

INTERESTING CASE

INFECTIVE ENDOCARDITIS



Outline



1

Patient history

2

**Physical
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**Problem list
& Approach**

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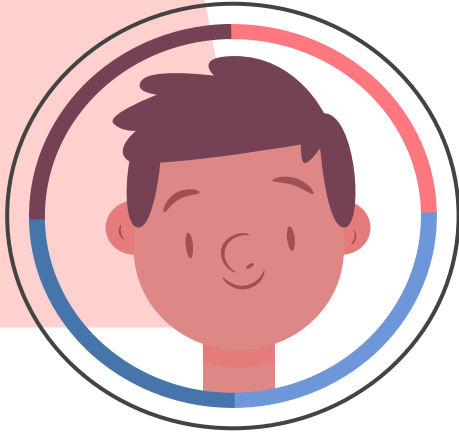
Hospital coarse

6

Topic review

Patient history





AGE: 44 year
GENDER: Male
U/D: Unknown



ABOUT PATIENT

CC: ไข้สูงหนาวสั่น 3 wk PTA

Case Thai male 44 yr, Unknown U/D

CC: ใช้สุงหนาวสั้น 3 wk PTA 

PRESENT ILLNESS

3 wk PTA มีใช้สุงหนาวสั้น (ไม่มีฟันกระทบกัน) เป็นๆหายๆ กิน Paracetamol แล้วอาการไม่ดีขึ้น เป็นมากช่วงอากาศเย็น แต่ยังไปทำงานได้ตามปกติ ไม่มีไอ ไม่มีเสมหะ ไม่ปวดท้อง ไม่มีปวดเอว ไม่มีคลื่นไส้อาเจียน ไม่มีท้องเสียถ่ายเหลว ไม่มีปัสสาวะแสบขัด ไม่มีปวดเมื่อยตามร่างกาย กินอาหารได้ตามปกติ ไม่มีน้ำหนักลด ไม่มีผื่น

2 wk PTA ไปซื้อยามาจาก clinic อาการไม่ดีขึ้น

4 day PTA มีใช้สุงหนาวสั้นตลอด รู้สึกใจสั้น อ่อนเพลียเหมือนจะวูบ อาการเป็นมากขึ้นเรื่อยๆ ไปทำงานไม่ไหว จึงมารพ.

ให้ประวัติว่า มีเดินเข้าสวน ไม่ได้เดินเข้าป่าหรือพุ่มหญ้า มีเดินย่ำน้ำสกปรกบ้าง



PAST HISTORY

- Unknown U/D
- Alcohol: เบียร์ 1 ขวด/วัน, 3 วัน/สัปดาห์
- Smoking: ปฏิเสธการสูบบุหรี่
- ปฏิเสธการใช้สารเสพติด รวมถึงการฉีดสารเสพติดเข้าสู่หลอดเลือดดำ
- ปฏิเสธประวัติแพ้ยาหรือแพ้อาหาร
- ปฏิเสธประวัติการผ่าตัดในอดีต
- ให้ประวัติว่าเคยกินถึงเช้าของยั้งยงเมื่อ 3 moPTA กินอยู่ 2 mo หยุดมา 1 mo

Physical examination



Physical examination



Vital sign : BT RR HR BP

GA : Good consciousness, well cooperative

HEENT : not pale conjunctiva, anicteric sclera, no injected conjunctiva,
few oral caries

CVS : no heave, **thrill at LLPSB, PSM grade IV at LLPSB radiate to apex**

RS : no accessory m.use, equal chest movement, resonance on
percussion, equal breath sound

Physical examination



Abdomen : no abdominal distension, no dilated vein, normoactive bowel sounds, no palpable mass, no hepatosplenomegaly, no CVA tenderness

Extremities : no bruise or petechiae, no joint swelling, no edema

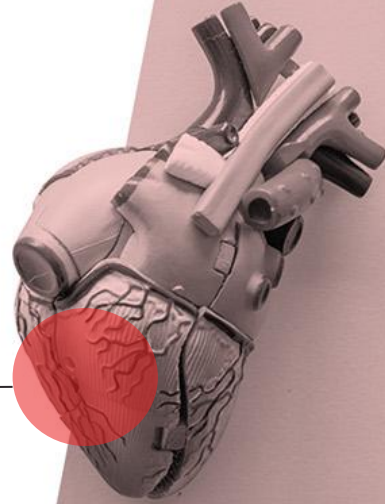
Neurological examination : Mental status - alert, oriented to time, place and person , CN Intact, Motor power - grade 5 all extremities, Normal sensation

Problem list & Approach



Problem list

Prolong fever with unknown origin
with New onset murmur



Prolong fever
with unknown origin

Infection

Non-Infection

Localized abscess

Vascular Infection

Systemic Infection

GI
Hepatobiliary
Gu

- **Bacterial endocarditis**
- Vascular catheter
related infection

- Virus: Infectious mononucleosis, HIV
- **Bacteria**: Salmonellosis, Legionnaires' disease,...
- Microbacteria: Tuberculosis, NTM
- **Tropical infection**: Melioidosis, Leptospirosis,
Rickettsial disease, Malaria, Tularemia
- Fungus: Aspergillosis, PCP, Histoplasmosis

Prolong fever
with unknown origin

Infection

Non-Infection

Connective tissue
disease

Tumor

Other

- Rheumatoid arthritis
- Vasculitis
- SLE

- Malignant
 - Hematologic
 - RCC
 - Hepatocellular carcinoma
- Benign

- Drug fever
- Thermoregulatory disorder



Provisional Diagnosis : Infective endocarditis

Different diagnosis : Systemic infection

TIMELINE



23/4-6/5/64

16-23/4/64

12-16/4/64

Presented with
prolonged fever with
new onset murmur
Imp : IE

Refer to PPK

- consult Cardio
(18/4/64) >> Dx : IE
- 1st Echocardiogram
(23/4/64)

Refer back to Soidao

- continue ATB 2 wks



TIMELINE



12/5/64-Now

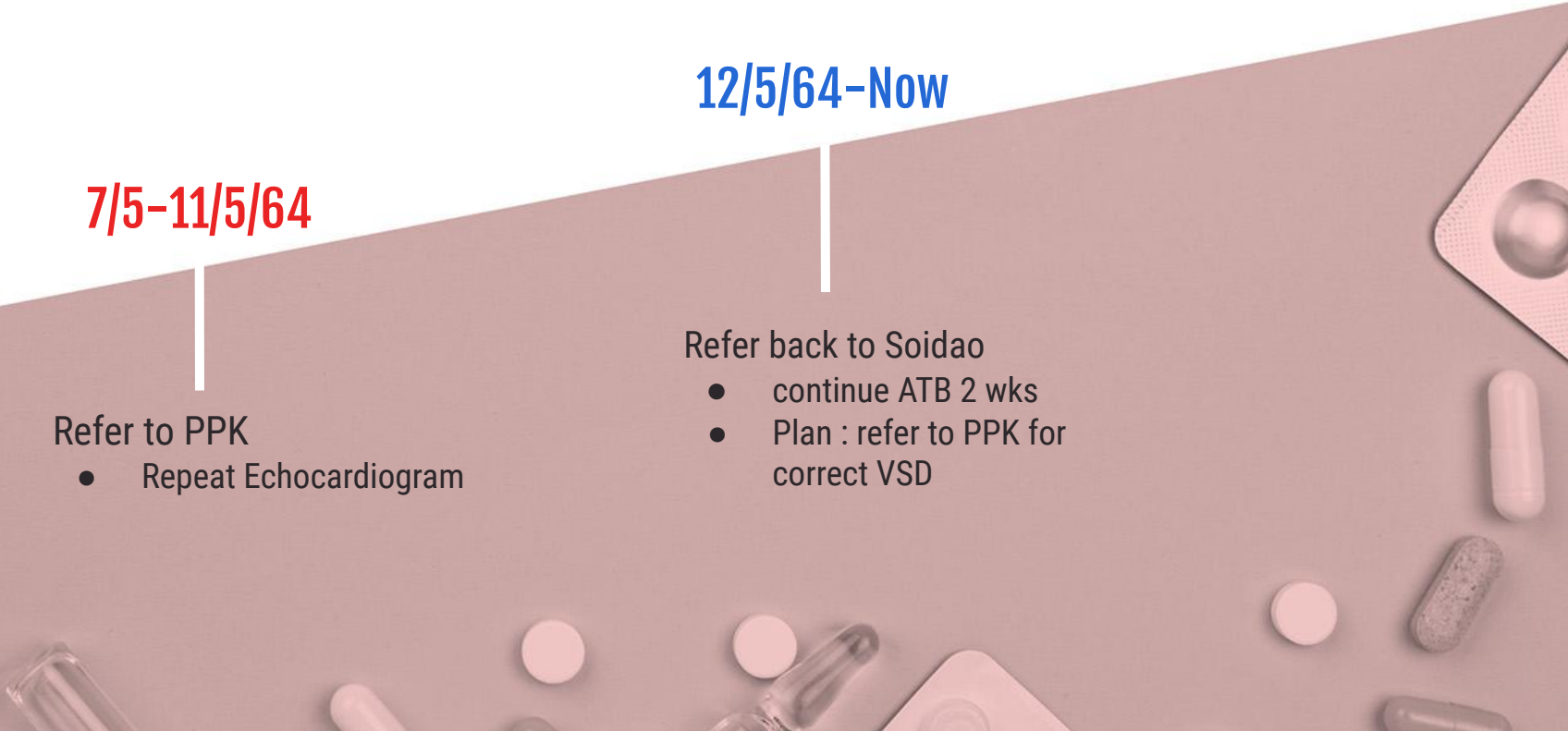
7/5-11/5/64

Refer to PPK

- Repeat Echocardiogram

Refer back to Soidao

- continue ATB 2 wks
- Plan : refer to PPK for correct VSD



12-16/4/64 at Soidao



- Admit
- Investigation
 - H/C 2 ชั่วโมง then next 1 hr apart (ทั้งหมด 3 ขวด)
 - Lepto Ab
 - Weil felix test
 - HIV Ab
 - Melioid titer
 - Malaria film
 - Sputum AFB x III

