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Management of infectious endocarditis from the perspective of the Infectious Diseases specialist – a 2023 update

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ABSTRACT

An increase in the number and the complexity of cardiac surgery has brought on a rise in the proportion of healthcare-associated Infectious Endocarditis (IE), and as a result, today *S. aureus* is the most common causative pathogen for this condition.
Clinical suspicion for IE should be raised in front of a patient with predisposing risk factors, a new heart murmur and/or vasculitic/embolic events.
The Duke Criteria have been long used to diagnose IE. However, they underwent several changes in order to improve their sensitivity in the diagnosis of Q-fever IE and to decrease the size of the possible IE group.
Our primary goal is to enhance the knowledge regarding the diagnosis and treatment of infective endocarditis.
In acute IE, prior to beginning antibiotic therapy, at least three sets of blood cultures must be taken, ideally from three distinct sites, as determining the etiologic agent is of highest importance. The diagnosis of IE cannot be made based just on a single positive blood culture. To diagnose subacute IE, three to five sets of blood cultures must be drawn over the course of 24 hours.
Transthoracic echocardiography (TTE) remains the preferred investigation when the diagnosis of IE is suspected. Transoesophageal echocardiography (TOE) is recommended when TTE is unremarkable but the suspicion is still high. A whole-body CT scan, an MRI, a cardiac CT, PET-CT, or radiolabelled leucocyte single-photon emission computed tomography may be helpful when TTE and TOE are inconclusive.
Recommended empirical therapy for Native Valve Endocarditis (NVE) and late Prosthetic Valve Endocarditis (PVE) consists of IV Amoxicillin, Oxacillin and Gentamicin administered until blood culture results are available. If a patient is allergic to penicillin, IV Vancomycin and Gentamicin should be given.
The recommended empirical antibiotic regimen for early PVE includes IV Vancomycin, Gentamicin, and Rifampin.
Once the results of blood cultures are available, the treatment will depend on the isolated organism, its sensitivity to antibiotics, and whether it is an NVE or a PVE.

Keywords: febrile neutropenia, onco-hematologic patients, infections, chemoprophylaxis

INTRODUCTION. DEFINITIONS

Infection of the cardiac endothelium, known as infective endocarditis (IE), has an annual incidence of up to 12.7/100 000 and a mortality rate of up to 30% at 30 days. Over time, the epidemiology of IE has altered progressively, with a rise in the proportion of healthcare-associated IE (which now accounts for 25–30% of IE in recent studies). This is

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brought on by an increase in the number of cardiac surgeries and greater use of intravenous lines and intracardiac devices. Furthermore, in industrialized countries, we witness a drop in the number of post-rheumatic valvulopathies, so IE affects mainly young adults (IV drug abuse patients → IVDA IE) and older patients (maximum incidence between 70 and 80 years of age – mean age of patients – 60.8 years). More than half of the patients are above 50 [1,2,3].

Our primary goal is to enhance the knowledge regarding the diagnosis and treatment of IE. Additionally, we sought to compare the AHA (American Heart Association) and ESC (European Society of Cardiology) guidelines, which are the two major guidelines regarding the treatment of this condition.

ETIOLOGY OF INFECTIVE ENDOCARDITIS

Each type of IE has a different etiologic agent. The responsible microorganism relies on the entry site – dental (oral streptococci), cutaneous (staphylococci), urinary (enterococci) etc. Overall, today *S. aureus* infection is the most common cause of IE - IE complicates between 35.6 and 60.5% of staphylococcal bacteremia.

Native Valve Infective Endocarditis (NVE)

Streptococcus species, such as *S. viridans, Streptococcus gallolyticus* (ex. *S. bovis*), and enterococci, are responsible for over 70% of NVE cases. 25% of cases are brought on by Staphylococcus species, which typically have an acute course that is more aggressive [2].

Prosthetic Valve Endocarditis (PVE)

Early prosthetic valve endocarditis, which occurs during the first year after cardiac surgery, shows differently than late PVE, which manifests as a subacute condition comparable to NVE.

