daily ³	4 weeks	—
$\leq 2 \text{ mg/L}$, rifampicin-sensitive	Rifampicin orally	300-600 mg twice daily	4 weeks	—
Staphylococci – prosthetic valve				
Meticillin-sensitive	Flucloxacillin IV	2g 4–6 times daily	_	6 weeks
	and gentamicin IV	1 mg/kg twice daily ²	_	6 weeks
	and rifampicin orally	300-600 mg twice daily	_	6 weeks
Meticillin-resistant, vancomycin MIC	Vancomycin IV	1 g twice daily ³	_	6 weeks
$\leq 2 \text{ mg/L}$, rifampicin-sensitive	and rifampicin orally	300-600 mg twice daily	_	6 weeks

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16.98 Indications for cardiac surgery in infective endocarditis

- Heart failure due to valve damage
- Failure of antibiotic therapy (persistent/uncontrolled infection)
- Large vegetations on left-sided heart valves with echo appearance suggesting high risk of emboli
- Previous evidence of systemic emboli
- Abscess formation

*Patients with prosthetic valve endocarditis or fungal endocarditis often require cardiac surgery.

IE prophylaxis:

- Antibiotic prophylaxis
- Non specific preventive measures

A/Antibiotic prophylaxis:

Cardiac conditions
High riskProcedures
High riskFor infective endocarditisImage: Condition of the section of th

Antibiotic prophylaxis should <u>only be</u> considered for:

- (1) Prosthetic valve
- (2) Previous episode of IE.
- (3) CHD (congenital heart disease)
 - (a) Cyanotic CHD.
 - (b) CHD repaired with a prosthetic material
 - (up to 6 months if complete repair / lifelong if residual shunt remains.)

Antibiotic prophylaxis *should* <u>only be</u> considered for:

Dental procedures requiring :

- manipulation of the gingival or periapical region of the teeth
- or perforation of the oral mucosa

While Antibiotic prophylaxis is <u>NOT</u> recommended for

1. Other dental procedures :

local anaesthetic injections in non-infected tissues, treatment of superficial caries, removal of sutures, dental X-rays, placement or adjustment of removable prosthodontic or orthodontic appliances or braces or following the shedding of deciduous teeth or trauma to the lips and oral mucosa

- 1. Respiratory tract procedures
- 2. Gastrointestinal or urogenital procedures
- 3. Skin and soft tissue procedures

Recommended prophylaxis for high-risk dental procedures in high-risk patients

Situation	Antibiotic	Single-dose 30–60 minutes before procedure		
		Adults	Children	
No allergy to penicillin or ampicillin	Amoxicillin or ampicillinª	2 g orally or i.v.	50 mg/kg orally or i.v.	
Allergy to penicillin or ampicillin	Clindamycin	600 mg orally or i.v.	20 mg/kg orally or i.v.	

^aAlternatively, cephalexin 2 g i.v. for adults or 50 mg/kg i.v. for children, cefazolin or ceftriaxone 1 g i.v. for adults or 50 mg/kg i.v. for children.

Cephalosporins should not be used in patients with anaphylaxis, angio-oedema, or urticaria after intake of penicillin or ampicillin due to cross-sensitivity.

These measures should ideally be applied to the general population and particularly reinforced in high-risk patients:

- Strict dental and cutaneous hygiene. Dental follow-up should be performed twice a year in high-risk patients and yearly in the others.
- Disinfection of wounds.
- Curative antibiotics for any focus of bacterial infection.
- No self-medication with antibiotics.
- Strict infection control measures for any at-risk procedure.
- Discourage piercing and tattooing.

Non infective endocarditis:

Libman-Sacks endocarditis characterise which of the followings:

- A-Rheumatoid arthritis B- SLE
- **C- Scleroderma**
- **D- Bahcet disease**

Non infective endocarditis:

Marantic endocarditis characterise which of the followings:

- A- DIC
- **B- Metastatic carcinomas**
- **C-** Chronic infection like TB
- **D- All of the above**

Q // 40 years old female, hypertensive presented with 4 weeks history of fever, night sweating and hand pain.

<u>Clinical examination</u> :

Pallor

- Temperature 39 C , BP= 150/90 , HR=100 regular
- Precordial examination : Grade 2 systolic murmur at apex with soft S1
- Abdominal examination : Mild splenomegaly

Hands examination : arthritis of interphalangeal and metacarpophalangeal joints

<u>Echocardiography</u> : thickened prolapsed mitral valve leaflets with vegetations and moderate mitral regurgitation



THANK YOU