Empirical ATB Treatment for IE

- Cloxacilin 2 g IV q 4 hr
- Gentamycin 180 mg IV OD
- Ampicillin 2 g IV q 4 hr

H/C : *Ganella haemolysans*

Clinical ปัจจุบัน : มีไข้เป็นๆหายๆ ไอบ้างเล็กน้อย เหนื่อยเล็กน้อย
Imp : IE Plan : refer to PPK for work up

16-23/5/64 at PPK



ช่วงที่ Admit

- Repeat H/C : NG x III
- Continue Antibiotic ตามรพ.สอยดาว : Cloxacillin, Gentamicin, Ampicillin
- Consult Cardio (18/5/64)

Dx : IE

Suggest

- ชักประวัติ IVDU
- ให้ Antibiotic ตาม Sense จนครบ
- Plan ส่ง Echo (Plan Sx)

1st Echocardiogram (23/4/64)

- Sinus rhythm, good LV contraction without RWMA.
- Large vegetative mass (3.6x1.8 cm) at TR.
- Small VSD (perimembranous type)

Clinical ปัจจุบัน : ไม่มีไข้ ไม่หอบเหนื่อย Clinical stable ดี

Plan : refer กลับรพช. for continue Antibiotics ต่ออีก 2 wks และให้ refer กลับไป PPK เพื่อ repeat Echocardiogram (Size IE เข้า criteria ของการผ่าตัด แต่เนื่องด้วยสถานการณ์โควิด การผ่าตัดจึงทำได้ยาก)

Pt. Name : **YAEMMALI SOMJAN**
Cardiologist : **Wiwat Kanjanarutjawi**, MD.
Echo No. : **1684-64**

Pt. HN : **6413438**
Age : **06/12/1976 (44 years)**
Echo machine :

Exam Date : **23/04/2021**
Sex : **male**
Room/OPD :

ศูนย์โรคหัวใจ
พญ. วิวัฒน์ จาวี

SCAN แล้ว

Physical Exam Data

Height 165 cm, 5 ft 5 in. Weight 61 kg, 9 st 8 lb. BMI 22.41 kg/m². BSA 1.67 m².

Measure

Doppler

TR Vmax 3.29 m/s TR max PG 43.21 mmHg

Other

Patient Characteristics 1.67 m²

Body Surface Area

Patient Characteristics 44 a

Subject Age

Patient Characteristics 1.65 m

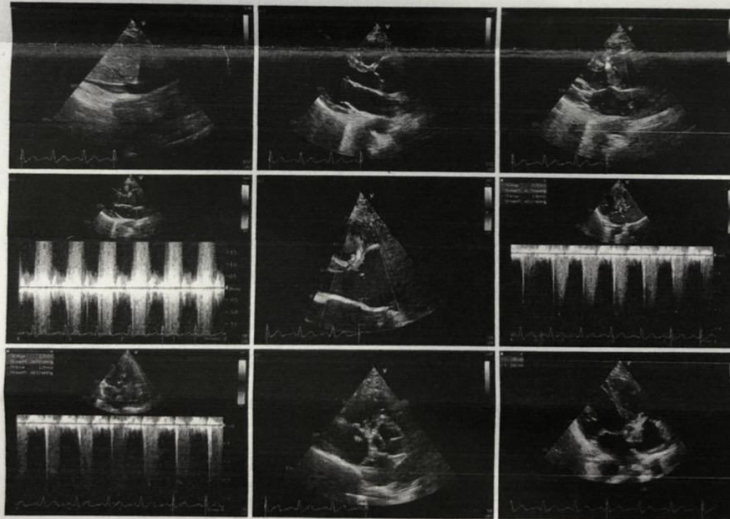
Patient Height

Patient Characteristics 61 kg

Patient Weight

Comment

Sinus rhythm, good LV contraction without RWMA. Presented large vegetative mass (3.6 x 1.8 cm) at TV but trivial TR. Presented small VSD (perimembranous type). Normal pericardium.



23/4/64-6/5/64 at รพ.สอยดาว



Refer กลับจาก PPK

- continue Antibiotics : Gentamicin, Cloxacillin, Ampicillin จนครบ 14 วัน
- Consult ทันตกรรม
 - Imp : dental caries, chronic periodontitis
 - Mx : ถอนฟัน, อุดฟัน, ขูดหินน้ำลาย

Clinical ปัจจุบัน : ไม่มีไข้ ไม่หอบเหนื่อย Clinical stable ดี

Plan : continue Antibiotics จนครบ 2 wks และให้ refer กลับไป PPK เพื่อ repeat Echocardiogram

7-11/5/64 at PPK



2nd Echocardiogram (11/5/64)

- Mild LV dilatation, LVEF 65%
- Thickening of TV leaflet, decrease vegetation size, mild TR with PHT
- No AS,AR, MR
- Small perimembranous VSD with left to Right Shunt

Consult cardio (11/5/64)

- ให้ Antibiotics เหลือแค่ Ampicillin เนื่องจาก Cr rising
- continue Ampicillin ต่ออีก 2 wks
- ให้ติดต่อ refer ไป รพ.จุฬารัตน์ 3 for VSD closure (ถ้าไม่แก้ไขมีโอกาสเป็น recurrent IE อีก)

Clinical ปัจจุบัน : ไม่มีไข้ ไม่หอบเหนื่อย clinical stable ดี
Plan : refer กลับรพช. for continue Ampicillin IV 2 wks

Aortic Valve

Trileaflet and structurally normal aortic valve. No evidence of aortic stenosis. No aortic regurgitation.

Tricuspid Valve

Mild tricuspid regurgitation.
Moderately increased pulmonary pressure.

Aorta

Normal aortic root, ascending aorta and aortic arch.

Pulmonic Valve

Structurally normal pulmonic valve.

Pericardium

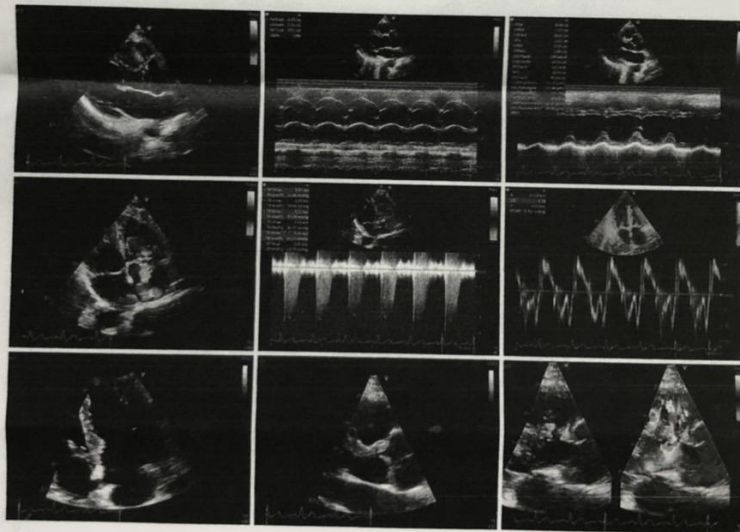
Normal. Effusion: none.

Comment

1. Mild LV dilate, LVEF 65%, no RWMA, diastolic dysfunction grade 1, $E/E' = 6$, LA 3.7 cm.
2. Mild RA dilate, good RV contraction
3. Thickening of TV leaflet, decrease vegetation size, mild TR with PHT, RVSP 51 mmHg
4. No AS, no AR, no MR
5. Presence of small perimembranous VSD with left to right shunt with PHT
6. No pericardial effusion

Impression

VSD with PHT, improve IE at TV



12/5/64 – Now at รพ.สอยดาว



Refer กลับจาก PPK

- continue Antibiotics : Ampicillin จนครบ 14 วัน

Clinical ปัจจุบัน : ไม่มีไข้ ไม่หอบเหนื่อย Clinical stable ดี
Plan : ให้ ATB ครบ 14 วัน then Refer ไป PPK for correct VSD

Gemella endocarditis



[Avicenna J Med.](#) 2019 Oct-Dec; 9(4): 164–168.