The organisms that are typically inferred when discussing early PVE are *S. aureus* and *S. epidermidis*, both of which are frequently methicillin-resistant (e.g., MRSA). Streptococci are the most frequent cause of late illness. In general, CoNS account for 30% of PVE cases[2].

Intravenous Drug Abuse Infective Endocarditis (IVDA IE)

In individuals with IVDA IE, *Staphylococcus aureus* is the most frequent etiologic organism (MRSA accounting for many of the cases, mainly in patients with prior hospitalizations, long-term use of IVD, and non-prescribed antibiotic use. Groups A, C, and G streptococci and enterococci also are recovered from patients with IVDA IE.

Gram-negative organisms are rarely implicated – members of the HACEK family and *Pseudomonas aeruginosa* are the most often isolated etiologic agents [2].

Nosocomial/healthcare-associated infective endocarditis

Endocarditis can occur because of medical procedures involving intravascular devices, including hemodialysis shunts and catheters, chemotherapeutic and hyperalimentation lines, central or peripheral intravenous catheters, and rhythm control devices implantation, such as pacemakers and defibrillators. The most prevalent pathogens are gram-positive cocci, such as *S. aureus*, CoNS, enterococci, and non-enterococcal streptococci [2].

Fungal endocarditis

Patients using broad-spectrum antibiotics in intensive care units and IV drug users have the greatest risk of fungal endocarditis. Unfortunately, blood cultures typically yield negative results [2].

Blood cultures are negative in 5–10% of IE cases, and the etiologic agent cannot be determined without the use of serologic testing or genetic amplification assays on bioptic tissue *(Coxiella burnetii, Bartonella spp.).*

The entrance site determines the etiologic agent (Table 1). The entry point cannot be identified in roughly half of the cases. An infection site, whether active or latent, or an intervention that results in bacteraemia can serve as the entry point [3].

TABLE 1. Etiologic agents according to the entry site [4]

Entry site	Involved organisms
Dental (Chronic infectious foci, dental avulsions, oral surgical procedures, scaling)	Oral streptococci, HACEK group
Cutaneous (furuncles, burns, dermatitis, infected wounds, IV drug abuse)	Staphylococci
Urinary (UTIs)	Enterococci, *Str. gallolyticus*
Digestive (tumors, diverticulosis, surgery) **! Colonoscopy is mandatory in *Str. gallolyticus* IE**	Enterococci, *Str. gallolyticus*
Intravenous catheters	Staphylococci, fungi

RISK FACTORS FOR INFECTIVE ENDOCARDITIS

Regardless of the type of IE, two conditions must exist for IE to occur: one that allows the microorganism to enter the bloodstream and another that enables the organism to set place in the cardiac endothelium. We already covered the etiologic agents and their different sites of entry, so next we will

point out the conditions that predispose the patient to IE.

Remaining endocarditis-related valve damage from an earlier episode is the main risk factor for IE [3].

Almost half of **NVE** cases occur in apparently healthy individuals, who do not know of any previous heart condition. The most common precursors of NVE are valvulopathies, whether congenital, atheromatous, or degenerative, with valvular regurgitation and mitral valve prolapse with an associated murmur being more frequently implicated than stenosis. Compared to mitral valve disease, aortic valve disease is more prevalent. Other risk factors for IE include congenital heart defects such as tetralogy of Fallot, ventricular septal defect, patent ductus arteriosus, and aortic bicuspid valve. Atrial septal defect is not considered a risk factor for IE.

The risk of developing IE in patients with a valvular prosthesis is 1000 times greater than in the general population. Early **PVE** is more frequently the consequence of perioperative inoculation, especially if it occurs in the first few months after the procedure. However, the risk of developing IE persists for a long time after the intervention [3].

