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Infective endocarditis

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ABSTRACT

Infective endocarditis preoccupies a substantial place in infectious emergencies, and treatment delays are likely to cause increased mortality and morbidity. This paper attempts to explore and discuss the current knowledge on the diagnosis, treatment, and prophylaxis of infective endocarditis in light of the relevant literature. Infective endocarditis is an infectious condition that still keeps its significance and requires a multidisciplinary approach from infectious diseases, clinical microbiology, cardiology, and cardiovascular surgery.

Keywords: Infective endocarditis, epidemiology, etiology, diagnosis, treatment

DEFINITION

Infective endocarditis is an infection of the endocardial tissue that may affect the heart valves or prosthetic (artificial) valves. While it was previously classified as acute, subacute, and chronic endocarditis, it is contemporarily categorized as natural or prosthetic valve endocarditis and community-acquired or healthcare-associated (formerly hospital-acquired) endocarditis (1).

EPIDEMIOLOGY

The annual incidence of infective endocarditis is estimated to be about 3-10 per 100,000 people. The incidence, which becomes about 15 per 100,000 people in the United States, is predicted to be high due to the prevalence of rheumatic heart disease in Turkey, despite a paucity of reseach. Besides, the annual mortality rate in endocarditis appears to be around 30%. Thus, infective endocarditis ranks fourth among the causes of infectious diseases (1, 2).

In countries with low socioeconomic status, rheumatic heart disease is the major risk factor in two-thirds of cases. The disease usually occurs in young adults and appears mostly as a community-acquired infection. In high-income countries, on the other hand, degenerative valve disorders, diabetes, hemodialysis, cancer, HIV, intravenous drug use, congenital heart disease, and intracardiac devices are the leading causes of the infection. In high-income countries, it constitutes 25-30% of healthcare-associated conditions (1). Infective endocarditis is frequently reported in patients aged 60 years and above (1). The mean age for endocarditis is currently known to be 47 years in Turkey (2). **Table 1** presents the common risk factors for infective endocarditis (3).

Table 1. Risk factors for endocarditis
Patients with natural valve disease
Bicuspid aortic valve
Mitral valve prolapse
Congenital heart disease
Rheumatic valve disease
Previous episode of infective endocarditis
Chronic hemodialysis
Intravenous drug use
Permanent venous line
Immunocompromised state
Human immunodeficiency virus infection (HIV)
Implanted cardiac device or prosthetic valve
Mid-operative complications
Pre-operative signs/symptoms of infection
Hematoma following device insertion
Need for revision in device layout
Chronic anticoagulation
Larger numbers of permanent prosthetic materials
Heart failure with a reduced ejection fraction
Corticosteroid use
General population comorbidities associated with endocarditis
Hypertension
Poorly managed diabetes
Coronary artery disease
Chronic obstructive pulmonary disease
Renal failure (especially when needed for dialysis)
Chronic liver disease
Malignancy
Advanced age

(*) Adapted from: Vincent L L. Otto CM Current Cardiology Reports 2018; 20:86. Doi.10.1007/s11886-018-1043-2.

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ETIOLOGY

It is well-known that Gram-positive bacteria are accounted for 80-90% of cases of native valve infective endocarditis. Of them, 35 to 40% are *Staphylococcus aureus*, 30 to 40% are streptococci (about 20% consist of viridans streptococcus and *Streptococcus gallolyticus* [formerly *S. bovis*], and about 15% are other streptococci), and 10% are composed of enterococci. Coagulase-negative staphylococci, prevalent in prosthetic valve infective endocarditis, are rare in native valve infective endocarditis, except for *S. lugdunensis*. HACEK (*Haemophilus* spp., *Agregatibacter* [formerly *Actinobacillus*] spp., *Cardiobacterium* spp., *Eikenella corrodens* spp., and *Kingella* spp.), fungi, polymicrobial infection, and rarely aerobic Gram-negative bacilli are accounted for 3%-5% of cases (1,4).