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Gemella endocarditis: A case report and a review of the literature

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Table 1

Characteristics of cases of Gemella infective endocarditis

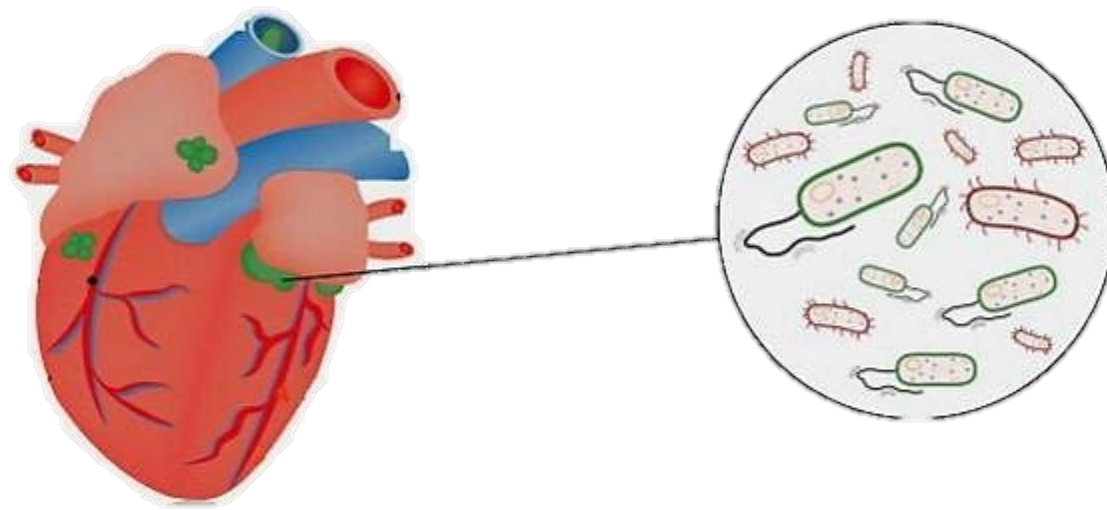
Characteristics	Participants (N = 66)
Age group (years; N = 64)	50.5 ± 23
0–10	3 (5%)
11–20	5 (8%)
21–30	6 (9%)
31–40	7 (11%)
41–50	8 (13%)
≥51	35 (55%)
Gender (N = 64)	
Male	46 (72%)
Female	18 (28%)
Source (N = 30)	
Dental/oral	22 (73%)
Intravenous drug abuse	4 (13%)
Colonic	4 (13%)
Presentation	
Fever	40 (61%)
Fatigue	7 (11%)
Dyspnea	6 (9%)
Miscellaneous	13 (19%)

Table 2

Valve affected, surgery, and outcomes of Gemella infective endocarditis

Characteristics	Participants (N = 66)
Valve affected (N = 62)	
Mitral valve	24 (39.1%)
Aortic valve	15 (24%)
Prosthetic mitral valve	9 (14%)
Others	14 (23%)
Surgery	
No	31 (50%)
Yes	31 (50%)
Aortic valve	13 (42%)
Mitral valve	13 (42%)
Mitral and aortic valve	5 (16%)
Others	7 (23%)
Outcomes (N = 57)	
Survived	47 (82%)
Died	10 (18%)
Outcomes based on treatment type (N = 53)	
Required surgery and died	24 (45%)
Conservative approach and died	23 (43%)
Required surgery and survived	5 (9%)
Conservative approach and survived	1 (2%)

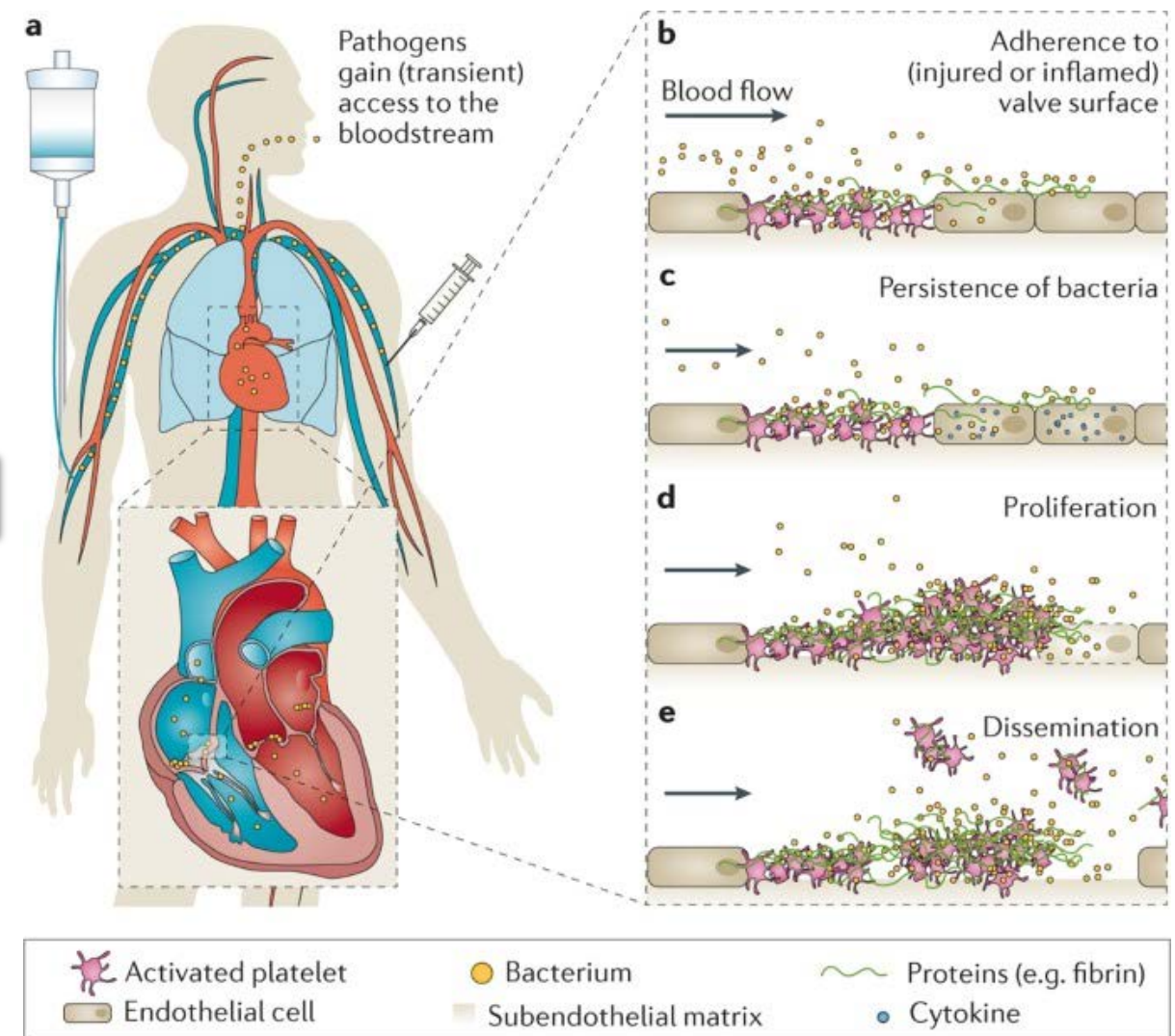
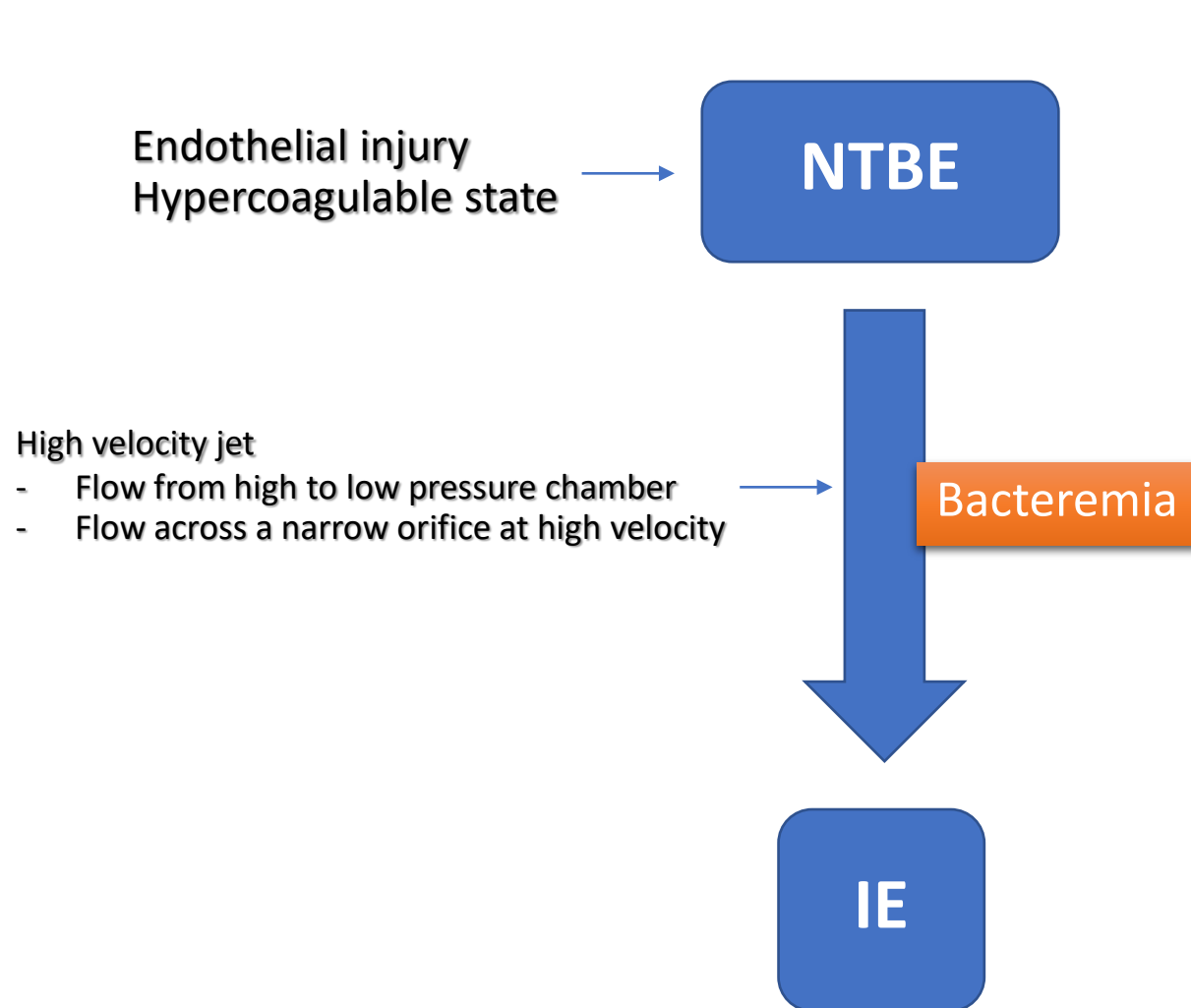
INFECTIVE ENDOCARDITIS



