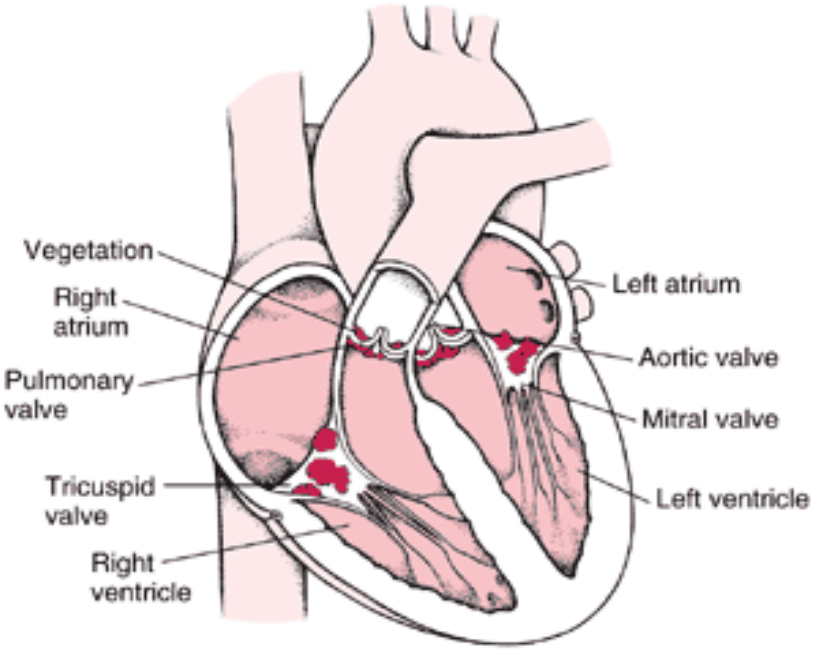

Welcome
NATIONAL HEART FOUNDATION HOSPITAL

INFECTIVE ENDOCARDITIS:

WHERE WE ARE AT 2005?



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DEFINITION OF INFECTIVE ENDOCARDITIS

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 microorganisms and moderate inflammatory cells are enmeshed.

Heart valves are most commonly involved; however, septal defects, chordae tendineae or mural endocardium may be involved.

The analogous process involving arteriovenous shunts, arterioarterial shunts (patent ductus arteriosus), or a coarctation of the aorta is called ***infective endarteritis*****.**

EPIDEMIOLOGY

The spectrum of IE continue to change. Approximately 10,000 to 15,000 cases annually in the USA.

The median age of patients has increased from an average of 30 years in 1926 to over 50.

Degenerative valve disease and mitral valve prolapse have replaced rheumatic heart disease as the most common substrate for endocarditis.

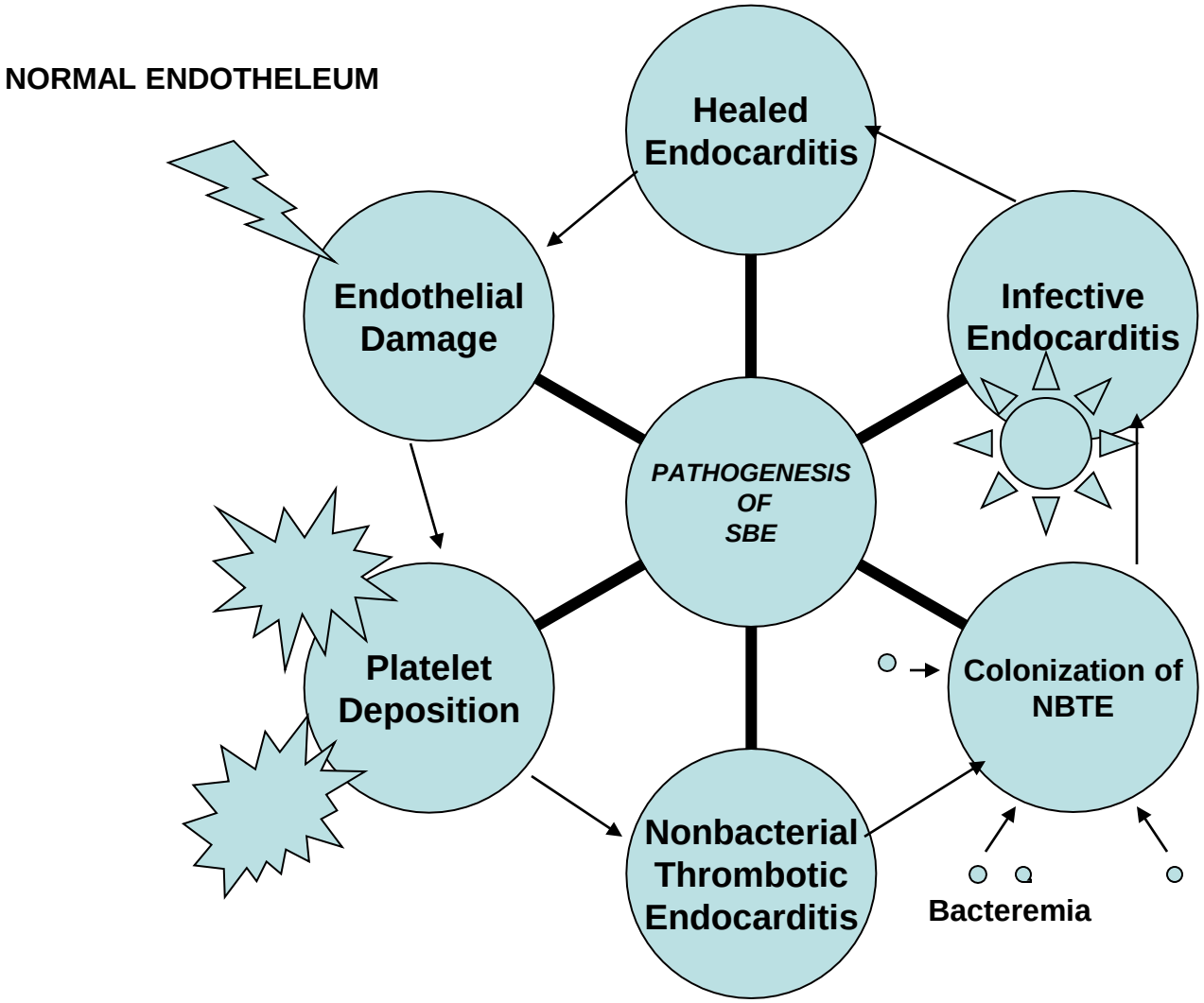
The use of IV drugs is also associated with a high risk. New bioprosthetic material to correct congenital or acquired valvular disease has predisposed many patients with prosthetic heart valves to the risk of IE. The risk appears similar in patients with mechanical or bioprosthetic valves.

A prior H/O endocarditis is an additional important risk factor.

A growing number of patients have no identifiable cardiac lesions; mostly in the elderly. Nosocomial infections due indwelling IV devices and catheters, procedures involving the GIT and Genitourinary tracts also facilitate bacteremia in this group.

Immunosuppressed like HIV and persons undergone organ transplantation are also susceptible.

PATHOGENETIC MODEL OF INFECTIVE ENDOCARDITIS



CLASSIFICATION OF IE

Endocarditis may be classified according to the temporal evolution of disease, the site of infection, the cause of infection, or a predisposing risk factor.

Temporal evolution and clinical grounds:

- ***Acute:*** is a hectically febrile illness, rapidly damages cardiac structures, hematogenously seeds extra-cardiac sites and if untreated, progresses to death within weeks.
- ***Sub-acute:*** the disease follows an indolent course; causes structural cardiac damage only slowly, if at all; rarely causes metastatic infection. And is gradually progressive unless complicated by a major embolic event or ruptured mycotic aneurysm.