Staphylococcal infective endocarditis may affect natural and prosthetic valves in risk groups (e.g., hemodialysis patients and intravenous drug users). Viridans group streptococci (17%) and enterococci (11%) are other causes of natural valve infection. Besides, coagulase-negative staphylococci have gained popularity in prosthetic valves and heart devices. Coagulase-negative staphylococci (e.g., *Staphylococcus epidermidis*, *Staphylococcus lugdunensis*) are often found in skin flora and cause prosthetic valve endocarditis by colonizing indwelling catheters and devices. Coagulase-negative staphylococci are a prevalent cause of hospital-acquired native valve endocarditis. Viridans streptococci (e.g., *Streptococcus mutans*, *Streptococcus salivarius*, *Streptococcus mitis*) seen in the oral wort are the most common cause of infective endocarditis in low-income countries. Viridans streptococci are usually located in the oral, gastrointestinal, and urogenital systems. Group D streptococci (e.g., *Streptococcus gallolyticus*, *Streptococcus bovis*) may lead to colon tumor-associated infective endocarditis; *Streptococcus bovis* is common particularly among patients with colon cancer. Enterococci account for 10% of cases and cause natural or prosthetic valve endocarditis among older adults or those with chronic diseases. Of them, the most common agent is *Enterococcus faecalis*.

Other factors in infective endocarditis are slow-growing bacteria, zoonotic bacteria, and fungi. For example, HACEK group bacteria (*Haemophilus* spp. (*Haemophilus* parainfluenzae), *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella* spp.) colonize the oropharynx and are Gram-negative bacteria that lead to infective endocarditis and are difficult to reproduce in culture. In zoonotic endocarditis, *Coxiella burnetii* (the agent of Q fever) and *Brucella* spp. (spp) may be transmitted to humans from farm animals, while cats transmit *Bartonella henselae*, and parrots and pigeons carry *Chlamydia psittaci*. Gram-negative bacteria (e.g., *Acinetobacter* spp., *Pseudomonas aeruginosa*), *Legionella* spp., *Mycoplasma* spp., and *Tropheryma whippelii* may be other causes of endocarditis. Fungal endocarditis is usually caused by *Candida* or *Aspergillus*; despite being rare, it often becomes fatal. It is diagnosed in immunocompromised patients or those undergoing cardiac surgery and with prosthetic valves. The diagnosis of fungal infective endocarditis caused by HACEK, *Candida*, and *Aspergillus* is rather challenging due to the poor susceptibility of blood cultures (1).

On the other hand, 10% of cases in which the agent cannot be defined are called culture-negative endocarditis (5). In these cases, one needs to avoid detecting the agent by blood culture, vegetation culture, intracardiac foreign bodies, cultures obtained from implants, and polymerase chain reaction (PCR) for diagnosis. There is also polymicrobial endocarditis with a rate of approximately 3%, and more than one factor can be detected behind it (4). **Table 2** shows culture-negative endocarditis agents. Accordingly, taking antibiotics before the diagnosis is the most common cause of culture-negative endocarditis.

Table 2. Culture-negative endocarditis agents*

Bartonella spp.
Tropheryma whipleii
Coxiella burnetti
Chlamydophila
Corynebacterium spp.
HACEK organisms
Fungal agents

(*) Adapted from: İnkaya AÇ, Akova M. Enfektif endokardit, miyokardit, perikardit. Wilke AT, Söyletir G, Doğanay M. Enfeksiyon Hastalıkları ve Mikrobiyolojisi, 4. Baskı, Nobel Tıp Kitabevleri, İstanbul, 2017; 951-972.

The frequency of microorganisms causing infective endocarditis varies by underlying disorder. The endocarditis agents by underlying disease are shown in **Table 3**.

Table 3. Infective endocarditis agents by underlying diseases *

Cardiovascular pathology	Agents
Rheumatic valve disease	
	Viridans streptococci, enterococci
	Other streptococci, *S. aureus*
Congenital valve lesion	
	Viridans streptococci, enterococci, enterococci, other streptococci, *S. aureus*
Normal pericardium	
	S. aureus, Viridans streptococci, enterococci
Prosthetic valve - Early stage	
	S. aureus
	Coagulase-negative staphylococci (CNS), Gram-negative bacillus, diphtheroid, *Candida*
Prosthetic valve - Late stage	
	CNS
	Enterococcus, viridans streptococcus, *S. aureus*
Intravenous drug addiction	
	S. aureus, *P. aeruginosa*, enterococci, *C. albicans*

(*) Adapted from: İnkaya AÇ, Akova M. Enfektif endokardit, miyokardit, perikardit. Wilke AT, Söyletir G, Doğanay M. Enfeksiyon Hastalıkları ve Mikrobiyolojisi, 4. Baskı, Nobel Tıp Kitabevleri, İstanbul, 2017; 951-972.

