

INFECTIVE ENDOCARDITIS

CAUSES OF INFECTIVE ENDOCARDITIS

TYPE OF VALVE	MOST COMMON CAUSES	LESS COMMON
Native valve infective endocarditis (NVE)	Viridans streptococci (~50–70%)	Gram-positive bacilli
Late prosthetic valve endocarditis (PVE)	<i>Staphylococcus aureus</i> (~25%) Enterococci (~10%)	Gram-negative bacilli HACEK group of organisms (<i>Haemophilus</i> , <i>Actinobacillus</i> , <i>Cardiobacterium</i> , <i>Eikenella</i> and <i>Kingella</i> species)
Early prosthetic valve endocarditis (PVE)	<i>S. epidermidis</i> <i>S. aureus</i>	Fungi

RISK FACTORS FOR INFECTIVE ENDOCARDITIS

- Risk factors for infective endocarditis (IE) include:
 - Cardiac risk factors:
 - prior infective endocarditis
 - presence of a prosthetic valve or cardiac device
 - history of valvular or congenital heart disease
 - Non-cardiac risk factors:
 - intravenous drug use
 - intravenous lines
 - immunosuppression
 - recent dental or surgical procedure

DIAGNOSIS OF INFECTIVE ENDOCARDITIS


- The accepted criteria for diagnosing IE are modified Duke criteria – a diagnostic guide to be used together with good clinical judgment.
- The diagnosis is based on:
 - clinical manifestations: fever (with or without bacteremia) and/or relevant risk factors
 - blood cultures are the primary diagnostic test for infective endocarditis:
 - three sets of blood cultures each containing 10 mL of blood give a good diagnostic yield
 - must be taken aseptically
 - blood cultures should be taken prior to starting antimicrobials
 - bacteraemia in IE is almost constant, therefore no need to delay blood sampling to coincide with peaks of fever
 - other microbiological evidence
 - echocardiography

- Additional evaluation for suspected infective endocarditis:
 - serology for *Coxiella*, *Bartonella* and *Brucella* if the blood cultures are negative
 - electrocardiography
 - chest radiography and other radiographic imaging tailored to clinical manifestations
 - dental evaluation

INVESTIGATION OF RARE CAUSES OF BLOOD-CULTURE NEGATIVE INFECTIVE ENDOCARDITIS

PATHOGEN	RECOMMENDED LABORATORY TESTS
<i>Brucella</i> spp.	Blood cultures, serology, culture + histology + PCR of resected valve material (<i>Brucella</i> PCR and/or broad range bacterial 16s rRNA PCR)
<i>Coxiella burnetii</i>	Serology, tissue culture + histology + PCR of resected valve material (broad range bacterial 16s rRNA PCR)
<i>Bartonella</i> spp.	Blood cultures, serology, culture + histology + PCR of resected valve material (<i>Bartonella</i> PCR and/or broad range bacterial 16s rRNA PCR)
<i>Tropheryma whipplei</i>	Histology and PCR of resected valve material (<i>Tropheryma whipplei</i> PCR and/or broad range bacterial 16s rRNA PCR)
<i>Mycoplasma</i> spp.	Serology, culture + histology + PCR of resected valve material (broad range bacterial 16s rRNA PCR)
<i>Legionella</i> spp.	Serology, culture + histology + PCR of resected valve material (broad range bacterial 16s rRNA PCR)
Fungi	Blood cultures, culture + PCR of resected valve material (broad range fungal PCR)

EMPIRIC TREATMENT REGIMENS FOR INFECTIVE ENDOCARDITIS

 NVE-INDOLENT PRESENTATION	
Ampicillin 2 g IV 4 hourly AND Gentamicin 3 mg/kg IV every 24 hours	If the patient is stable, ideally await blood cultures. Ampicillin has better activity against enterococci and many HACEK microorganisms compared with benzylpenicillin. Use vancomycin if genuine penicillin allergy.
NVE, SEVERE SEPSIS (NO RISK FACTORS FOR ENTEROBACTERIACEAE, PSEUDOMONAS)	
Vancomycin 1 g IV 12 hourly AND Gentamicin 3 mg/kg IV every 24 hours	In severe sepsis, staphylococci (including methicillin-resistant staphylococci) need to be covered. If there are concerns about nephrotoxicity/acute kidney injury, use ciprofloxacin in place of gentamicin.