Aging, diabetes mellitus, the use of anticoagulants or steroids, and other risk factors have all been mentioned as potential causes of pacemaker IE. Surgery on any element of the pacemaker system, especially elective battery replacements, is probably the biggest risk factor. Infection rates related to battery replacements are around five times higher than those of initial implantation (6.5% vs. 1.4%).

A postoperative hematoma, an inexperienced surgeon, and a previous temporary transvenous pacing are some other important risk factors for pacemaker IE [2].

CLINICAL PRESENTATION OF INFECTIVE ENDOCARDITIS

Almost all of the patients experience fever, nocturnal diaphoresis, fatigue, loss of weight, and loss of appetite. At presentation, 25% of patients already have an embolic complication.

Clinical suspicion for IE should be raised in front of a patient with predisposing risk factors (listed above), a new heart murmur, and/or vasculitic/embolic events [3].

IE can present as an acute or subacute condition.

Acute IE is characterized by rapid (within days) development of symptoms, including high fever, chills, heart failure, splenomegaly, lumbar pains, arthralgias, and systemic complications, including stroke.

With *subacute IE*, the symptoms develop more slowly (over weeks or months) and include fatigue, difficulty breathing, weight loss, and sometimes fever. On average, six weeks pass between the time of the disease's onset and its diagnosis.

A new heart murmur, although highly suggestive of IE, is present in less than half of the patients [4]. Underlying cardiac disease may present with signs of congestive heart failure brought on by valvular regurgitation. Back pain brought on by spinal osteomyelitis or focal neurologic symptoms from an embolic stroke are examples of secondary phenomena.

People who use intravenous drugs frequently complain of dyspnea, coughing, and chest pain. This is because this group has a high prevalence of tricuspid valve endocarditis with secondary embolic showering of the pulmonary vasculature [2].

Clinical signs and complications of IE will be synthesized in Table 2.

TABLE 2. Clinical signs and complications of IE [5]

Clinical signs	Prevalence %
Fever	86-96
New heart murmur	48
Worsening/change of a known heart murmur	20
Hematuria	26
Embolic events	17
Splenomegaly	11
Splinter hemorrhages	8
Osler nodules	3
Janeway lesions	5
Roth spots	2
Complications	**Prevalence %**
Stroke	17-20
Embolic events (other than stroke)	23-33
Cardiac failure	14-33
Intracardiac abscess	14-20
New conduction abnormality	8

DIAGNOSIS OF INFECTIVE ENDOCARDITIS

1. Modified Duke criteria (Table 3)

The sensitivity of Duke criteria is typically 80%. Their sensitivity in PVE or implanted device endocarditis is significantly reduced. CT and cerebral MRI may be helpful in such circumstances [3].

2. Microbiological diagnosis

In acute IE, prior to beginning antibiotic therapy, at least three sets of blood cultures must be taken, ideally from three distinct sites, as determining the etiologic agent is of the highest importance. One set of blood cultures consists of two tubes: one for aerobic and one for anaerobic bacteria. 10 ml of blood should be collected in each tube. The first and third blood cultures must be prelevated one hour apart. The diagnosis of IE cannot be made based just on a single positive blood culture [3].

To diagnose subacute IE, three to five sets of blood cultures must be drawn over the course of 24 hours [2].

TABLE 3. Modified Duke criteria [4]