Outline

- Pathogenesis
- Clinical presentation
- Investigation
- Diagnosis
- Treatment
- Prevention

Infective endocarditis – Pathogenesis



Clinical presentation

- Fever (90%)
- Heart murmur (85%)
- Chill and sweats
- Anorexia, weight loss, malaise
- Vascular phenomena
 - Subconjunctival hemorrhage, Janeway's lesion, splinter hemorrhage, intracranial hemorrhage, arterial emboli, splenic infarct, renal infarct
- Immunological phenomena
 - Hematuria, Osler's node, Roth's spot

Infective endocarditis – Clinical presentation



Janeway's lesion



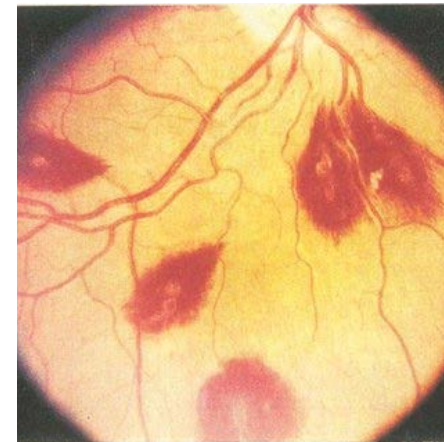
Osler's node



Conjunctival hemorrhage

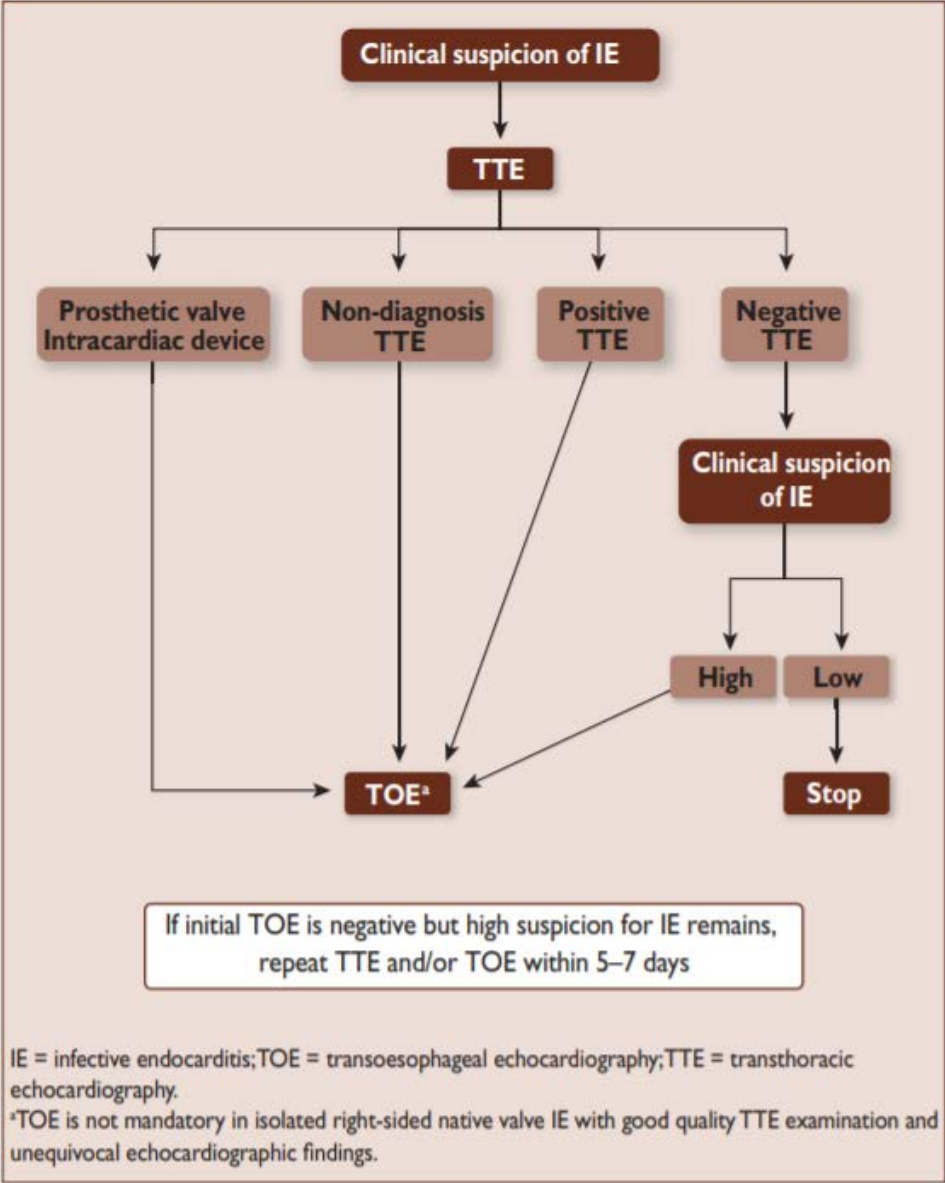


Splinter hemorrhage



Roth's spot

Infective endocarditis – Investigation



Recommendations	Class ^a	Level ^b	Ref. ^c
A. Diagnosis			
• TTE is recommended as the first-line imaging modality in suspected IE.	I	B	64,65
• TOE is recommended in all patients with clinical suspicion of IE and a negative or non-diagnostic TTE.	I	B	64, 68–71
• TOE is recommended in patients with clinical suspicion of IE, when a prosthetic heart valve or an intracardiac device is present.	I	B	64,71
• Repeat TTE and /or TOE within 5–7 days is recommended in case of initially negative examination when clinical suspicion of IE remains high.	I	C	
• Echocardiography should be considered in <i>Staphylococcus aureus</i> bacteraemia.	IIa	B	66,67
• TOE should be considered in patients with suspected IE, even in cases with positive TTE, except in isolated right-sided native valve IE with good quality TTE examination and unequivocal echocardiographic findings.	IIa	C	

B. Follow-up under medical therapy			
• Repeat TTE and/or TOE are recommended as soon as a new complication of IE is suspected (new murmur, embolism, persisting fever, HF, abscess, atrioventricular block).	I	B	64,72
• Repeat TTE and/or TOE should be considered during follow-up of uncomplicated IE, in order to detect new silent complications and monitor vegetation size. The timing and mode (TTE or TOE) of repeat examination depend on the initial findings, type of microorganism, and initial response to therapy.	IIa	B	64,72
C. Intraoperative echocardiography			
• Intraoperative echocardiography is recommended in all cases of IE requiring surgery.	I	B	64,73
D. Following completion of therapy			
• TTE is recommended at completion of antibiotic therapy for evaluation of cardiac and valve morphology and function.	I	C	

Echocardiography

- Vegetation
- Abscess or pseudoaneurysm
- Dehiscence of prosthetic valve

- Diagnosis of vegetation
 - Sensitivity of TTE – NVE 70% PVE 50%
 - Sensitivity of TOE – NVE 96% PVE 92%
 - Specificity of both – 90%

- Diagnosis of abscess
 - Sensitivity of TTE – 50%
 - Sensitivity of TOE – 90%
 - Specificity of both – >90%

Additional imaging technique

- Real-time 3-dimensional (3D) TOE
- Multi-slice computed tomography (MSCT)
- Magnetic resonance imaging (MRI)
- Nuclear imaging

Microbiological diagnosis

Blood culture-negative infective endocarditis

- 31% of all cases of infective endocarditis
- BCNIE most commonly arises as a consequence of previous antibiotic administration
- BCNIE can be caused by fungi or fastidious bacteria, notably obligatory intracellular bacteria
- Isolation of these microorganisms requires culturing them on specialized media

Table 12 Investigation of rare causes of blood culture negative infective endocarditis