PATHOGENESIS

Infective endocarditis bursts with valvular endothelial or endocardial damage caused by valvular sclerosis, rheumatic valvulitis, or direct bacterial activity (particularly *S. aureus*). The damage exposes subendothelial collagen, to which platelets and fibrin adhere and form a microthrombotic lesion - called sterile vegetation - and other matrix molecules. Then, the release of inflammatory cytokines and tissue factors initiates a platelet-fibrin thrombus is formed, facilitating bacterial adhesion. With bacterial colonization, additional endothelial damage and thrombus accumulation trigger cycles, eventually resulting in infected vegetation. Bacteria in the blood bind to the lesion and colonize it. In the absence of an effective host response, the bacteria multiply in situ and stimulate further platelet and fibrin deposition to form infected vegetation that is the hallmark of infective endocarditis. Vegetation creates an inaccessible protective microenvironment for neutrophils and host defense molecules (1). Mycotic aneurysms can particularly emerge in endocarditis due to Viridans streptococci (5).

CLINICAL FINDINGS

The clinical manifestations of infective endocarditis are varied and non-specific; thus, endocarditis needs to be investigated in patients with unexplained persistent bacteremia. In particular, *S. aureus* bacteremia is associated with endocarditis in 25-30% of cases, and all patients need to undergo echocardiography. In the first clinical evaluation of the patient with suspected infective endocarditis, a comprehensive anamnesis including risk factors and physical examination findings become critical for the diagnosis. Cardiac risk factors are prior infective endocarditis, prosthetic valve or cardiac devices, and congenital heart disease, while non-cardiac risk factors refer to intravenous drug use, indwelling intravenous catheters, immunosuppression, or a recent dental or surgical intervention. In clinical examination, fever (90% of cases) and a heart murmur (about 75-85% detectable) are the significant findings of the disease (1). While fever rises with chills, usually at 39°C and above (5), symptoms of the heart murmur present as a change in an existing murmur or a new murmur. Most of the new murmurs develop heart failure, showing a poor prognosis. Peripheral findings in two-thirds of the patients are petechiae, splinter hemorrhage, Osler's nodules, Janeway lesions, Roth's stain on the retina, clubbing (not seen in acute diseases), and splenomegaly. Splenomegaly or skin findings (e.g., petechiae and splinter hemorrhage) may be supportive. Complications such as heart failure, stroke, and metastatic infections (e.g., vertebral osteomyelitis, peripheral abscess) are also common. Microembolic or immunological phenomena, splinter hemorrhage, conjunctival hemorrhage, Osler's nodes (distal vasculitic lesions of the fingers and toes), Janeway lesions (vasculitic lesions of the palms and soles), and Roth spots (hemorrhagic retinal lesions) are rare, occurring in 5% to 10% of cases (1,4). In general, any finding has low susceptibility and specificity, and the diagnosis should not be excluded based on only clinical examination.

LABORATORY FINDINGS

Routine laboratory tests may not be specific for endocarditis. Leukocytosis, increased inflammatory markers (erythrocyte sedimentation rate [ESR], C-reactive protein), and normocytic normochromic anemia (as anemia of chronic disease) may occur. ESR is elevated and can often be found at 100 mm/hr and above. Rheumatoid factor positivity can be detected as well as microscopic hematuria and sometimes erythrocyte cylinders or pyuria/proteinuria in urine examination. New-onset conduction disturbance (e.g., first-degree atrioventricular block, bundle branch block, or complete heart block) indicates the paravalvular or myocardial spread of infection, requiring an inpatient or intermittent ECG to be detected. Serum complement levels may decrease. Immune complexes are the cause of glomerulopathy (1,4,5).