MAJOR CRITERIA
1. Positive blood cultures
Typical microorganisms consistent with IE from two separate blood cultures: • Oral streptococci, *Streptococcus gallolyticus* (previously known as *Str. bovis*), HACEK group, *Staphylococcus aureus* • Community-acquired enterococci, in the absence of a primary infectious focus
Positive blood cultures with an etiologic agent that might cause IE: • At least two positive blood cultures drawn at least 12 h apart *or* • Three blood cultures out of three or the majority of blood cultures are positive (if there were more than 4 drawn), the first and the last samples being drawn at least 1h apart *or* • One positive blood culture with *Coxiella burnetii* or phase I IgG antibody titre >1:800
2. Imagistic evidence of endocardial injury
Echocardiography showing lesions that are compatible with IE: • Vegetation (floating mass attached to a valve/subvalvular structure) • Perivalvular abscess • Valvular perforation • Intracardiac aneurysm or pseudoaneurysm • New partial dehiscence of a prosthetic valve
Abnormal activity around the site of a prosthetic valve detected by 18F-FDG PET/CT (only if >3 months after surgery) or **radiolabelled leucocyte-SPECT/CT**
Paravalvular lesions identified by **cardiac CT**
MINOR CRITERIA
1. Predisposing factors present: cardiac conditions associated with high risk of IE, IV drug consumption
2. Fever (T >38°)
3. Vascular events: major arterial septic emboli, pulmonary infarcts, mycotic aneurysms, intracranial hemorrhage, conjunctival hemorrhage, Janeway lesions, vascular abnormality identified by imaging
4. Immunologic phenomena: glomerulonephritis, Osler nodules, Roth spots, positive rheumatoid factor
5. Microbiological evidence: positive blood cultures that do not meet the mentioned above major criteria, or serological evidence of an infection with organism consistent with IE (other than *C. burnetii*)
DEFINITE IE
Histopathologic criteria • Microorganism isolated from cultures or histopathologic examination of a vegetation/intracardiac abscess • Intracardiac vegetation or abscess with histopathologic aspect compatible with 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 2 minor criteria or • 3 minor criteria
REJECTED IE
• Alternative diagnosis explaining the clinical signs or • Resolution of clinical manifestations in the absence or with antibiotic therapy that lasts 4 days or fewer or • Absence of histological evidence of endocarditis in case of surgery/autopsy, in the absence or with antibiotic therapy that lasts 4 days or fewer

If blood cultures show no growth and the clinical suspicion of IE is still high, additional serological, molecular biology, and histopathologic tests should be carried out. This is especially important if the patient hasn't previously been exposed to antibiotics. Since multiplex PCR from blood has limited sensitivity, it is not recommended [3,5].

Diagnostic tests used in culture negative endocarditis are shown in Table 4.

TABLE 4. Diagnostic tests used in culture negative endocarditis [5]

Diagnostic test	Etiologic agent	Comments
Serologic tests	*Coxiella burnetii* *Bartonella spp.* *Chlamydophila spp.* *Brucella spp.* *Mycoplasma spp.* *Legionella pneumophila* *Aspergillus spp.*	Serology particularly useful in *C. burnetii* and *Bartonella* IE **NB!** Many cross reactions between *Bartonella* and *Chlamydophila*
Histopathology of resected valvular tissue	*Bartonella spp.* *Tropheryma whipplei* *Coxiella burnetii* Fungi *(Candida spp., Aspergillus spp.)*	HP also useful in case of IE caused by streptococci or staphylococci, if blood cultures were negative due to preexposure to antibiotics
PCR tests from valvular tissue	*Bartonella spp.* *Tropheryma whipplei* *Coxiella burnetii* Fungi *(Candida spp., Aspergillus spp.)*	HP also useful in case of IE caused by streptococci or staphylococci, if blood cultures were negative due to preexposure to antibiotics

3. Cardiac imaging

Transthoracic echocardiography (TTE) is essential when the diagnosis of IE is suspected. Transoesophageal echocardiography (TOE) is recommended when TTE is unremarkable but the suspicion is still high. A whole-body CT scan, an MRI, a cardiac CT, PET-CT, or radiolabelled leucocyte single-photon emission computed tomography may be helpful when TTE and TOE are inconclusive [4].

Cardiac CT scans can provide important information about perivalvular lesions, playing an important role in the diagnosis of PVE and intracardiac device endocarditis.

When echocardiography is unclear and there is a high clinical suspicion of PVE, a PET-CT may become useful.

Depending on the clinical presentation, the following tests may help diagnose complications: ECG, thoracic X-ray, serum creatinine levels, whole body CT, and brain MRI. Before cardiovascular surgery, cerebral imaging must be systematically undertaken [4].