The cause of infection:

- Bacterial: streptococcal (viridans, Bovis), enterococcal, staphylococcal, etc
- Fungal: candidias infection
- Blood culture negative endocarditis

Predisposing risk factors

- ***Native valve endocarditis***
- ***Prosthetic valve endocarditis***
- ***Endocarditis in injection drug abusers***

ETIOLOGY

The viridans group of streptococci (strep. Mitis, strep. Sanguis, a hemolytic streptococci) are commensals in the upper respiratory tract that may enter the blood stream on the chewing, brushing or any dental procedure and are common cause of sub-acute endocarditis.

Other organisms including Enterococcus faecalis, strep. Milleri and strep bovis may enter the blood from the bowel or urinary tract.

Other causes are Strep. pneumoniae and Neisseria gonorrheae

ETIOLOGY

Staph aureus is a common cause of acute endocarditis, originating from skin infections, abscess or vascular access sites (i,v or central lines) or from intravenous drug misuse. It is highly virulent organism and invasive usually producing florid vegetations, rapid valve destruction and abscess formation.
.

Post operative, follows cardiac surgery and may affect native or prosthetic heart valves or other prosthetic materials. The most common causes are coagulase negative staphylococci (Staph. Epidermidis), which is a normal skin contaminant. *Staph lugdenensis* is other cause of destructive acute endocarditis.

ETIOLOGY

Q fever endocarditis (Coxiella Burnetti) usually associated with hepatitis and purpura and pt usually has history of contact with farm animals.

HACEK groups are slow growing fastidious and resistant to penicillin.

Yeasts and fungi (Candida, Aspergillus) may attack previously normal or prosthetic valves, abscesses and emboli are common, therapy is difficult and often surgery is required.

TABLE 1A. Definition of Infective Endocarditis According to the Modified Duke Criteria

Definite infective endocarditis

Pathological criteria

Microorganisms demonstrated by culture or 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

Firm alternative diagnosis explaining evidence of IE; or

Resolution of IE syndrome 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

Modifications shown in boldface. Reprinted with permission from Clinical Infectious Diseases.35

TABLE 1B. Definition of Terms Used in the Modified Duke Criteria for the Diagnosis of Infective Endocarditis

Major criteria

Blood culture positive for IE

Typical microorganisms consistent with IE from 2 separate blood cultures: Viridans streptococci, *Streptococcus bovis*, HACEK group, ***Staphylococcus aureus***; or community-acquired enterococci in the absence of a primary focus; or

Microorganisms consistent with IE from persistently positive blood cultures defined as follows: At least 2 positive 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 sample drawn at least 1 h apart)

Major criteria Contd.

Single positive blood culture for *Coxiella burnetii* ***or anti–phase 1 IgG antibody titer >1:800***

Evidence of endocardial involvement

Echocardiogram positive for IE **(TEE recommended for patients with prosthetic valves, rated at least "possible IE" by clinical criteria, or complicated IE paravalvular abscess; TTE as first test in other patients)** defined as follows: oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation; or abscess; or new partial dehiscence of prosthetic valve; new valvular regurgitation (worsening or changing or preexisting murmur not)

TABLE 1B CONTD.