DIAGNOSIS

Making the diagnosis of infective endocarditis requires evaluating all clinical findings, microbiological tests, and imaging results. The modified Duke clinical diagnostic criteria focus on three areas and address the findings as major or minor criteria (**Table 5**). The susceptibility of these criteria in infective endocarditis is approximately 80% in definite cases and becomes higher when considering suspected cases. Yet, they have low susceptibility in the case of prosthetic valve or cardiac device-related infections, right-sided endocarditis, and culture-negative infective endocarditis. The negative predictive value is about 90% when the criteria are not met in definitive or suspected infective endocarditis. A definitive pathological diagnosis can be made if organisms are identified in an intracardiac abscess or peripheral embolism in histological analysis or culture of vegetation and if the presence of vegetation or intracardiac abscess is confirmed by histological analysis indicating active endocarditis.

A blood culture is a significant microbiological test in the diagnosis and treatment of endocarditis and an important Duke criterion since antimicrobial therapy is highly dependent on blood culture isolates and their antimicrobial susceptibility. Almost all (90-95%) blood

cultures produce a positive result in native valve infective endocarditis. To maximize recovery, three separate sets of blood cultures 30 minutes apart are recommended prior to starting antibiotics. Blood culture-negative cases are caused by the recent use of antimicrobial agents or organisms growing poorly or not at all in standard blood cultures (e.g., *Bartonella* spp., *Coxiella burnetii*, *Tropheryma whippleii*, and *Legionella*). Yet, in the cases of negative blood cultures, serological and molecular testing should be performed, guided by nucleic acid amplification by PCR with specific primers for a particular species or genus or with broad-range primers targeting the 16S ribosomal RNA (rRNA) gene for bacterial pathogens or the 18S rRNA gene for fungal pathogens (e.g., C. burnetii may be associated with an exposure to livestock, while *Bartonella quintana* infection may be linked with homelessness). For PCR, the susceptibility ranges between 33% and 90%, while the specificity falls between 77% and 100%. An excised valve tissue or vegetation is preferred for molecular testing. Plasma DNA amplification tests can aid microbiological diagnosis against the difficulty in identifying pathogens.

Echocardiography is considered a prominent technique in the diagnosis, management, and monitoring of complications of infective endocarditis. In native valve infective endocarditis, while the susceptibility for vegetation detection ranges between 50% and 70% with transthoracic echocardiography (TTE), it is 90% or more with transesophageal echocardiography (TEE). TTE has low resolution and produces a susceptibility of 50% in prosthetic valve endocarditis. The specificities of these techniques, on the other hand, vary between 90% and 95%. TTE is less susceptible than TEE to detecting intracardiac complications (e.g., paravalvular abscess). TEE is often adopted in suspected patients to exclude infective endocarditis and evaluate intracardiac complications.

TTE yields a low susceptibility in the diagnosis of an intracardiac abscess; therefore, TEE should be performed in all endocarditis with suspected abscess requiring surgery. In addition, cardiac computed tomographic angiography provides visualization of paravalvular complications such as abscesses or aneurysms. It has potentially fewer artifacts from a prosthetic valve than TEE; yet, it is less susceptible than TEE in small-size vegetation.

The most common of the novel forms of imaging may be 18F-fluorodeoxyglucose (FDG) cardiac positron emission tomography (FDG-PET) or FDG/computed tomography (FGD-CT). FGD-CT becomes more suitable for the diagnosis and evaluation of prosthetic valve infective endocarditis; however, its role in native valve endocarditis remains veiled. Peripheral embolic, cardiac, and extracardiac infection sites can be detected using FDG-PET/CT (1,4).