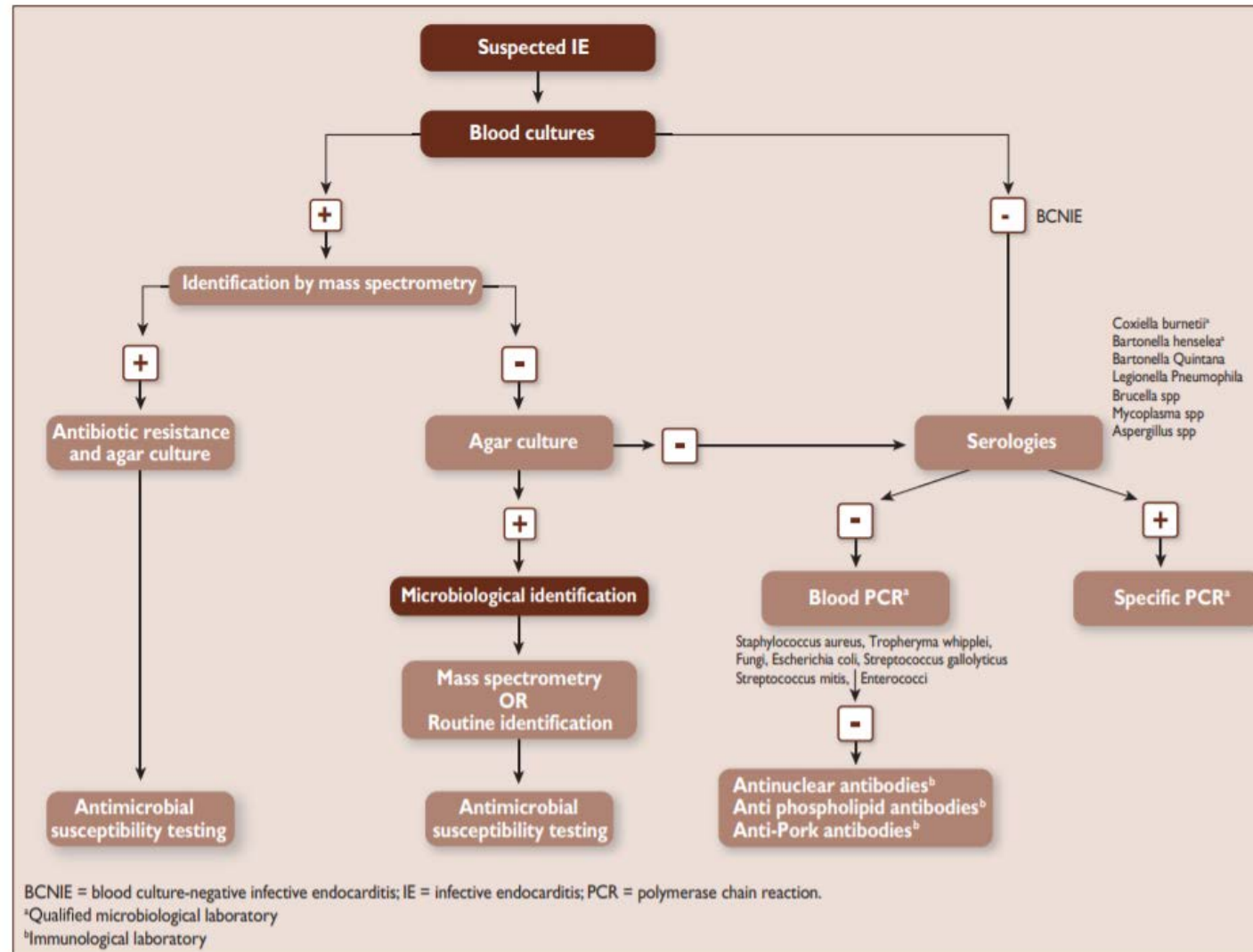
Pathogen	Diagnostic procedures
<i>Brucella</i> spp.	Blood cultures, serology, culture, immunohistology, and PCR of surgical material.
<i>Coxiella burnetii</i>	Serology (IgG phase I > 1:800), tissue culture, immunohistology, and PCR of surgical material.
<i>Bartonella</i> spp.	Blood cultures, serology, culture, immunohistology, and PCR of surgical material.
<i>Tropheryma whipplei</i>	Histology and PCR of surgical material.
<i>Mycoplasma</i> spp.	Serology, culture, immunohistology, and PCR of surgical material.
<i>Legionella</i> spp.	Blood cultures, serology, culture, immunohistology, and PCR of surgical material.
Fungi	Blood cultures, serology, PCR of surgical material.

Infective endocarditis – Diagnosis

Table 6. Epidemiological Clues That May be Helpful in Defining the Etiological Diagnosis of Culture-Negative Endocarditis

Epidemiological Feature	Common Microorganism	Epidemiological Feature	Common Microorganism			
IDU	<i>S aureus</i> , including community-acquired oxacillin-resistant strains	Dog or cat exposure	<i>Bartonella</i> sp	Alcoholism, cirrhosis	<i>Bartonella</i> sp	
	Coagulase-negative staphylococci		<i>Pasteurella</i> sp		<i>Aeromonas</i> sp	
	β-Hemolytic streptococci		<i>Capnocytophaga</i> sp		<i>Listeria</i> sp	
	Fungi	Contact with contaminated milk or infected farm animals	<i>Brucella</i> sp	Burn	<i>S pneumoniae</i>	
	Aerobic Gram-negative bacilli, including <i>Pseudomonas aeruginosa</i>		<i>Coxiella burnetii</i>		β-Hemolytic streptococci	
Polymicrobial	<i>Erysipelothrix</i> sp		<i>S aureus</i>			
Indwelling cardiovascular medical devices	<i>S aureus</i>	Homeless, body lice	<i>Bartonella</i> sp	Diabetes mellitus	Aerobic Gram-negative bacilli, including <i>P aeruginosa</i>	
	Coagulase-negative staphylococci	AIDS	<i>Salmonella</i> sp		Fungi	
	Fungi	<i>S pneumoniae</i>	<i>S aureus</i>			
	Aerobic Gram-negative bacilli	Pneumonia, meningitis	<i>S aureus</i>	Early (≤1 y) prosthetic valve placement	β-Hemolytic streptococci	
	<i>Corynebacterium</i> sp		<i>S pneumoniae</i>		<i>S pneumoniae</i>	
<i>Enterococcus</i> sp	<i>S aureus</i>		Coagulase-negative staphylococci			
Genitourinary disorders, infection, and manipulation, including pregnancy, delivery, and abortion	Group B streptococci (<i>S agalactiae</i>)	Solid organ transplantation	<i>Aspergillus fumigatus</i>	Late (>1 y) prosthetic valve placement	<i>S aureus</i>	
	<i>Listeria monocytogenes</i>		<i>Enterococcus</i> sp		Aerobic Gram-negative bacilli	
	Aerobic Gram-negative bacilli		<i>Candida</i> sp		Fungi	
	Chronic skin disorders, including recurrent infections	<i>Neisseria gonorrhoeae</i>	Gastrointestinal lesions	<i>S gallolyticus (bovis)</i>		<i>Corynebacterium</i> sp
		<i>S aureus</i>		<i>Enterococcus</i> sp		<i>Legionella</i> sp
β-Hemolytic streptococci		<i>Clostridium septicum</i>		Coagulase-negative staphylococci		
Poor dental health, dental procedures		VGS	HACEK indicates <i>Haemophilus</i> species, <i>Aggregatibacter</i> species, <i>Cardiobacterium hominis</i> , <i>Eikenella corrodens</i> , and <i>Kingella</i> species; IDU, injection drug use; and VGS, viridans group streptococci.			<i>S aureus</i>
		Nutritionally variant streptococci				Viridans group streptococci
	<i>Abiotrophia defectiva</i>	<i>Enterococcus</i> species				
	<i>Granulicatella</i> sp	Fungi				
	<i>Gemella</i> sp	<i>Corynebacterium</i> sp				
	HACEK organisms					

Microbial diagnostic algorithm



MODIFIED DUKE CRITERIA

Major criteria

1. Blood cultures positive for IE

- a. Typical microorganisms consistent with IE from 2 separate blood cultures:
 - *Viridans streptococci*, *Streptococcus gallolyticus* (*Streptococcus bovis*), *HACEK group*, *Staphylococcus aureus*; or
 - Community-acquired enterococci, in the absence of a primary focus; or
- b. Microorganisms consistent with IE from persistently positive blood cultures:
 - ≥ 2 positive blood cultures of blood samples drawn >12 h apart; or
 - All of 3 or a majority of ≥ 4 separate cultures of blood (with first and last samples drawn ≥ 1 h apart); or
- c. Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titre $>1:800$

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 ^{18}F -FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabelled leukocytes SPECT/CT.
- c. Definite paravalvular lesions by cardiac CT.

Minor criteria

1. Predisposition such as predisposing heart condition, or injection drug use.
2. Fever defined as temperature $>38^{\circ}\text{C}$.
3. Vascular phenomena (including those detected by imaging only): major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions.
4. Immunological phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor.
5. Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE.

Diagnosis

MODIFIED DUKE CRITERIA

Definite IE

Pathological criteria

- Microorganisms demonstrated by culture or on histological examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or
- Pathological lesions; vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis

Clinical criteria

- 2 major criteria; or
- 1 major criterion and 3 minor criteria; or
- 5 minor criteria