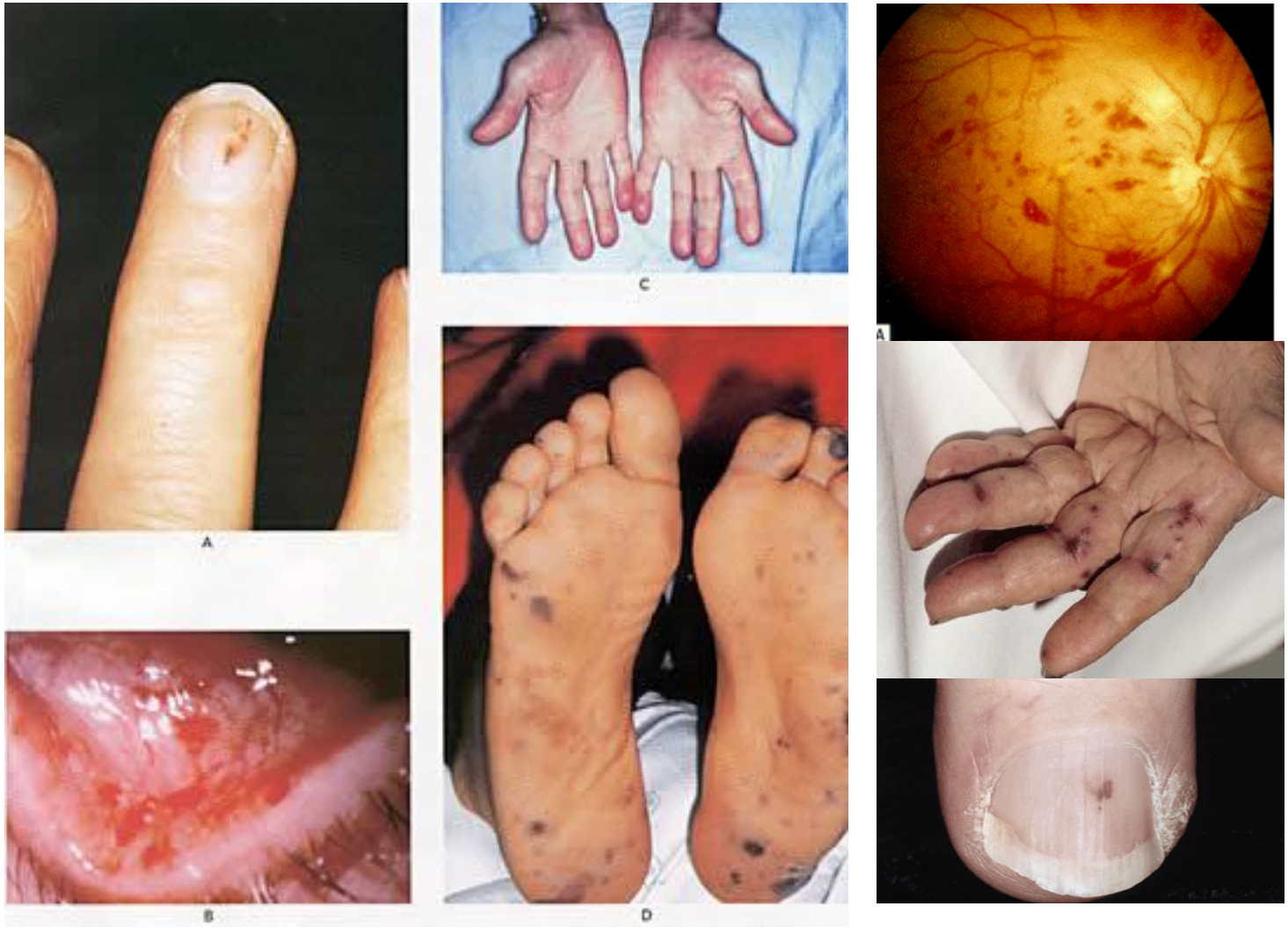
Minor criteria

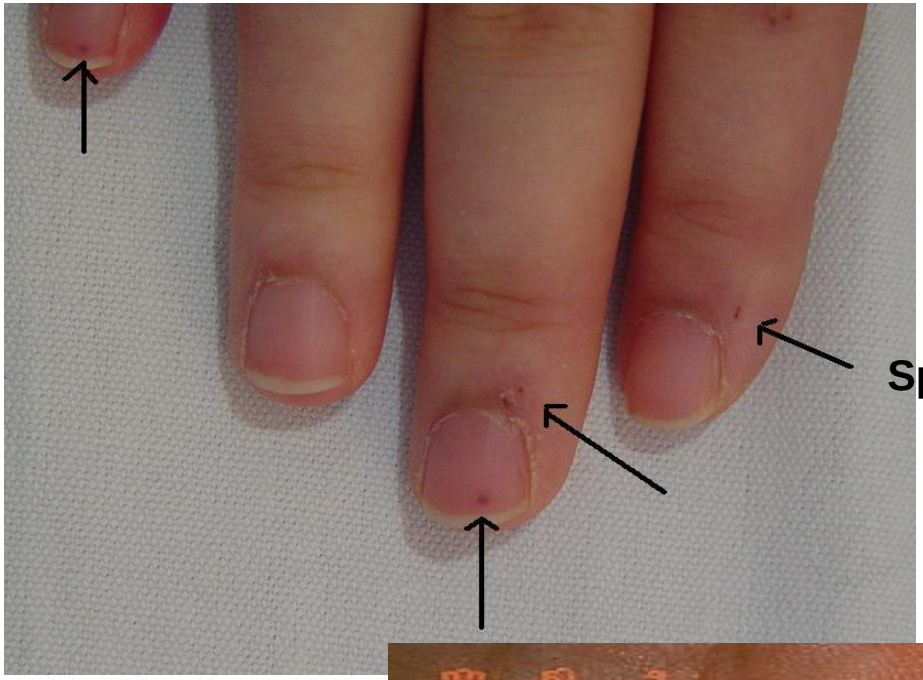
Predisposition, predisposing heart condition, or IDU
Fever, temperature 38°C
Vascular phenomena, major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway's lesions
Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor
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

Echocardiographic minor criteria eliminated

Modifications shown in boldface.
*Excludes single positive cultures for coagulase-negative staphylococci and organisms that do not cause endocarditis.
TEE indicates transesophageal echocardiography; TTE, transthoracic echo-cardiography.

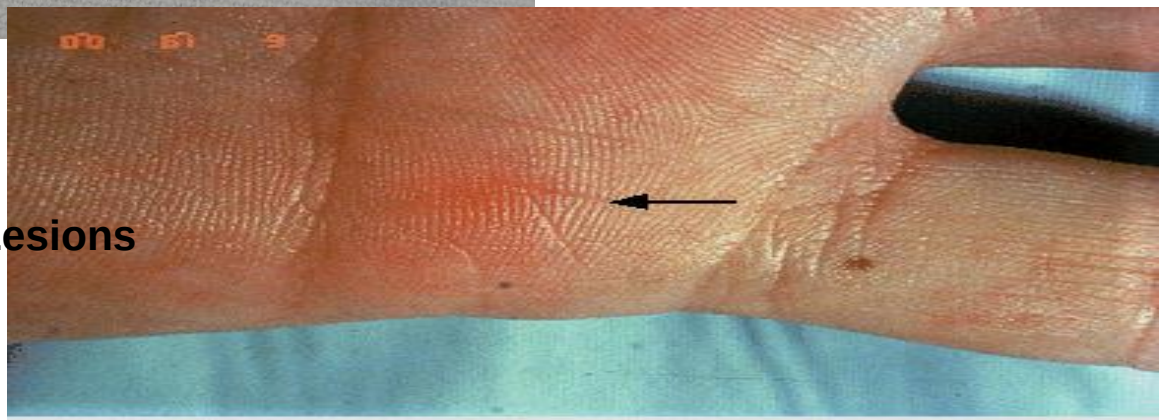
CLINCAL STIGMATA





Splinter Hemorrhages

Janeway Lesions

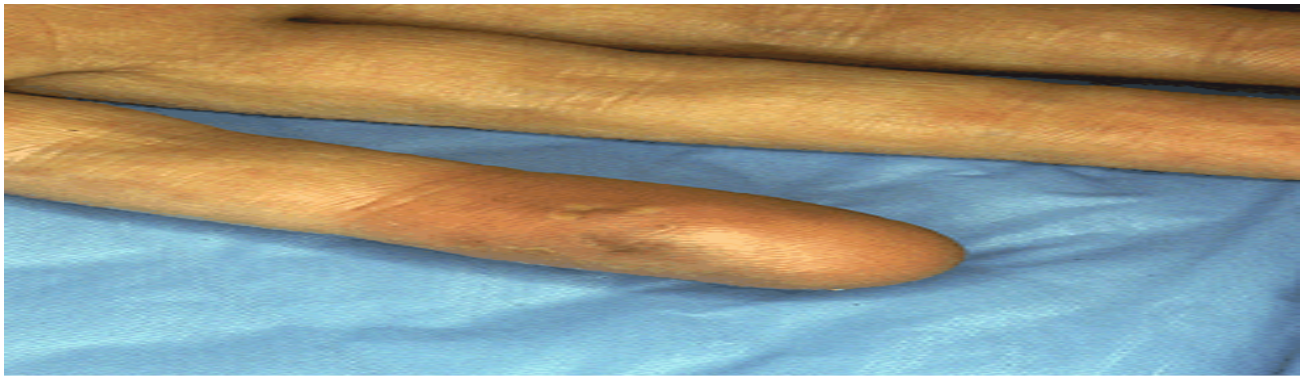


Janeway lesion in infective endocarditis A Janeway lesion (arrow) occurred on the palm in this patient with bacterial endocarditis due to Streptococcus bovis. These lesions are macular, blanching, and nonpainful, and are located on the palms and soles. Courtesy of Jan V Hirschmann. (The Skin and Infection: A Color Atlas and Text, Sanders, CV, Nesbitt, LT Jr (Eds), Williams & Wilkins, Baltimore, 1995.)