Table 4. Modified Duke criteria for the diagnosis of infective endocarditis*

Definitive Infective Endocarditis
Pathological Criteria
Microorganisms demonstrated by culture or histological examination of vegetation, embolized vegetation, or an example of an intracardiac abscess OR
Pathological lesions; vegetation or intracardiac abscess showing active endocarditis confirmed by histological examination
Clinical Criteria
2 major criteria OR
1 major criterion and 3 minor criteria OR
5 minor criteria
Suspected Infective Endocarditis
1 major criterion and 1 minor criterion OR
3 minor criteria
Rejection;
definitive alternative diagnosis explaining evidence of infective endocarditis
endocarditis OR
antibiotic treatment of infective endocarditis syndrome
resolution within 4 or fewer days OR
No pathological evidence of infective endocarditis at the time of surgery or autopsy after 4 or fewer days of antibiotic therapy OR
Not meeting criteria for suspected infective endocarditis as above
Major Criteria
Blood Culture Positivity for Infective Endocarditis
Typical microorganisms for infective endocarditis from two separate blood cultures:
Viridans streptococci, *Streptococcus bovis* or HACEK (*Haemophilus* spp., *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella* spp.), *S. aureus*, or community-acquired enterococci, in the absence of a primary focus or
Microorganisms consistent with infective endocarditis from persistently positive blood cultures are identified as follows:
At least 2 positive cultures of blood samples after > 12 hours OR
All three or the majority of four or more separate blood cultures
(≥ 1-hour intervals between the first and last sampling)
Single positive blood culture for *Coxiella burnetti* or antiphase I IgG antibody titer greater than 1:800
Evidence of Endocardial Involvement
Echocardiogram positivity for infective endocarditis is defined as follows:
Intracardiac mass or abscess released on a valve or supporting structures, in the path of insufficient jet streams, or implanted material in the absence of an alternative anatomical explanation, or partial detachment of the prosthetic valve
New valve regurgitation (worsening or changing of a pre-existing murmur is not enough)
Minor Criteria
1. Susceptibility to heart disease, underlying heart disease, or intravenous drug addiction
2. Fever, temperature more than 38°C
3. Vascular phenomena: major arterial embolism, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway lesions
4. Immunological phenomena: glomerulonephritis
5. Microbiological evidence: Blood culture positivity that does not meet the above-mentioned major criteria a or serological evidence for active infection with microorganisms compatible with endocarditis

a Excludes single positive cultures for coagulase-negative staphylococci and organisms not causing infective endocarditis. (*) Adapted from (Wang A, Gaca JG, Chu VH. Management Considerations in Infective Endocarditis. JAMA. 2018;320(1):72-83.)

TREATMENT

Treatment of infective endocarditis requires a multidisciplinary approach by a team of infectious diseases specialists, cardiologists, and cardiovascular surgeons. Empirical antimicrobial therapy should be started immediately for possible causative agents as soon as blood cultures are obtained. The antimicrobial treatment regimen can be altered according to culture findings, resistance patterns, infection severity, and the presence of a prosthetic valve. In general, combination intravenous therapy is preferred over monotherapy to reduce the development of resistance and provide synergistic antimicrobial activity (1).

Principles of antibiotic therapy

1. Multidisciplinary approach: a collaboration of infectious diseases, cardiology, and cardiovascular surgery,
2. Microbiological diagnosis,
3. Should be started after taking three blood cultures in acute empirical cases,
4. The minimal inhibitory concentration (MIC) value of the isolated agent should be determined,
5. Bactericidal and IV antibiotics should be selected for the agent,
6. The focus of entry of the agent should be investigated (tooth abscess for *viridans streptococcus* and colon tumor for S.bovis)
7. Unless a clinical response, blood culture follow-up is performed.
8. Necessary diagnostic examinations (e.g., ECHO, cardiac CT) should be performed.
9. Patients should be informed about prophylaxis (5).

Antimicrobial therapy recommendations for infective endocarditis are based on observational research rather than randomized clinical trials and adopt four key principles: the regimen's ability to eliminate the pathogen, a prolonged course of treatment (i.e., weeks instead of days), intensive dosing to ensure adequate drug exposure, and source control. In general, ceftriaxone in combination with vancomycin is considered appropriate for empirical therapy in native valve infective endocarditis to cover possible pathogens while awaiting culture findings. Infective endocarditis caused by Viridans streptococci, *S. gallolyticus*, *Abiotrophia* spp., or *Granulicatella* spp., which are not susceptible to penicillin, can be treated with penicillin or a combination of ceftriaxone and gentamicin. Vancomycin monotherapy is also an option despite less experience.