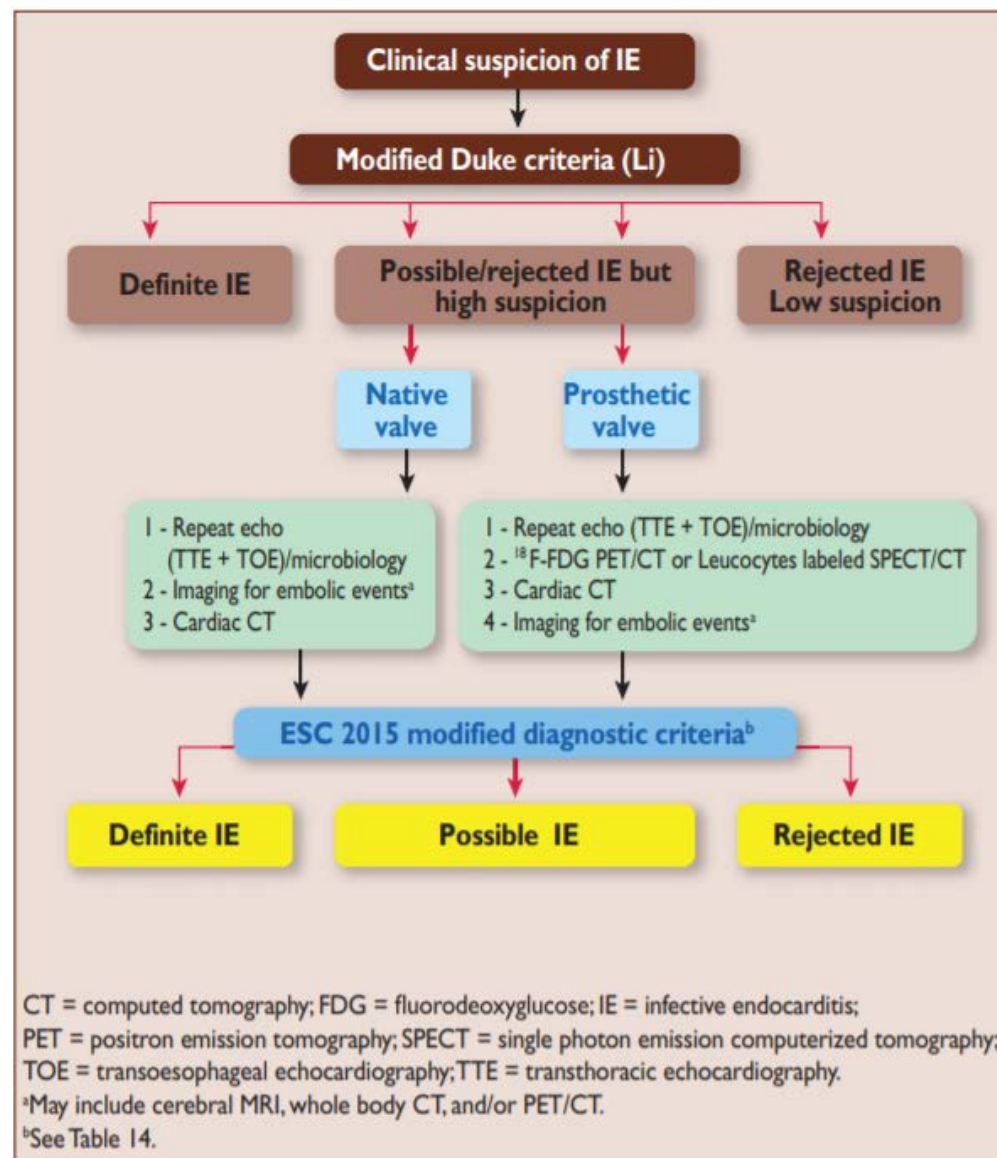
Possible IE

- 1 major criterion and 1 minor criterion; or
- 3 minor criteria

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

Algorithm for diagnosis



Predictors of poor outcome

Table 15 Predictors of poor outcome in patients with infective endocarditis

Patient characteristics

- Older age
- Prosthetic valve IE
- Diabetes mellitus
- Comorbidity (e.g., frailty, immunosuppression, renal or pulmonary disease)

Clinical complications of IE

- Heart failure
- Renal failure
- >Moderate area of ischaemic stroke
- Brain haemorrhage
- Septic shock

Microorganism

- *Staphylococcus aureus*
- Fungi
- Non-HACEK Gram-negative bacilli

Echocardiographic findings

- Periannular complications
- Severe left-sided valve regurgitation
- Low left ventricular ejection fraction
- Pulmonary hypertension
- Large vegetations
- Severe prosthetic valve dysfunction
- Premature mitral valve closure and other signs of elevated diastolic pressures

Infective endocarditis – Antimicrobial therapy

Empirical ATB treatment

Table 20 Proposed antibiotic regimens for initial empirical treatment of infective endocarditis in acute severely ill patients (before pathogen identification)^a

Antibiotic	Dosage and route	Class ^b	Level ^c	Comments
Community-acquired native valves or late prosthetic valves (≥ 12 months post surgery) endocarditis				
Ampicillin with (Flu)cloxacillin or oxacillin with Gentamicin ^d	12 g/day i.v. in 4–6 doses 12 g/day i.v. in 4–6 doses 3 mg/kg/day i.v. or i.m. in 1 dose	IIa	C	Patients with BCNIE should be treated in consultation with an ID specialist.
Vancomycin ^d with Gentamicin ^d	30–60 mg/kg/day i.v. in 2–3 doses 3 mg/kg/day i.v. or i.m. in 1 dose			
Early PVE (<12 months post surgery) or nosocomial and non-nosocomial healthcare associated endocarditis				
Vancomycin ^d with Gentamicin ^d with Rifampin	30 mg/kg/day i.v. in 2 doses 3 mg/kg/day i.v. or i.m. in 1 dose 900–1200 mg i.v. or orally in 2 or 3 divided doses	IIb	C	Rifampin is only recommended for PVE and it should be started 3–5 days later than vancomycin and gentamicin has been suggested by some experts. In healthcare associated native valve endocarditis, some experts recommend in settings with a prevalence of MRSA infections >5% the combination of cloxacillin plus vancomycin until they have the final S. aureus identification

- NVE
- Late PVE (>12 mo)

- Early PVE (<12 mo)
- Nosocomial infection

Infective endocarditis – Antimicrobial therapy

Streptococcus group

Table 16 Antibiotic treatment of infective endocarditis due to oral streptococci and *Streptococcus bovis* group^a

Antibiotic	Dosage and route	Duration (weeks)	Class ^b	Level ^c	Ref. ^d	Comments
Strains penicillin-susceptible (MIC ≤ 0.125 mg/L) oral and digestive streptococci						
Standard treatment: 4-week duration						
Penicillin G or Amoxicillin ^e or Ceftriaxone ^f	12–18 million U/day i.v. either in 4–6 doses or continuously	4	I	B	6,8, 135– 139	Preferred in patients > 65 years or with impaired renal or VIII (vestibulocochlear) cranial nerve functions. 6-week therapy recommended for patients with PVE
	100–200 mg/kg/day i.v. in 4–6 doses	4	I	B		
	2 g/day i.v. or i.m. in 1 dose	4	I	B		
Paediatric doses:^g Penicillin G 200,000 U/kg/day i.v. in 4–6 divided doses Amoxicillin 300 mg/kg/day i.v. in 4–6 equally divided doses Ceftriaxone 100 mg/kg/day i.v. or i.m. in 1 dose						
Standard treatment: 2-week duration						
Penicillin G or Amoxicillin ^e or Ceftriaxone ^f combined with Gentamicin ^h or Netilmicin	12–18 million U/day i.v. either in 4–6 doses or continuously	2	I	B	6,8, 127, 135– 138	Only recommended in patients with non-complicated NVE with normal renal function. Netilmicin is not available in all European countries.
	100–200 mg/kg/day i.v. in 4–6 doses	2	I	B		
	2 g/day i.v. or i.m. in 1 dose	2	I	B		
	3 mg/kg/day i.v. or i.m. in 1 dose	2	I	B		
	4–5 mg/kg/day i.v. in 1 dose	2	I	B		
Paediatric doses:^g Penicillin G, amoxicillin, and ceftriaxone as above Gentamicin 3 mg/kg/day i.v. or i.m. in 1 dose or 3 equally divided doses						
In beta-lactam allergic patientsⁱ						
Vancomycin ^l	30 mg/kg/day i.v. in 2 doses	4	I	C		6-week therapy recommended for patients with PVE
Paediatric doses:^g Vancomycin 40 mg/kg/day i.v. in 2 or 3 equally divided doses						

- Age > 65
- Impaired renal function, CN8 functions
- 6-week Tx in PVE
- Non-complicated NVE + Normal renal function
- 6-week Tx in PVE

Infective endocarditis – Antimicrobial therapy

Streptococcus group

Strains relatively resistant to penicillin (MIC 0.250–2 mg/l) ^k						
Standard treatment						
Penicillin G or Amoxicillin ^e or Ceftriaxone ^f combined with Gentamicin ^h	24 million U/day i.v. either in 4–6 doses or continuously	4	I	B	6,8, 135, 136	6-week therapy recommended for patients with PVE
	200 mg/kg/day i.v. in 4–6 doses	4	I	B		
	2 g/day i.v. or i.m. in 1 dose	4	I	B		
	3 mg/kg/day i.v. or i.m. in 1 dose	2	I	B		
In beta-lactam allergic patients ^l						
Vancomycin ^l with Gentamicin ^k	30 mg/kg/day i.v. in 2 doses	4	I	C		6-week therapy recommended for patients with PVE
	3 mg/kg/day i.v. or i.m. in 1 dose	2	I	C		
	Paediatric doses: ^g As above					

- 6-week Tx in PVE

- 6-week Tx in PVE

Streptococcus group

Streptococcus pneumoniae

- Associated with meningitis in up to 30%
- Penicillin-susceptible strain : MIC ≤ 0.06 mg/L
 - 2-week therapy similar to oral streptococci
- Penicillin-intermediate strain : MIC 0.125 - 2 mg/L or resistant strains MIC ≥ 4 mg/L
 - High dose cephalosporins or vancomycin
- In case with meningitis
 - penicillin must be avoided because of its poor penetration of the cerebrospinal fluid
 - ceftriaxone or cefotaxime alone or in association with vancomycin

Beta-hemolytic streptococcus (Group A, B, C, G)

- Group B, C, G streptococcus and *S. anginosus* produce abscesses and thus may require adjunctive surgery
- ATB Tx is similar to oral streptococcus
- Short term therapy is not recommended
- Gentamicin should be given for 2 weeks.