REAL IMAGE OF VEGETATION

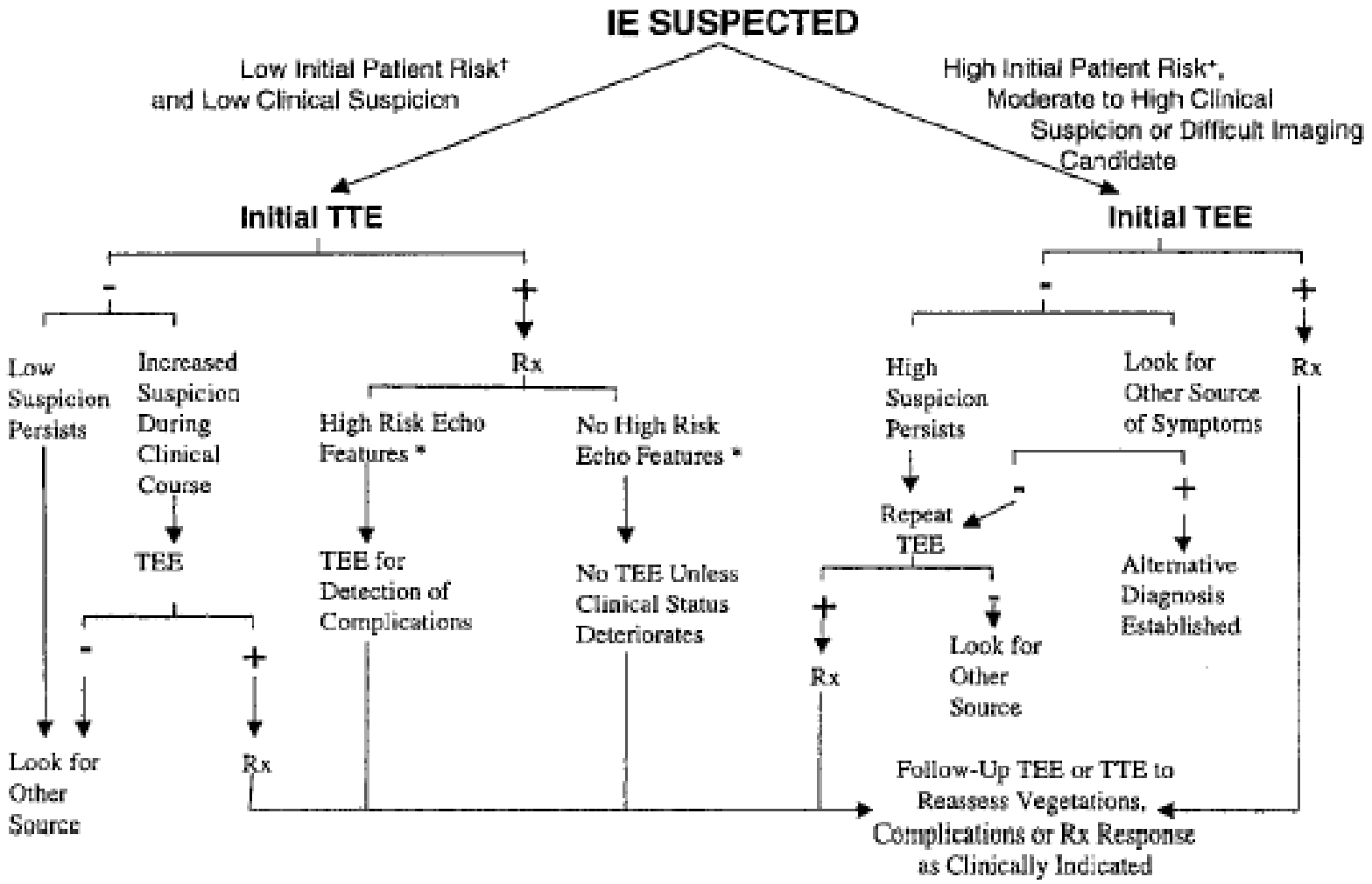
Mitral Valve Vegetation
(Courtesy of Vance G. Fowler, Jr., MD
Duke University Medical Center
Durham, NC)

Osler's nodes



Osler's nodes in infective endocarditis Osler's nodes are tender, papulopustules located on the pulp of the finger in a patient with bacterial endocarditis caused by Staphylococcus aureus. Courtesy of Charles V Sanders. (The Skin and Infection: A Color Atlas and Text, Sanders, CV, Nesbitt, LT Jr (Eds), Williams & Wilkins, Baltimore, 1995.)

ALGORITHM OF ECHO-DIAGNOSIS



Recommended use of TTE and TEE

TTE is the first diagnostic test in most patients with suspected IE. However, it is reasonable to proceed to TEE directly in selected settings:

-Limited transthoracic windows (eg, due to obesity, chest wall deformity, or mechanical ventilation.

-Prosthetic valves, especially prosthetic aortic valves in which shadowing may make visualization difficult by TTE

-A prior valvular abnormality (including previous endocarditis)

-S. aureus bacteremia

-Bacteremia due to an organism known to be a common cause of IE such as S. sanguis

For patients with a normal TTE (both morphology and function), the likelihood of IE is very low.A subsequent TEE is not necessary unless one or more of the following is present:

-A high clinical suspicion of IE (persistently positive blood cultures and/or multiple minor criteria for endocarditis)

-A technically limited TTE study

Abnormal findings on TTE that may require further evaluation by TEE include significant valvular regurgitation and/or vegetations. In addition, patients with a diagnosis of IE should have a TEE if they are at increased risk of a paravalvular abscess, which includes the following settings:

-Conduction delay by ECG that is not known to be old
-Persistent fever despite appropriate antimicrobial therapy
-Aortic valve endocarditis

-History of intravenous drug use

TRANSESOPHAGEAL ECHO HAS A UNIQUE ROLE !

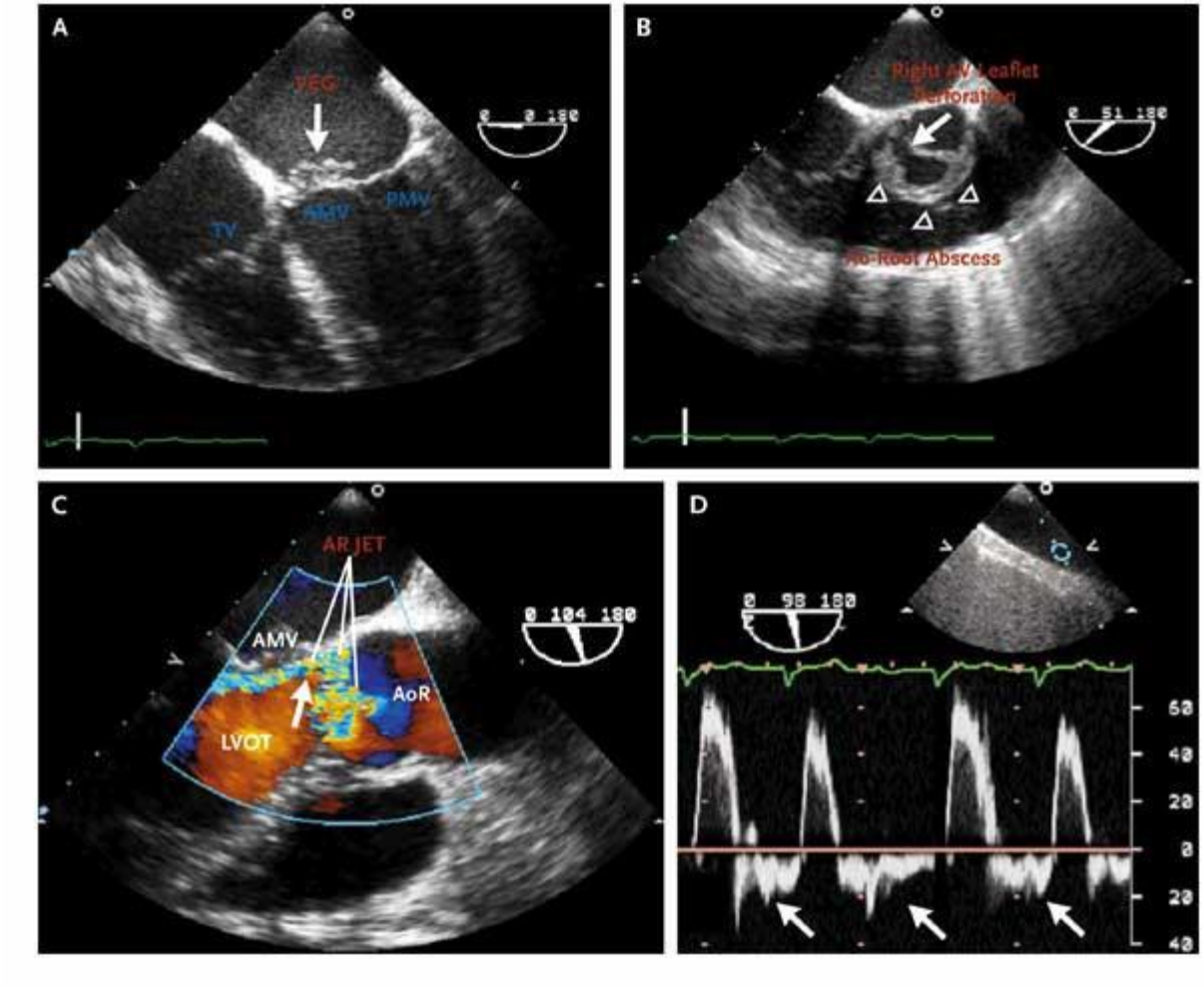


TABLE 2. Use of Echocardiography During Diagnosis and Treatment of Endocarditis

Early
Echocardiography as soon as possible (12 h after initial evaluation)
TEE preferred; obtain TTE views of any abnormal findings for later comparison
TTE if TEE is not immediately available
TTE may be sufficient in small children
Repeat echocardiography
TEE after positive TTE as soon as possible in patients at high risk for complications
TEE 7–10 d after initial TEE if suspicion exists without diagnosis of IE or with worrisome clinical course during early treatment of IE
Intraoperative
Prepump
Identification of vegetations, mechanism of regurgitation, abscesses, fistulas, and pseudoaneurysms
Postpump
Confirmation of successful repair of abnormal findings
Assessment of residual valve dysfunction
Elevated afterload if necessary to avoid underestimating valve insufficiency or presence of residual abnormal flow
Completion of therapy
Establish new baseline for valve function and morphology and ventricular size and function
TTE usually adequate; TEE or review of intraoperative TEE may be needed for complex anatomy to establish new baseline

TEE indicates transesophageal echocardiography; TTE, transthoracic echocardiography.