Antibiotic therapy for *S. aureus* infective endocarditis is dependent on its antibiotic resistance. An antistaphylococcal beta-lactam (e.g., nafcillin) is recommended for the treatment of methicillin-susceptible *S. aureus* (MSSA), while vancomycin is recommended for methicillin-resistant *S. aureus* (MRSA). Daptomycin is an acceptable alternative; however, special attention is required for dosing. Guidelines of Infectious Diseases Society of America recommend daptomycin at doses of 8 to 10 mg/kg, while it is 10 mg/kg or above in European guidelines. Combination therapy (aminoglycoside and rifampin in combination with an antistaphylococcal beta-lactam or vancomycin) for prosthetic valves infected with *S. aureus*.

Daptomycin or vancomycin monotherapy is recommended in native valve endocarditis caused by MRSA. The benefit of combination therapy has not been proven yet.

While penicillin is recommended for the treatment of enterococcal infective endocarditis, ampicillin-gentamicin or ampicillin-ceftriaxone is recommended for the treatment of aminoglycoside-susceptible enterococcal infective endocarditis. Besides, ampicillin-ceftriaxone is recommended for ampicillin-susceptible and aminoglycoside-resistant enterococcal infective endocarditis. As stated in the guidelines, vancomycin can be adopted in return for ampicillin if the enterococcal strain is resistant to penicillin. If it is resistant to penicillin and vancomycin, linezolid or daptomycin can be used (4).

Candida and *Aspergillus* can cause fungal endocarditis, and the only fungicidal drug to be used in the treatment seems to be Amphotericin B. In fungal endocarditis, findings may demonstrate negative blood culture, large vegetation, large vessel embolism, and a metastatic infection; therefore, surgical intervention may be needed (5). **Table 5** summarizes antimicrobial therapy for the causative agent in infective endocarditis.

Table 5. Antimicrobial therapy for the causative agent in infective endocarditis *

Agent	Antibiotic
Penicilin-susceptible Viridans streptococci	Crystalline penicillin G + Gentamicin or Ceftriaxone (Vancomycin if allergic to penicillin)
Penicillin-susceptible enterococci	Crystalline Penicillin G + Gentamicin or Ampicillin + Gentamicin
Penicillin-resistant enterococci	Vancomycin + Gentamicin
Penicillin-resistant, glycopeptide-resistant enterococci	Daptomycin, Quinupristin/dalfopristin
MSSA in the natural valve	Antistaphylococcal Nafcillin or oxacillin + Gentamicin (Vancomycin if allergic to penicillin) - 4-6 weeks
MRSA in the natural valve	Vancomycin or Daptomycin IV
MSSA in the prosthetic valve	Nafcillin or oxacicillin + Gentamicin + Rifampicin - ≥ 6 weeks
MRSA in the prosthetic valve	Vancomycin + Rifampicin + Gentamicin - ≥6 weeks
MS-CNS in the prosthetic valve	Nafcillin or oxacillin + Gentamicin - 4-6 weeks
MR-CNS in the prosthetic valve	Vancomycin + Gentamycin + Rifampicin - ≥6 weeks

(*) Adapted from: İnkaya AÇ, Akova M. Enfektif endokardit, miyokardit, perikardit. Wilke AT, Söyletir G, Doğanay M. Enfeksiyon Hastalıkları ve Mikrobiyolojisi, 4. Baskı, Nobel Tıp Kitabevleri, İstanbul, 2017; 951-972.

SURGICAL TREATMENT

Indications for surgery in infective endocarditis are summarized in **Table 6**.

Table 6. Indications for early heart-valve surgery*

Heart failure
Refractory pulmonary edema or cardiogenic shock due to aortic-valve or mitral-valve dysfunction, obstruction, fistula, or shunt,
Aortic-inadequately compensated valve with hemodynamic function or mitral valve regurgitation or dysfunction,
Unmanaged infection,
Fungal endocarditis (ineffective treatment),
Multidrug-resistant pathogen,
A patient with blood cultures persistently positive for an antibiotic-susceptible pathogen despite adequate source control of other foci of infection, receiving appropriate antimicrobial therapy for 6 or 7 days,
Paravalvular complications (e.g., abscess),
Prevention of systemic embolization,
Aortic-valve or mitral-valve vegetation > 10 mm, especially when accompanied by ≥1 embolic events while the patient is receiving appropriate therapy.