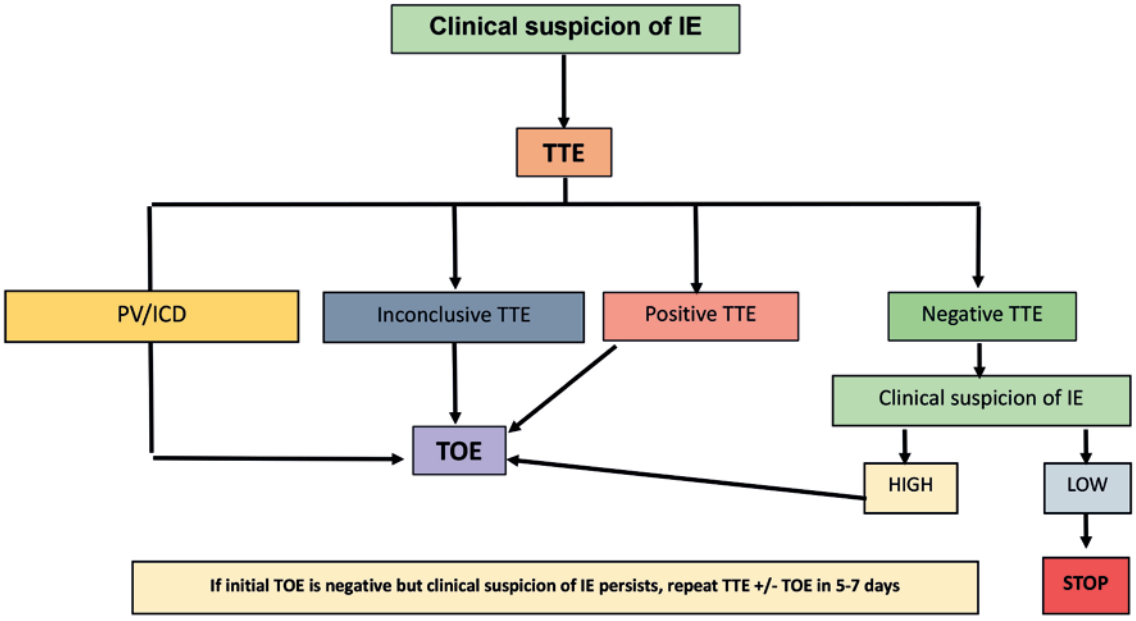

FIGURE 1. Indications for echocardiography in suspected infective endocarditis. Adapted from *Eur Heart J,* Volume 36, Issue 44, 21 November 2015, Pages 3075–3128, https://doi.org/10.1093/eurheartj/ehv319
TTE = transthoracic endoscopy; PV = prosthetic valve; ICD = intracardiac device; TOE = transoesophagean endoscopy.

TREATMENT OF INFECTIVE ENDOCARDITIS

Antibiotic therapy must be initiated after at least three sets of blood cultures are prelevated. In cases of sepsis or septic shock and when there is an urgent need for cardiac surgery, this restriction is disregarded. In all other situations, microbiological evidence must be provided in order to adjust antibiotic treatment plans following the results [4].

1. Empirical therapy in Infective Endocarditis

Recommended regimens for NVE and late PVE are IV Amoxicillin plus Oxacillin plus Gentamicin administered until blood culture results are available. If a patient is allergic to penicillin, IV Vancomycin and Gentamicin should be given.

The recommended antibiotic regimen for early PVE includes IV Vancomycin, Gentamicin, and Rifampin [4]. Posology is presented in Table 5.