TABLE 3. Echocardiographic Features That Suggest Potential Need for Surgical Intervention

Vegetation

Persistent vegetation after systemic embolization
Anterior mitral leaflet vegetation, particularly with size 10 mm*
1 embolic events during first 2 wk of antimicrobial therapy*
Increase in vegetation size despite appropriate antimicrobial therapy*†

Valvular dysfunction

Acute aortic or mitral insufficiency with signs of ventricular failure†
Heart failure unresponsive to medical therapy†
Valve perforation or rupture†

Perivalvular extension

Valvular dehiscence, rupture, or fistula†
New heart block†‡
Large abscess or extension of abscess despite appropriate antimicrobial therapy†
See text for more complete discussion of indications for surgery based on vegetation characterizations.

*Surgery may be required because of risk of embolization.
†Surgery may be required because of heart failure or failure of medical therapy.
‡Echocardiography should not be the primary modality used to detect or

Minor heart block

Recommendations for Echocardiography in Infective Endocarditis: Native Valves†

Indication	Class
1. Detection and characterization of valvular lesions, their hemodynamic severity, and/or ventricular compensation*	I
2. Detection of vegetations and characterization of lesions in patients with congenital heart disease in whom infective endocarditis is suspected	I
3. Detection of associated abnormalties (eg, abscesses, shunts).*	I
4. Reevaluation studies in complex endocarditis (eg, virulent organism, severe hemodynamic lesion, aortic valve involvement, persistent fever or bacteremia, clinical change, or symptomatic deterioration)	I
5. Evaluation of patients with high clinical suspicion of culture-negative endocarditis*	I
6. If TTE is equivocal, TEE evaluation of bacteremia, especially staphylococcus bacteremia and fungemia without a known source.	I
7. Evaluation of persistent nonstaphylococcus bacteremia without a known source*	IIa
8. Risk stratification in established endocarditis*	IIa
9. Routine reevaluation in uncomplicated endocarditis during antibiotic therapy	IIb
10. Evaluation of transient fever without evidence of bacteremia or new murmur.	III

*TEE may frequently provide incremental value in addition to information obtained by TTE. The role of TEE in first-line examination awaits further study.

ACC/AHA classification

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.
Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
Class IIa. Weight of evidence/opinion is in favor of usefulness/efficacy.
Class IIb. Usefulness/efficacy less well established by evidence/opinion.
Class III: Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful and in some cases may be harmful.

†Data from Cheitlin, MD, Armstrong, WF, Aurigemma, GP, et al, Circulation 2003; 108:1146.

Recommendations for Echocardiography in Infective Endocarditis: Prosthetic Valves†

Indication	Class
1. Detection and characterization of valvular lesions, their hemodynamic severity, and/or ventricular compensation*	I
2. Detection of associated abnormalties (eg, abscesses, shunts).*	I
3. Reevaluation in complex endocarditis (eg, virulent organism, severe hemodynamic lesion, aortic valve involvement, persistent fever or bacteremia, clinical change, or symptomatic deterioration).	I
4. Evaluation of suspected endocarditis and negative cultures*	I
5. Evaluation of bacteremia without a known source*	I
6. Evaluation of persistent fever without evidence of bacteremia or new murmur*	IIa
7. Routine reevaluation in uncomplicated endocarditis during antibiotic therapy	IIb
8. Evaluation of transient fever without evidence of bacteremia or new murmur	III

*TEE may provide incremental value in addition to that obtained by TTE.

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†Data from Cheitlin, MD, Armstrong, WF, Aurigemma, GP, et al, Circulation 2003; 108:1146.

Treatment of IE

If acute start empirical treatment. If subacute, can delay treatment till cultures are back.

Regardless of treatment, do serial exams to look for neurological deficits, emboli, heart failure and other complications while patient is in hospital.

Empiric therapy is usually begun with a beta lactam and aminoglycoside. We usually switch therapy once the causative organism has come back from culture. Only IV antibiotics at least for the first week.

Streptococcus Viridans- Penicillin G 12 million units (usually as 3 million units q6hr) for 4 weeks. If renal function is okay, then add gentamicin 1mg/kg q8hr for 2weeks. Pen. allergic then Vancomycin or Ceftriaxone 1gQD or 2g QD resp. for 4 weeks.

Enterococcus- can use Vancomycin/Gentamicin combo or can use Linezolid or Synersid. Usually for 4-6 weeks

Staph. aureus- Nafcillin 2gIVq4hr with gentamicin for first 3-5days. If MRSA- Vancomycin for 6 weeks. HACEK-Ceftriaxone

TABLE 4. Therapy of Native Valve Endocarditis Caused by Highly Penicillin-Susceptible Viridans Group Streptococci and *Streptococcus bovis*

Regimen	Dosage* and Route	Duration, wk	Strength of Recommendation	Comments
Aqueous crystalline penicillin G sodium	12–18 million U/24 h IV either continuously or in 4 or 6 equally divided doses	4	IA	Preferred in most patients >65 y or patients with impairment of 8th cranial nerve function or renal function
or				
Ceftriaxone sodium	2 g/24 h IV/IM in 1 dose *Pediatric dose*†: penicillin 200 000 U/kg per 24 h IV in 4–6 equally divided doses; ceftriaxone 100 mg/kg per 24 h IV/IM in 1 dose	4	IA	
Aqueous crystalline penicillin G sodium	12–18 million U/24 h IV either continuously or in 6 equally divided doses	2	IB	2-wk regimen not intended for patients with known cardiac or extracardiac abscess or for those with creatinine clearance of <20 mL/min, impaired 8th cranial nerve function, or *Abiotrophia*, *Granulicatella*, or *Gemella* spp infection; gentamicin dosage should be adjusted to achieve peak serum concentration of 3–4 μg/mL and trough serum concentration of <1 μg/mL when 3 divided doses are used; nomogram used for single daily dosing§
or				
Ceftriaxone sodium	2 g/24 h IV/IM in 1 dose	2	IB	
plus				
Gentamicin sulfate‡	3 mg/kg per 24 h IV/IM in 1 dose *Pediatric dose*: penicillin 200 000 U/kg per 24 h IV in 4–6 equally divided doses; ceftriaxone 100 mg/kg per 24 h IV/IM in 1 dose; gentamicin 3 mg/kg per 24 h IV/IM in 1 dose or 3 equally divided doses‖	2		
Vancomycin hydrochloride¶	30 mg/kg per 24 h IV in 2 equally divided doses not to exceed 2 g/24 h unless concentrations in serum are inappropriately low *Pediatric dose*: 40 mg/kg per 24 h IV in 2–3 equally divided doses	4	IB	Vancomycin therapy recommended only for patients unable to tolerate penicillin or ceftriaxone; vancomycin dosage should be adjusted to obtain peak (1 h after infusion completed) serum concentration of 30–45 μg/mL and a trough concentration range of 10–15 μg/mL

Minimum inhibitory concentration ≤0.12 μg/mL.