Adapted from: Chambers HF, and Bayer AS.. Native-valve infective endocarditis. N Engl J Med 2020;383:567-76.

PROPHYLAXIS

Dental interventions are considered to be the primary source of bacteremia, requiring antimicrobial prophylaxis among patients at risk of developing infective endocarditis. **Table 7** lists dental procedures requiring prophylaxis for infective endocarditis.

Interventional Procedures Requiring Infective Endocarditis Prophylaxis

Dental interventions: Gingival tissue/oral mucosa perforation, periapical region manipulations

Prophylaxis is not recommended for bronchoscopy or laryngoscopy, endotracheal, or transnasal respiratory interventions.

Prophylaxis is not recommended for gastrointestinal or urogenital procedures.

Prophylaxis is not required for invasive airway procedures, incision or biopsy, or tonsillectomy and adenectomy procedures.

Prophylaxis is not recommended for gastrointestinal or urogenital procedures.

Oral hygiene is essential since certain oral hygiene habits (e.g., not brushing after meals) are associated with infective endocarditis due to oral streptococci.

The American Heart Association and the European Society of Cardiology recommend prophylaxis when dental procedures are performed in those with cardiac conditions that may result in the worst outcome when infective endocarditis develops.

However, antibiotic prophylaxis may be recommended in patients with prosthetic valves or other conditions at high risk for adverse outcomes. **Table 8** summarizes antibiotics (with doses) to be used in the prophylaxis of infective endocarditis.

In prophylaxis, it is essential to maintain adequate dental care and oral hygiene at the best possible level (7).

PROGNOSIS

Infective endocarditis is a fatal condition; in-hospital mortality in infective endocarditis is reported to be about 20% and about 30% at six months. Despite advances in health care, the rates have hardly changed in the last 20 years. Increased mortality is often due to epidemiological shifts in types of infective endocarditis (e.g., healthcare-associated infective endocarditis), greater numbers of older adult patients with significant comorbidities, and pathogens with higher antibiotic resistance. Host factors (e.g., age and hemodialysis), prosthetic valve involvement, infective endocarditis features (e.g., healthcare-associated), and complications (e.g., severe heart failure, stroke, and abscess) may be considered prognostic factors for poor outcomes resulting from infective endocarditis. Yet, early surgical intervention reduces mortality (1,2,4,6).

Table 7. Recommendations for dental procedures requiring infective endocarditis prophylaxis

Type of dental intervention	Class	Level of Evidence
In dental interventions of the gingival or periapical region of the tooth and perforations in the oral mucosa	IIa Prophylaxis recommended	C
Local anesthesia to uninfected tissue Dental radiography Suture removal Placement of removable dentures, orthodontic appliances, or braces	III Prophylaxis not recommended	C
Loss of baby teeth Following lip and oral mucosal traumas	III Prophylaxis not recommended	

Table 8. Antibiotics used in infective endocarditis prophylaxis

Indications	Presence of prosthetic valve, aortic stenosis, uncorrected VSD, congenital heart diseases (uncorrected cyanotic heart disease), patients with valve damage following heart transplant
Clinical Status	Antibiotic/Dose
Standard general prophylaxis	Amoxicillin 2 g - an hour before the intervention
Those with an inability of oral intake or problems with GIS absorption	Ampicillin 2 g intravenous - an hour before the intervention or ceftriaxone 1 g - an hour before the intervention
Penicillin allergy	Clindamycin 600 mg (oral) - an hour before the intervention or azithromycin 500 mg - an hour before the intervention or clarithromycin 500 mg - an hour before the intervention

CONCLUSION

Endocarditis is an infectious disease that still maintains its significance, brings a high mortality rate, and requires a multidisciplinary approach from infectious diseases, clinical microbiology, cardiology, and cardiovascular surgery. Its epidemiology and management have constantly been changing, and uncertainties still persist. The relevant guidelines provide specific recommendations for the management of infective endocarditis. When making treatment decisions, one needs to focus great attention on patient characteristics, type of pathogen, and risk of infective endocarditis sequelae.

ETHICAL DECLARATIONS

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