**NVE, SEVERE SEPSIS AND RISK FACTORS FOR MULTI-RESISTANT ENTEROBACTERIACEAE, PSEUDOMONAS**

Vancomycin 1 g IV 12 hourly
AND
 Meropenem 2 g IV 8 hourly

Will provide cover against MRSA, MRSE, streptococci, enterococci, HACEK, Enterobacteriaceae and *P. aeruginosa*.

PVE PENDING BLOOD CULTURES OR WITH NEGATIVE BLOOD CULTURES

Vancomycin 1 g IV 12 hourly
AND
 Gentamicin 3 mg/kg IV every 24 hours
AND
 Rifampicin 300–600 mg PO or IV 12 hourly

TREATMENT REGIMENS FOR SPECIFIC BACTERIA CAUSING ENDOCARDITIS**STAPHYLOCOCCAL ENDOCARDITIS**

INDICATION	ANTIBIOTIC(S)	DOSE/ROUTE	DURATION (WEEKS)
NVE: cloxacillin/methicillin-susceptible <i>Staphylococcus</i> spp.	Flucloxacillin	2 g IV 4–6 hourly	4
NVE: cloxacillin/methicillin-resistant and rifampicin-susceptible <i>Staphylococcus</i> spp. or penicillin allergy	Vancomycin*	1 g IV 12 hourly	4
	Rifampicin	300–600 mg PO 12 hourly	4
PVE: cloxacillin/methicillin and rifampicin-susceptible <i>Staphylococcus</i> spp.	Flucloxacillin	2 g IV 4–6 hourly	6
	Rifampicin	300–600 mg PO 12 hourly	6
	Gentamicin	3 mg/kg IV/IM every 24 hours	6
PVE: cloxacillin/methicillin-resistant, <i>Staphylococcus</i> spp. or penicillin allergy	Vancomycin*	1 g IV 12 hourly	6
	Rifampicin	300–600 mg PO 12 hourly	6
	Gentamicin	3 mg/kg IV/IM every 24 hours	2 weeks or more

*Vancomycin levels should be monitored and the dose adjusted to maintain a serum trough level between 15 and 20 mg/L.

**STREPTOCOCCAL ENDOCARDITIS (BASED ON MIC AND THE SPECIES)**

INDICATION	ANTIBIOTIC(S)	DOSE/ROUTE	DURATION (WEEKS)
Viridans streptococci: Penicillin MIC \leq 0.125 mg/L	Benzylpenicillin	1.2 g IV 4 hourly	4–6
	OR		
	Ceftriaxone	2 g IV/IM every 24 hours	4–6
	OR		
	Benzylpenicillin AND	1.2 g IV 4 hourly	2
	Gentamicin	3 mg/kg IV/IM every 24 hours	2
Viridans streptococci: Penicillin MIC > 0.125 to \leq 0.5 mg/L	OR		
	Ceftriaxone*	2 g IV/IM every 24 hours	2
	AND		
	Gentamicin	3 mg/kg IV/IM every 24 hours	2
Abiotrophia and <i>Granulicatella</i> spp. (nutritionally variant streptococci)	Benzylpenicillin	2.4 g IV 4 hourly	4–6
	AND		
Streptococci in patients with significant penicillin allergy	Gentamicin	3 mg/kg IV every 24 hours	4–6
	AND		
	Vancomycin**	1 g IV 12 hourly	4–6
	AND		
	Gentamicin	3 mg/kg IV every 24 hours	2
	OR		
	Teicoplanin	10 mg/kg IV every 24 hours	4–6
	AND		
	Gentamicin	3 mg/kg IV every 24 hours	2

*Regimen can be used for outpatient therapy.