*Dosages recommended are for patients with normal renal function.

†Pediatric dose should not exceed that of a normal adult.

‡Other potentially nephrotoxic drugs (eg, nonsteroidal antiinflammatory drugs) should be used with caution in patients receiving gentamicin therapy.

§See reference 280 in full statement.

‖Data for once-daily dosing of aminoglycosides for children exist, but no data for treatment of IE exist.

¶Vancomycin dosages should be infused during course of at least 1 h to reduce risk of histamine-release "red man" syndrome.

TABLE 5. Therapy of Native Valve Endocarditis Caused by Strains of Viridans Group Streptococci and *Streptococcus bovis* Relatively Resistant to Penicillin

Regimen	Dosage* and Route	Duration, wk	Strength of Recommendation	Comments
Aqueous crystalline penicillin G sodium	24 million U/24 h IV either continuously or in 4–6 equally divided doses	4	IB	Patients with endocarditis caused by penicillin-resistant (MIC >0.5 μg/mL) strains should be treated with regimen recommended for enterococcal endocarditis (see Table 9)
or				
Ceftriaxone sodium	2 g/24 h IV/IM in 1 dose	4	IB	
plus				
Gentamicin sulfate†	3 mg/kg per 24 h IV/IM in 1 dose	2		
	Pediatric dose‡: penicillin 300 000 U/24 h IV in 4–6 equally divided doses; ceftriaxone 100 mg/kg per 24 h IV/IM in 1 dose; gentamicin 3 mg/kg per 24 h IV/IM in 1 dose or 3 equally divided doses			
Vancomycin hydrochloride‡	30 mg/kg per 24 h IV in 2 equally divided doses not to exceed 2 g/24 h, unless serum concentrations are inappropriately low	4	IB	Vancomycin§ therapy recommended only for patients unable to tolerate penicillin or ceftriaxone therapy
	Pediatric dose: 40 mg/kg 24 h in 2 or 3 equally divided doses			

Minimum inhibitory concentration (MIC) >0.12 μg/mL–≤0.5 μg/mL.

*Dosages recommended are for patients with normal renal function.

†See Table 4 for appropriate dosage of gentamicin.

‡Pediatric dose should not exceed that of a normal adult.

§See Table 4 for appropriate dosage of vancomycin.

TABLE 6. Therapy for Endocarditis of Prosthetic Valves or Other Prosthetic Material Caused by Viridans Group Streptococci and *Streptococcus bovis*

Regimen	Dosage* and Route	Duration, wk	Strength of Recommendation	Comments
Penicillin-susceptible strain (minimum inhibitory concentration ≤0.12 μg/mL)				
Aqueous crystalline penicillin G sodium	24 million U/24 h IV either continuously or in 4–6 equally divided doses	6	IB	Penicillin or ceftriaxone together with gentamicin has not demonstrated superior cure rates compared with monotherapy with penicillin or ceftriaxone for patients with highly susceptible strain; gentamicin therapy should not be administered to patients with creatinine clearance of <30 mL/min
or				
Ceftriaxone	2 g/24 h IV/IM in 1 dose	6	IB	
with or without				
Gentamicin sulfate†	3 mg/kg per 24 h IV/IM in 1 dose	2		
	Pediatric dose‡: penicillin 300 000 U/kg per 24 h IV in 4–6 equally divided doses; ceftriaxone 100 mg/kg IV/IM once daily; gentamicin 3 mg/kg per 24 h IV/IM, in 1 dose or 3 equally divided doses			
Vancomycin hydrochloride§	30 mg/kg per 24 h IV in 2 equally divided doses	6	IB	Vancomycin therapy recommended only for patients unable to tolerate penicillin or ceftriaxone
	Pediatric dose: 40 mg/kg per 24 h IV or in 2 or 3 equally divided doses			
Penicillin relatively or fully resistant strain (minimum inhibitory concentration >0.12 μg/mL)				
Aqueous crystalline penicillin sodium	24 million U/24 h IV either continuously or in 4–6 equally divided doses	6	IB	
or				
Ceftriaxone	2 g/24 h IV/IM in 1 dose	6	IB	
plus				
Gentamicin sulfate	3 mg/kg per 24 h IV/IM in 1 dose	6		
	Pediatric dose: penicillin 300 000 U/kg per 24 h IV in 4–6 equally divided doses			
Vancomycin hydrochloride	30 mg/kg per 24 h IV in 2 equally divided doses	6	IB	Vancomycin therapy is recommended only for patients unable to tolerate penicillin or ceftriaxone
	Pediatric dose: 40 mg/kg per 24 h IV in 2 or 3 equally divided doses			

*Dosages recommended are for patients with normal renal function.
†See Table 4 for appropriate dosage of gentamicin.
‡Pediatric dose should not exceed that of a normal adult.
§See text and Table 4 for appropriate dosage of vancomycin.

TABLE 7. Therapy for Endocarditis Caused by Staphylococci in the Absence of Prosthetic Materials

Regimen	Dosage* and Route	Duration	Strength of Recommendation	Comments
Oxacillin-susceptible strains				
Nafcillin or oxacillin†	12 g/24 h IV in 4–6 equally divided doses	6 wk	IA	For complicated right-sided IE and for left-sided IE; for uncomplicated right-sided IE, 2 wk (see text)
with				
Optional addition of gentamicin sulfate‡	3 mg/kg per 24 h IV/IM in 2 or 3 equally divided doses	3–5 d		
	Pediatric dose§: Nafcillin or oxacillin 200 mg/kg per 24 h IV in 4–6 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses			Clinical benefit of aminoglycosides has not been established
For penicillin-allergic (nonanaphylactoid type) patients:				Consider skin testing for oxacillin-susceptible staphylococci and questionable history of immediate-type hypersensitivity to penicillin
Cefazolin	6 g/24 h IV in 3 equally divided doses	6 wk	IB	Cephalosporins should be avoided in patients with anaphylactoid-type hypersensitivity to β-lactams; vancomycin should be used in these cases§
with				
Optional addition of gentamicin sulfate	3 mg/kg per 24 h IV/IM in 2 or 3 equally divided doses	3–5 d		Clinical benefit of aminoglycosides has not been established
	Pediatric dose: cefazolin 100 mg/kg per 24 h IV in 3 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses			
Oxacillin-resistant strains				
Vancomycin‖	30 mg/kg per 24 h IV in 2 equally divided doses	6 wk	IB	Adjust vancomycin dosage to achieve 1-h serum concentration of 30–45 μg/mL and trough concentration of 10–15 μg/mL (see text for vancomycin alternatives)
	Pediatric dose: 40 mg/kg per 24 h IV in 2 or 3 equally divided doses			

*Dosages recommended are for patients with normal renal function.

†Penicillin G 24 million U/24 h IV in 4 to 6 equally divided doses may be used in place of nafcillin or oxacillin if strain is penicillin susceptible (minimum inhibitory concentration ≤0.1 μg/mL) and does not produce β-lactamase.

‡Gentamicin should be administered in close temporal proximity to vancomycin, nafcillin, or oxacillin dosing.

§Pediatric dose should not exceed that of a normal adult.

‖For specific dosing adjustment and issues concerning vancomycin, see Table 4 footnotes.