Staphylococcus group

Antibiotic	Dosage and route	Duration (weeks)	Class ⁱ	Level ^j	Ref. ^k	Comments
Native valves						
Methicillin-susceptible staphylococci						
(Flu)cloxacillin or oxacillin	12 g/day i.v. in 4–6 doses	4–6	I	B	6,8, 128, 135, 136, 158	Gentamicin addition is not recommended because clinical benefit has not been demonstrated and there is increased renal toxicity
	Paediatric doses: ^g 200–300 mg/kg/day i.v. in 4–6 equally divided doses					
Alternative therapy* Cotrimoxazole ^a	Sulfamethoxazole 4800 mg/day and Trimethoprim 960 mg/day (i.v. in 4–6 doses)	1 i.v. + 5 oral intake	IIb	C		*for <i>Staphylococcus aureus</i>
with						
Clindamycin	1800mg/day i.v. in 3 doses	1	IIb	C		
	Paediatric doses: ^g Sulfamethoxazole 60 mg/kg/day and Trimethoprim 12 mg/kg/day (i.v. in 2 doses) Clindamycin 40 mg/kg/day (i.v. in 3 doses)					
Penicillin-allergic patients^h or methicillin-resistant staphylococci						
Vancomycin ^{b, **}	30–60 mg/kg/day i.v. in 2–3 doses	4–6	I	B	6,8, 135, 136	Cephalosporins (cefazolin 6 g/day or cefotaxime 6 g/day i.v. in 3 doses) are recommended for penicillin-allergic patients with non-anaphylactic reactions with methicillin-susceptible endocarditis
	Paediatric doses: ^g 40 mg/kg/day i.v. in 2–3 equally divided doses					
Alternative therapy**: Daptomycin ^{c,d}	10 mg/kg/day i.v. once daily	4–6	IIa	C		Daptomycin is superior to vancomycin for MSSA and MRSA bacteraemia with vancomycin MIC > 1 mg/L
	Paediatric doses: ^g 10 mg/kg/day i.v. once daily					
Alternative therapy* Cotrimoxazole ^a	Sulfamethoxazole 4800 mg/day and Trimethoprim 960 mg/day (i.v. in 4–6 doses)	1 i.v. + 5 oral intake	IIb	C		*for <i>Staphylococcus aureus</i>
with						
Clindamycin	1800mg/day IV in 3 doses	1	IIb	C		

- No longer recommended for aminoglycoside
- Short term Tx (2 weeks) and oral Tx
 - For Uncomplicated Rt-sided native MSSA

Infective endocarditis – Antimicrobial therapy

Staphylococcus group

Prosthetic valves						
Methicillin-susceptible staphylococci						
(Flu)cloxacillin or oxacillin with Rifampin ^e and Gentamicin ^f	12 g/day i.v. in 4–6 doses	≥ 6	I	B	6,8, 135, 136	Starting rifampin 3–5 days later than vancomycin and gentamicin has been suggested by some experts. Gentamicin can be given in a single daily dose in order to reduce renal toxicity
	900–1200 mg i.v. or orally in 2 or 3 divided doses	≥ 6	I	B		
	3 mg/kg/day i.v. or i.m. in 1 or 2 doses	2	I	B		
	Paediatric doses: ^g Oxacillin and (flu)cloxacillin as above Rifampin 20 mg/kg/day i.v. or orally in 3 equally divided doses					
Penicillin-allergic patients ^h and methicillin-resistant staphylococci						
Vancomycin ^b with Rifampin ^e and Gentamicin ^f	30–60 mg/kg/day i.v. in 2–3 doses	≥ 6	I	B	6,8, 135, 136	Cephalosporins (cefazolin 6 g/day or cefotaxime 6 g/day i.v. in 3 doses) are recommended for penicillin-allergic patients with non-anaphylactic reactions with methicillin-susceptible endocarditis. Starting rifampin 3–5 days later than vancomycin and gentamicin has been suggested by some experts. Gentamicin can be given in a single daily dose in order to reduce renal toxicity
	900–1200 mg i.v. or orally in 2 or 3 divided doses	≥ 6	I	B		
	3 mg/kg/day i.v. or i.m. in 1 or 2 doses	2	I	B		
	Paediatric dosing: ^g As above					

PVE

- Add Rifampin + Gentamicin

Infective endocarditis – Antimicrobial therapy

Enterococcus group

Table 18 Antibiotic treatment of infective endocarditis due to *Enterococcus* spp.

Antibiotic	Dosage and route	Duration, weeks	Class ^g	Level ^h	Ref. ⁱ	Comments
Beta-lactam and gentamicin-susceptible strains (for resistant isolates see ^{a,b,c})						
Amoxicillin* with Gentamicin ^d	200 mg/kg/day i.v. in 4–6 doses	4–6	I	B	6,8, 129, 135, 136, 186	6-week therapy recommended for patients with >3 months symptoms or PVE
	3 mg/kg/day i.v. or i.m. in 1 dose	2–6**	I	B		
	Paediatric doses: ^e Ampicillin 300 mg/kg/day i.v. in 4–6 equally divided doses Gentamicin 3 mg/kg/day i.v. or i.m. in 3 equally divided doses					
Ampicillin with Ceftriaxone	200 mg/kg/day i.v. in 4–6 doses	6	I	B	183– 185	This combination is active against <i>Enterococcus faecalis</i> strains with and without HLAR, being the combination of choice in patients with HLAR <i>E. faecalis</i> endocarditis.
	4 g/day i.v. or i.m. in 2 doses	6	I	B		
	Paediatric doses: ^e Amoxicillin as above Ceftriaxone 100 mg/kg/12 h i.v. or i.m.					This combination is not active against <i>E. faecium</i>
Vancomycin ^f with Gentamicin ^d	30 mg/kg/day i.v. in 2 doses	6	I	C		
	3 mg/kg/day i.v. or i.m. in 1 dose	6	I	C		
	Paediatric doses: ^e Vancomycin 40 mg/kg/day i.v. in 2–3 equally divided doses. Gentamicin as above					

Highly resistance

- Eradication requires prolonged ATB therapy (6-week)

High-level aminoglycoside resistance

- Synergistic bactericidal combination

Gram negative - HACEK group

Antibiotic

- Ceftriaxone 2 g/d IV for 4 weeks in NVE
- Ceftriaxone 2 g/d IV for 6 weeks in PVE

Alternative therapy

- Ampicillin 12 g/d IV in 4 or 6 doses + Gentamicin 3 mg/kg/d IV in 2 or 3 doses for 4-6 wks
- Ciprofloxacin 400 mg/8-12 hr IV or 750 mg/12 h orally

- *Haemophilus species*
- *Aggregatibacter species*
- *Cardiobacterium species*
- *Eikenella species*
- *Kingella species*

Gram negative – Non-HACEK group

- Early surgery + Long-term ATB therapy (at least 6 weeks)
- Bactericidal combinations of Beta-lactams and aminoglycosides
- Sometimes with additional quinolones or cotrimoxazole

Infective endocarditis – Antimicrobial therapy

Blood culture-negative group

Table 19 Antibiotic treatment of blood culture-negative infective endocarditis (adapted from Brouqui et al.¹⁹³)

Pathogens	Proposed therapy ^a	Treatment outcome
<i>Brucella</i> spp.	Doxycycline (200 mg/24 h) plus cotrimoxazole (960 mg/12 h) plus rifampin (300–600/24 h) for ≥3–6 months ^b orally	Treatment success defined as an antibody titre <1:60. Some authors recommend adding gentamicin for the first 3 weeks.
<i>C. burnetii</i> (agent of Q fever)	Doxycycline (200 mg/24 h) plus hydroxychloroquine (200–600 mg/24 h) ^c orally (>18 months of treatment)	Treatment success defined as anti-phase I IgG titre <1:200, and IgA and IgM titres <1:50.
<i>Bartonella</i> spp. ^d	Doxycycline 100 mg/12 h orally for 4 weeks plus gentamicin (3 mg/24 h) i.v. for 2 weeks	Treatment success expected in ≥90%.
<i>Legionella</i> spp.	Levofloxacin (500 mg/12 h) i.v. or orally for ≥6 weeks or clarithromycin (500 mg/12 h) i.v. for 2 weeks, then orally for 4 weeks plus rifampin (300–1200 mg/24 h)	Optimal treatment unknown.
<i>Mycoplasma</i> spp.	Levofloxacin (500 mg/12 h) i.v. or orally for ≥6 months ^e	Optimal treatment unknown.
<i>T. whipplei</i> (agent of Whipple's disease) ^f	Doxycycline (200 mg/24 h) plus hydroxychloroquine (200–600 mg/24 h) ^c orally for ≥18 months	Long-term treatment, optimal duration unknown.

ID = infectious disease; IE = infective endocarditis; Ig = immunoglobulin; i.v. = intravenous; U = units.

^aOwing to the lack of large series, the optimal duration of treatment of IE due to these pathogens is unknown. The presented durations are based on selected case reports.

Consultation with an ID specialist is recommended.

^bAddition of streptomycin (15 mg/kg/24 h in 2 doses) for the first few weeks is optional.

^cDoxycycline plus hydroxychloroquine (with monitoring of serum hydroxychloroquine levels) is significantly superior to doxycycline.¹⁹⁴

^dSeveral therapeutic regimens have been reported, including aminopenicillins (ampicillin or amoxicillin, 12 g/24 h i.v.) or cephalosporins (ceftriaxone, 2 g/24 h i.v.) combined with aminoglycosides (gentamicin or netilmicin).¹⁹⁵ Dosages are as for streptococcal and enterococcal IE (Tables 16 and 18).^{196,197}

^eNewer fluoroquinolones (levofloxacin, moxifloxacin) are more potent than ciprofloxacin against intracellular pathogens such as *Mycoplasma* spp., *Legionella* spp., and *Chlamydia* spp.