**Vancomycin levels should be monitored and the dose adjusted to maintain a serum trough level between 15 and 20 mg/L.

**ENTEROCOCCAL ENDOCARDITIS**

INDICATION	ANTIBIOTIC(S)	DOSE/ROUTE	DURATION (WEEKS)
For amoxicillin-susceptible enterococci (MIC \leq 4 mg/L), penicillin MIC \leq 4 mg/L AND gentamicin-susceptible (MIC \leq 128 mg/L) isolates	Ampicillin	2 g IV 4 hourly	4–6
	AND		
	Gentamicin	3 mg/kg IV every 24 hours	4–6
	OR		
	Penicillin	2.4 g IV 4 hourly	4–6
	AND		
	Gentamicin	3 mg/kg IV every 24 hours	4–6

Rx	For penicillin-allergic patients OR amoxicillin- or penicillin-resistant isolate. Ensure vancomycin MIC \leq 4 mg/L	Vancomycin* AND Gentamicin	1 g 12 hourly IV 3 mg/kg IV every 24 hours	4 -6 4-6
	An alternative to vancomycin AND gentamicin regimen	Teicoplanin AND Gentamicin	10 mg/kg daily IV 3 mg/kg IV every 24 hours	4-6 4-6
	For amoxicillin-susceptible (MIC \leq 4 mg/L) AND gentamicin-susceptible (MIC \leq 128 mg/L) isolates	Ampicillin alone	2 g IV 4 hourly	6

*Vancomycin levels should be monitored and the dose adjusted to maintain a serum trough level between 15 and 20 mg/L.

Rx SUGGESTED TREATMENT FOR BLOOD CULTURE-NEGATIVE IE			
PATHOGEN	ANTIBIOTIC(S)	DOSE/ROUTE	DURATION (WEEKS)
<i>Brucella</i>	Doxycycline AND Cotrimoxazole AND Rifampicin	200 mg PO daily 960 mg PO 12 hourly 300-600 mg PO daily	\geq 3
<i>Bartonella</i>	Ampicillin AND Gentamicin OR Doxycycline AND Gentamicin	2 g IV 4 hourly 3 mg/kg IV every 24 hours 200 mg PO daily 3 mg/kg IV every 24 hours	6
<i>Coxiella burnetii</i> (Q fever)	Doxycycline AND Hydroxy-chloroquine OR Doxycycline AND Ciprofloxacin	100 mg PO 12 hourly 200 mg PO 8 hourly 100 mg PO 12 hourly 250 mg PO 12 hourly	\geq 18

**SUGGESTED TREATMENT FOR INFECTIVE ENDOCARDITIS CAUSED BY THE HACEK* GROUP**

ANTIBIOTIC	DOSE/ROUTE	DURATION (WEEKS)
Ceftriaxone AND Gentamicin OR Ampicillin AND Gentamicin	1 g IV/IM daily 3 mg/kg IV/IM every 24 hours 2 g IV 4 hourly 3 mg/kg IV/IM every 24 hours	4 4

**Haemophilus, Actinobacillus, Cardiobacterium, Eikenella* and *Kingella* species

FUNGAL ENDOCARDITIS**CANDIDA ENDOCARDITIS**

- *Candida* endocarditis is one of the most serious manifestations of candidiasis. *Candida* is the most common cause of fungal endocarditis, causing over half of all cases.
- Initial treatment should be with an echinocandin or amphotericin B (preferably a lipid preparation), and modified once the species and susceptibility profile is known.
- Surgical valve replacement is recommended for both native and prosthetic valve endocarditis.
- Treatment should be continued for at least six weeks following surgery.
- Initial treatment is typically followed by long-term suppressive therapy to prevent relapses.

**CANDIDA ENDOCARDITIS: INITIAL ANTIFUNGAL THERAPY**

Caspofungin 150 mg IV daily
OR
Micafungin 150 mg IV daily
OR
Anidulafungin 200 mg IV daily
OR
Liposomal amphotericin B 3 to 5 mg/kg IV daily
OR
Amphotericin B deoxycholate 1 mg/kg IV daily (if a lipid formulation is not available)

ASPERGILLUS ENDOCARDITIS

- Aspergillus accounts for approximately 25% of fungal endocarditis cases.
- Successful treatment of endocarditis requires the combination of antifungal therapy and surgical debridement.
- Initial treatment should be with voriconazole, with confirmation of susceptibility of the isolate to voriconazole and therapeutic drug monitoring.
- Duration of treatment is not known and should be at least six weeks after surgical debridement and followed by long-term prophylaxis.



ASPERGILLUS ENDOCARDITIS: INITIAL ANTIFUNGAL THERAPY

Voriconazole 6 mg/kg IV every 12 hours for the first day, followed by 4 mg/kg IV every 12 hours