TABLE 8. Therapy for Prosthetic Valve Endocarditis Caused by Staphylococci

Regimen	Dosage* and Route	Duration, wk	Strength of Recommendation	Comments
Oxacillin-susceptible strains				
Nafcillin or oxacillin	12 g/24 h IV in 6 equally divided doses	≥6	IB	Penicillin G 24 million U/24 h IV in 4 to 6 equally divided doses may be used in place of nafcillin or oxacillin if strain is penicillin susceptible (minimum inhibitory concentration ≤0.1 μg/mL) and does not produce β-lactamase; vancomycin should be used in patients with immediate-type hypersensitivity reactions to β-lactam antibiotics (see Table 3 for dosing guidelines); cefazolin may be substituted for nafcillin or oxacillin in patients with non–immediate-type hypersensitivity reactions to penicillins
plus				
Rifampin	900 mg per 24 h IV/PO in 3 equally divided doses	≥6		
plus				
Gentamicin†	3 mg/kg per 24 h IV/IM in 2 or 3 equally divided doses	2		
	Pediatric dose‡: nafcillin or oxacillin 200 mg/kg per 24 h IV in 4–6 equally divided doses; rifampin 20 mg/kg per 24 h IV/PO in 3 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses			
Oxacillin-resistant strains				
Vancomycin	30 mg/kg 24 h in 2 equally divided doses	≥6	IB	Adjust vancomycin to achieve 1-h serum concentration of 30–45 μg/mL and trough concentration of 10–15 μg/mL (see text for gentamicin alternatives)
plus				
Rifampin	900 mg/24 h IV/PO in 3 equally divided doses	≥6		
plus				
Gentamicin	3 mg/kg per 24 h IV/IM in 2 or 3 equally divided doses	2		
	Pediatric dose: vancomycin 40 mg/kg per 24 h IV in 2 or 3 equally divided doses; rifampin 20 mg/kg per 24 h IV/PO in 3 equally divided doses (up to adult dose); gentamicin 3 mg/kg per 24 h IV or IM in 3 equally divided doses			

*Dosages recommended are for patients with normal renal function.

†Gentamicin should be administered in close proximity to vancomycin, nafcillin, or oxacillin dosing.

‡Pediatric dose should not exceed that of a normal adult.

TABLE 9. Therapy for Native Valve or Prosthetic Valve Enterococcal Endocarditis Caused by Strains Susceptible to Penicillin, Gentamicin, and Vancomycin

Regimen	Dosage* and Route	Duration, wk	Strength of Recommendation	Comments
Ampicillin sodium	12 g/24 h IV in 6 equally divided doses	4–6	IA	Native valve: 4-wk therapy recommended for patients with symptoms of illness ≤3 mo; 6-wk therapy recommended for patients with symptoms >3 mo
or				
Aqueous crystalline penicillin G sodium	18–30 million U/24 h IV either continuously or in 6 equally divided doses	4–6	IA	Prosthetic valve or other prosthetic cardiac material: minimum of 6 wk of therapy recommended
plus				
Gentamicin sulfate†	3 mg/kg per 24 h IV/IM in 3 equally divided doses	4–6		
	Pediatric dose‡: ampicillin 300 mg/kg per 24 h IV in 4–6 equally divided doses; penicillin 300 000 U/kg per 24 h IV in 4–6 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses			
Vancomycin hydrochloride§	30 mg/kg per 24 h IV in 2 equally divided doses	6	IB	Vancomycin therapy recommended only for patients unable to tolerate penicillin or ampicillin
plus				
Gentamicin sulfate	3 mg/kg per 24 h IV/IM in 3 equally divided doses	6		6 wk of vancomycin therapy recommended because of decreased activity against enterococci
	Pediatric dose: vancomycin 40 mg/kg per 24 h IV in 2 or 3 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses			

*Dosages recommended are for patients with normal renal function.

†Dosage of gentamicin should be adjusted to achieve peak serum concentration of 3–4 μg/mL and a trough concentration of <1 μg/mL (see text). Patients with a creatinine clearance of <50 mL/min should be treated in consultation with an infectious diseases specialist.

‡Pediatric dose should not exceed that of a normal adult.

§See text and Table 4 for appropriate dosing of vancomycin.

TABLE 10. Therapy for Native or Prosthetic Valve Enterococcal Endocarditis Caused by Strains Susceptible to Penicillin, Streptomycin, and Vancomycin and Resistant to Gentamicin

Regimen	Dosage* and Route	Duration, wk	Strength of Recommendation	Comments
Ampicillin sodium	12 g/24 h IV in 6 equally divided doses	4–6	IA	Native valve: 4-wk therapy recommended for patients with symptoms of illness <3 mo; 6-wk therapy recommended for patients with symptoms >3 mo
or				
Aqueous crystalline penicillin G sodium	24 million U/24 h IV continuously or in 6 equally divided doses	4–6	IA	
plus				
Streptomycin sulfate†	15 mg/kg per 24 h IV/IM in 2 equally divided doses	4–6		Prosthetic valve or other prosthetic cardiac material: minimum of 6 wk of therapy recommended
	Pediatric dose‡: ampicillin 300 mg/kg per 24 h IV in 4–6 equally divided doses; penicillin 300 000 U/kg per 24 h IV in 4–6 equally divided doses; streptomycin 20–30 mg/kg per 24 h IV/IM in 2 equally divided doses			
Vancomycin hydrochloride§	30 mg/kg per 24 h IV in 2 equally divided doses	6	IB	Vancomycin therapy recommended only for patients unable to tolerate penicillin or ampicillin
plus				
Streptomycin sulfate	15 mg/kg per 24 h IV/IM in 2 equally divided doses	6		
	Pediatric dose: vancomycin 40 mg/kg per 24 h IV in 2 or 3 equally divided doses; streptomycin 20–30 mg/kg per 24 h IV/IM in 2 equally divided doses			

*Dosages recommended are for patients with normal renal function. Patients with creatinine clearance of <50 mL/min should be treated in consultation with an infectious diseases specialist.

†See text for appropriate dosing of streptomycin.

‡Pediatric dose should not exceed that of a normal adult.

§See text and Table 4 for appropriate dosing of vancomycin.

TABLE 11. Therapy for Native or Prosthetic Valve Enterococcal Endocarditis Caused by Strains Resistant to Penicillin and Susceptible to Aminoglycoside and Vancomycin

Regimen	Dosage* and Route	Duration, wk	Strength of Recommendation	Comments
β-Lactamase–producing strain				
Ampicillin-sulbactam	12 g/24 h IV in 4 equally divided doses	6	IIaC	Unlikely that the strain will be susceptible to gentamicin; if strain is gentamicin resistant, then >6 wk of ampicillin-sulbactam therapy will be needed
plus				
Gentamicin sulfate†	3 mg/kg per 24 h IV/IM in 3 equally divided doses	6		
	Pediatric dose‡: ampicillin-sulbactam 300 mg/kg per 24 h IV in 4 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses			
Vancomycin hydrochloride§	30 mg/kg per 24 h IV in 2 equally divided doses	6	IIaC	Vancomycin therapy recommended only for patients unable to tolerate ampicillin-sulbactam
plus				
Gentamicin sulfate†	3 mg/kg per 24 h IV/IM in 3 equally divided doses	6		
	Pediatric dose: vancomycin 40 mg/kg per 24 h in 2 or 3 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses			
Intrinsic penicillin resistance				
Vancomycin hydrochloride‡	30 mg/kg per 24 h IV in 2 equally divided doses	6	IIaC	Consultation with a specialist in infectious diseases recommended
plus				
Gentamicin sulfate†	3 mg/kg per 24 h IV/IM in 3 equally divided doses	6		
	Pediatric dose: vancomycin 40 mg/kg per 24 h IV in 2 or 3 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses			

*Dosages recommended are for patients with normal renal function; see Table 9 for patients with creatinine clearance of <50 mL/min.
†See text and Table 4 for appropriate dosing of gentamicin.
‡Pediatric dose should not exceed that of a normal adult.
§See Table 4 for appropriate dosing of vancomycin.