^fTreatment of Whipple's IE remains highly empirical. In the case of central nervous system involvement, sulfadiazine 1.5 g/6 h orally must be added to doxycycline. An alternative therapy is ceftriaxone (2 g/24 h i.v.) for 2–4 weeks or penicillin G (2 million U/4 h) and streptomycin (1 g/24 h) i.v. for 2–4 weeks followed by cotrimoxazole (800 mg/12 h) orally. Trimethoprim is not active against *T. whipplei*. Successes have been reported with long-term therapy (>1 year).

Complication of IE

Main complication of Lt-sided IE

- Heart failure
- Uncontrolled infection
- Systemic embolism

Other complication of IE

- Neurologic complication
- Infected aneurysm
- Splenic complication
- Myocarditis and pericarditis
- Acute renal failure
- Musculoskeletal manifestation
- Heart rhythm and conduction disturbance

Indication for surgery in Lt-sided IE

Table 22 Indications and timing of surgery in left-sided valve infective endocarditis (native valve endocarditis and prosthetic valve endocarditis)

Indications for surgery	Timing ^a	Class ^b	Level ^c	Ref. ^d
1. Heart failure				
Aortic or mitral NVE or PVE with severe acute regurgitation, obstruction or fistula causing refractory pulmonary oedema or cardiogenic shock	Emergency	I	B	111,115, 213,216
Aortic or mitral NVE or PVE with severe regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance	Urgent	I	B	37,115, 209,216, 220,221
2. Uncontrolled infection				
Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation)	Urgent	I	B	37,209, 216
Infection caused by fungi or multiresistant organisms	Urgent/ elective	I	C	
Persisting positive blood cultures despite appropriate antibiotic therapy and adequate control of septic metastatic foci	Urgent	IIa	B	123
PVE caused by staphylococci or non-HACEK gram-negative bacteria	Urgent/ elective	IIa	C	
3. Prevention of embolism				
Aortic or mitral NVE or PVE with persistent vegetations > 10 mm after one or more embolic episode despite appropriate antibiotic therapy	Urgent	I	B	9,58,72, 113,222
Aortic or mitral NVE with vegetations > 10 mm, associated with severe valve stenosis or regurgitation, and low operative risk	Urgent	IIa	B	9
Aortic or mitral NVE or PVE with isolated very large vegetations (> 30 mm)	Urgent	IIa	B	113
Aortic or mitral NVE or PVE with isolated large vegetations (> 15 mm) and no other indication for surgery ^e	Urgent	IIb	C	

HACEK = *Haemophilus parainfluenzae*, *Haemophilus aphrophilus*, *Haemophilus paraphrophilus*, *Haemophilus influenzae*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella kingae* and *Kingella denitrificans*; HF = heart failure; IE = infective endocarditis; NVE = native valve endocarditis; PVE = prosthetic valve endocarditis.

^aEmergency surgery: surgery performed within 24 h; urgent surgery: within a few days; elective surgery: after at least 1–2 weeks of antibiotic therapy.

^bClass of recommendation.

^cLevel of evidence.

^dReference(s) supporting recommendations.

^eSurgery may be preferred if a procedure preserving the native valve is feasible.

Management of neurological complications in IE

Table 23 Management of neurological complications of infective endocarditis

Recommendations	Class ^a	Level ^b	Ref. ^c
After a silent embolism or transient ischaemic attack, cardiac surgery, if indicated, is recommended without delay	I	B	105, 263
Neurosurgery or endovascular therapy is recommended for very large, enlarging or ruptured intracranial infectious aneurysms	I	C	
Following intracranial haemorrhage, surgery should generally be postponed for ≥ 1 month	IIa	B	264–266
After a stroke, surgery indicated for HF, uncontrolled infection, abscess, or persistent high embolic risk should be considered without any delay as long as coma is absent and the presence of cerebral haemorrhage has been excluded by cranial CT or MRI	IIa	B	9,263
Intracranial infectious aneurysms should be looked for in patients with IE and neurological symptoms. CT or MR angiography should be considered for diagnosis. If non-invasive techniques are negative and the suspicion of intracranial aneurysm remains, conventional angiography should be considered	IIa	B	267, 268

Indication for surgery in Rt-sided IE

Table 26 Indications for surgical treatment of right-sided infective endocarditis

Recommendation	Class ^a	Level ^b
Surgical treatment should be considered in the following scenarios: <ul style="list-style-type: none">• Microorganisms difficult to eradicate (e.g. persistent fungi) or bacteraemia for > 7 days (e.g. <i>S. aureus</i>, <i>P. aeruginosa</i>) despite adequate antimicrobial therapy or• Persistent tricuspid valve vegetations > 20 mm after recurrent pulmonary emboli with or without concomitant right heart failure or• Right HF secondary to severe tricuspid regurgitation with poor response to diuretic therapy	IIa	C

Infective endocarditis – Rt-sided IE

Rt-sided infective endocarditis

- IVU esp. with HIV, CHD
- *S. aureus* is the predominant organism (60–90%)
- The tricuspid valve is most frequently affected

2-week treatment of oxacillin(or cloxacillin) without gentamicin is effective for most patients with isolated tricuspid IE if all the following criteria are fulfilled:

- MSSA
- Good response to treatment
- Absence of metastatic sites of infection or empyema,
- Absence of cardiac and extracardiac complications
- Absence of associated prosthetic valve or left-sided valve infection
- < 20 mm vegetation
- Absence of severe immunosuppression (200 CD4 cells/mL) with or without acquired immune deficiency syndrome (AIDS)

4–6-week regimen of vancomycin must be used in the following situations:

- Slow clinical or microbiological response (>96 h) to antibiotic therapy
- Right-sided IE complicated by right HF
- vegetations >20 mm
- acute respiratory failure
- septic metastatic foci outside the lungs (including empyema)
- extracardiac complications, e.g. acute renal failure
- Therapy with antibiotics other than penicillinase-resistant penicillins
- IVDA with severe immunosuppression (CD4 count ,200 cells/ mL) with or without AIDS
- Associated left-sided IE

Follow-up and Long-term prognosis

- **Short-term follow-up**
 - Residual valve regurgitation can lead to heart failure
 - Risk of IE: oral health maintenance, dentistry and skin hygiene
- **Recurrence: actual risk 2-6%**
 - Relapse: cause by the same microorganism
 - Reinfection: cause by the different microorganism

Factor increased rate of relapse

Table 24 Factors associated with an increased rate of relapse

- | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| • Inadequate antibiotic treatment (agent, dose, duration) |
| • Resistant microorganisms, i.e. <i>Brucella spp.</i> , <i>Legionella spp.</i> , <i>Chlamydia spp.</i> , <i>Mycoplasma spp.</i> , <i>Mycobacterium spp.</i> , <i>Bartonella spp.</i> , <i>Coxiella Burnetii</i> , fungi |
| • Polymicrobial infection in an IVDA |
| • Empirical antimicrobial therapy for BCNIE |
| • Periannular extension |
| • Prosthetic valve IE |
| • Persistent metastatic foci of infection (abscesses) |
| • Resistance to conventional antibiotic regimens |
| • Positive valve culture |
| • Persistence of fever at the seventh postoperative day |
| • Chronic dialysis |

High-risk group for IE

Table 3 Cardiac conditions at highest risk of infective endocarditis for which prophylaxis should be considered when a high-risk procedure is performed

Recommendations	Class ^a	Level ^b
Antibiotic prophylaxis should be considered for patients at highest risk for IE: (1) Patients with any prosthetic valve, including a transcatheter valve, or those in whom any prosthetic material was used for cardiac valve repair. (2) Patients with a previous episode of IE. (3) Patients with CHD: (a) Any type of cyanotic CHD. (b) Any type of CHD repaired with a prosthetic material, whether placed surgically or by percutaneous techniques, up to 6 months after the procedure or lifelong if residual shunt or valvular regurgitation remains.	IIa	C
Antibiotic prophylaxis is not recommended in other forms of valvular or CHD.	III	C

Prophylaxis for at-risk procedure

Table 5 Recommendations for prophylaxis of infective endocarditis in the highest-risk patients according to the type of at-risk procedure

Recommendations	Class ^a	Level ^b
A. Dental procedures		
<ul style="list-style-type: none">Antibiotic prophylaxis should only be considered for dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa	IIa	C
<ul style="list-style-type: none">Antibiotic prophylaxis is not recommended for 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	III	C

Table 5 Continued

Recommendations	Class ^a	Level ^b
B. Respiratory tract procedures^c		
<ul style="list-style-type: none">Antibiotic prophylaxis is not recommended for respiratory tract procedures, including bronchoscopy or laryngoscopy, or transnasal or endotracheal intubation	III	C
C. Gastrointestinal or urogenital procedures or TOE^c		
<ul style="list-style-type: none">Antibiotic prophylaxis is not recommended for gastroscopy, colonoscopy, cystoscopy, vaginal or caesarean delivery or TOE	III	C
D. Skin and soft tissue procedures^c		
<ul style="list-style-type: none">Antibiotic prophylaxis is not recommended for any procedure	III	C

Prophylaxis for high-risk group

Table 6 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 ampicillin ^a	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.

Prevention measure

Table 4 Non-specific prevention measures to be followed in high-risk and intermediate-risk patients

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.
- Eradication or decrease of chronic bacterial carriage: skin, urine.
- 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.
- Limit the use of infusion catheters and invasive procedure when possible. Favour peripheral over central catheters, and systematic replacement of the peripheral catheter every 3–4 days. Strict adherence to care bundles for central and peripheral cannulae should be performed.

Reference

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- ❖ Holland, T., Baddour, L., Bayer, A. *et al.* Infective endocarditis. *Nat Rev Dis Primers* **2**, 16059 (2016).
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THANK YOU