TABLE 13. Therapy for Both Native and Prosthetic Valve Endocarditis Caused by HACEK* Microorganisms

Regimen	Dosage and Route	Duration, wk	Strength of Recommendation	Comments
Ceftriaxone† sodium	2 g/24 h IV/IM in 1 dose	4	IB	Cefotaxime or another third- or fourth-generation cephalosporin may be substituted
or				
Ampicillin-sulbactam‡	12 g/24 h IV in 4 equally divided doses	4	IIaB	
or				
Ciprofloxacin‡§	1000 mg/24 h PO or 800 mg/24 h IV in 2 equally divided doses *Pediatric dose*‖: Ceftriaxone 100 mg/kg per 24 h IV/IM once daily; ampicillin-sulbactam 300 mg/kg per 24 h IV divided into 4 or 6 equally divided doses; ciprofloxacin 20–30 mg/kg per 24 h IV/PO in 2 equally divided doses	4	IIbC	Fluoroquinolone therapy recommended only for patients unable to tolerate cephalosporin and ampicillin therapy; levofloxacin, gatifloxacin, or moxifloxacin may be substituted; fluoroquinolones generally not recommended for patients <18 y old Prosthetic valve: patients with endocarditis involving prosthetic cardiac valve or other prosthetic cardiac material should be treated for 6 wk

**Haemophilus parainfluenzae, H aphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens,* and *Kingella kingae.*

†Patients should be informed that IM injection of ceftriaxone is painful.

‡Dosage recommended for patients with normal renal function.

§Fluoroquinolones are highly active in vitro against HACEK microorganisms. Published data on use of fluoroquinolone therapy for endocarditis caused by HACEK are minimal.

‖Pediatric dose should not exceed that of a normal adult.

TABLE 14. Therapy for Culture-Negative Endocarditis Including *Bartonella* Endocarditis

Regimen	Dosage* and Route	Duration, wk	Strength of Recommendation	Comments
Native valve				
Ampicillin-sulbactam	12 g/24 h IV in 4 equally divided doses	4–6	IIbC	Patients with culture-negative endocarditis should be treated with consultation with an infectious diseases specialist
plus				
Gentamicin sulfate†	3 mg/kg per 24 h IV/IM in 3 equally divided doses	4–6		
Vancomycin‡	30 mg/kg per 24 h IV in 2 equally divided doses	4–6	IIbC	Vancomycin recommended only for patients unable to tolerate penicillins
plus				
Gentamicin sulfate	3 mg/kg per 24 h IV/IM in 3 equally divided doses	4–6		
plus				
Ciprofloxacin	1000 mg/24 h PO or 800 mg/24 h IV in 2 equally divided doses	4–6		
	Pediatric dose§: ampicillin-sulbactam 300 mg/kg per 24 h IV in 4–6 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses; vancomycin 40 mg/kg per 24 h in 2 or 3 equally divided doses; ciprofloxacin 20–30 mg/kg per 24 h IV/PO in 2 equally divided doses			
Prosthetic valve (early, ≤1 y)				
Vancomycin	30 mg/kg per 24 h IV in 2 equally divided doses	6	IIbC	
plus				
Gentamicin sulfate	3 mg/kg per 24 h IV/IM in 3 equally divided doses	2		
plus				
Cefepime	6 g/24 h IV in 3 equally divided doses	6		
plus				
Rifampin	900 mg/24 h PO/IV in 3 equally divided doses	6		
	Pediatric dose: vancomycin 40 mg/kg per 24 h IV in 2 or 3 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses; cefepime 150 mg/kg per 24 h IV in 3 equally divided doses; rifampin 20 mg/kg per 24 h PO/IV in 3 equally divided doses			
Prosthetic valve (late, >1 y)		6	IIbC	Same regimens as listed above for native valve endocarditis
Suspected *Bartonella*, culture negative				
Ceftriaxone sodium	2 g/24 h IV/IM in 1 dose	6	IIaB	Patients with *Bartonella* endocarditis should be treated in consultation with an infectious diseases specialist
plus				
Gentamicin sulfate	3 mg/kg per 24 h IV/IM in 3 equally divided doses	2		
with/without				
Doxycycline	200 mg/kg per 24 h IV/PO in 2 equally divided doses	6		
Documented *Bartonella*, culture positive				
Doxycycline	200 mg/24 h IV or PO in 2 equally divided doses	6	IIaB	If gentamicin cannot be given, then replace with rifampin, 600 mg/24 h PO/IV in 2 equally divided doses (see reference 187 in full statement)
plus				
Gentamicin sulfate	3 mg/kg per 24 h IV/IM in 3 equally divided doses	2		
	Pediatric dose: ceftriaxone 100 mg/kg per 24 h IV/IM once daily; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses; doxycycline 2–4 mg/kg per 24 h IV/PO in 2 equally divided doses; rifampin 20 mg/kg per 24 h PO/IV in 2 equally divided doses			

*Dosages recommended are for patients with normal renal function; see Table 9 for patients with creatinine clearance <50 mL/min.
†See text and Table 4 for appropriate dosing of gentamicin.
‡See Table 4 for appropriate dosing of vancomycin.
§Pediatric dose should not exceed that of a normal adult.

TABLE 15. Epidemiological Clues in Etiological Diagnosis of Culture-Negative Endocarditis

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

TABLE 16. Care During and After Completion of Antimicrobial Treatment

Initiate before or at completion of therapy
Obtain transthoracic echocardiogram to establish new baseline
Drug rehabilitation referral for patients who use illicit injection drugs
Educate regarding signs of endocarditis, need for antibiotic prophylaxis for certain dental/surgical/invasive procedures
Thorough dental evaluation and treatment if not performed earlier in evaluation
Prompt removal of IV catheter at completion of antimicrobial therapy
Short-term follow-up
Obtain at least 3 sets of blood cultures from separate sites for any febrile illness and before initiation of antibiotic therapy
Physical examination for evidence of congestive heart failure
Evaluate for toxicity resulting from current/previous antimicrobial therapy
Long-term follow-up
Obtain at least 3 sets of blood cultures from separate sites for any febrile illness and before initiation of antibiotic therapy
Evaluation of valvular and ventricular function (echocardiography)
Scrupulous oral hygiene and frequent dental professional office visits

CONCLUSION

IE IS AN OLD AND HETEROGENOUS DISEASE PRESENTS FREQUENTLY WITH DIVERSIFIED CLINICAL FEATURES

DIAGNOSTIC CRITERIA HHAS BEEN CHANGED WITH THE AVAILABLE EVIDENCES

IT IS THE CLINICIAN WHO WILL DECIDE WHETHER TO TREAT OR NOT TREAT AN INDIVIDUAL PATIENT, REGARDLESS OF WHETHER THEY MEET OR FAIL TO MEET THE CRITERIA FOR DEFINITE OR POSSIBLE IE BY THE DUKE SCHEMA

USE OF DNA TECHNOLOGY LIKE PCR CAN BE ADOPTED IN FUTURE AFTER STANDERIZATION AND VALIDATION IN THE DIANOSIS OF CULTURE NEGATIVE CASES

PROPHYLAXIS IN APPROPRIATE SITUATION HAVE NO ALTERNATIVE

SUSPICIOUS CLINICAL MIND, WELL COORDINATED EFFORTS AMONG INTERNISTS, CARDIOLOGISTS, PATHOLOGISTS & MICROBIOLOGISTS, AND CARE GIVERS ARE IN THE KEY TO MANAGEMENT OF IE


THANKS