TABLE 5. Empirical therapy in IE [4]

Antibiotic	Treatment plan	Comments
NVE		
Amoxicillin + Oxacillin + Gentamicin	200mg/kg/24h IV 200mg/kg/24h IV 3mg/kg/24h IV	If blood cultures remain negative, treatment plan must be indicated by an ID specialist
Vancomycin + Gentamicin	30-40mg/kg/24h IV 3mg/kg/24h IV	In case of penicillin allergy
Early PVE (less than 12 months after implantation of valve)		
Vancomycin + Gentamicin + Rifampin	30-40mg/kg/24h IV 3mg/kg/24h IV 15mg/kg/24h IV	A specialized medical team will be consulted to adjust the antibiotic medication and determine whether surgery is required if the treatment response is unfavourable
Late PVE (more than 12 months after implantation of valve)		
Identical treatment plan as NVE		

2. Pathogen-specific therapy

The isolated bacteria and its susceptibility to antibiotics are key factors in IE treatment. Whether it is NVE or PVE also affects how long the treatment will last. There is little variation in recommended regimens for common organisms in published guidelines [6].

Streptococcal Infective Endocarditis

Both European and American guidelines recommend a beta-lactam antibiotic (Penicillin G/Amoxicillin/Ampicillin/Ceftriaxone) in combination with Gentamicin when treating streptococcal IE caused by *S. viridans/gallolyticus* (CMI <0.12 mg/L to Penicillin). It takes two weeks to treat NVE with Gentamycin and a beta-lactam antibiotic, four weeks to treat NVE with a beta-lactam antibiotic alone, and six weeks to treat PVE or complicated NVE. Extracardiac involvement, a diagnosis made >3 months after the onset, and a need for surgery are all indicators of complicated NVE.

The regimens are the same for *S. viridans/gallolyticus* with a CMI >0.12 mg/L to Penicillin; the only differences are in the posology (higher doses of Penicillin/Amoxicillin), and the addition of gentamycin is not optional in this case.

The suggested treatments in cases of beta-lactam allergy include Vancomycin/Teicoplanin with or without Gentamicin. The course of treatment is the same length.

TABLE 6. Streptococcal IE treatment [4,7]

	ESC guidelines	AHA guidelines
CMI <0.12 mg/L streptococci	**Penicillin G** (12-18MU/24h) or **Amoxicillin** (100-200mg/kg/24h) or **Ceftriaxone** (2 g/24h) **+/- Gentamicin** (3mg/kg/24h) 2 weeks Gentamicin + BL or 4 weeks BL monotherapy (uncomplicated NVE) 4-6 weeks BL monotherapy (PVE or complicated NVE)	**Penicillin G** (12-18MU/24h in NVE 24MU/24h in PVE) or **Ampicillin** (12g/24h) or **Ceftriaxone** (2g/24h) **+/- Gentamicin** (3mg/kg/24h) 2 weeks Gentamicin + BL or 4 weeks BL monotherapy (NVE) 2 weeks Gentamicin + BL + 4 weeks BL monotherapy (PVE)
CMI >0.12 mg/L streptococci	**Penicillin G** (24MU/24h) or **Amoxicillin** (200mg/kg/24h) *PLUS* **Gentamicin** (3mg/kg/24h) 2 weeks Gentamicin + BL + 4-6 weeks BL monotherapy (NVE/PVE or complicated NVE)	**Penicillin G** (24 MU/24 h) or **Ampicillin** (12 g/24h) or **Ceftriaxone** (2 g/24 h) *PLUS* **Gentamicin** (3 mg/kg/24 h) 2 weeks Gentamicin + BL + 2-4 weeks BL monotherapy (NVE/PVE)
Beta-lactam allery	**Vancomycin** (30mg/kg/24h) or **Teicoplanin** (6mg/kg/24h) **+/- Gentamicin** (3mg/kg/24h) 2 weeks Gentamicin + GP (uncomplicated NVE) or 4 weeks GP monotherapy (uncomplicated NVE) 2 weeks Gentamicin + GP + 2-4 weeks GP monotherapy (PVE/complicated NVE)	**Vancomycin** (30 mg/kg/24h) 4 weeks GP monotherapy (NVE) 6 weeks GP monotherapy (PVE)

Staphylococcal Infective Endocarditis

TABLE 7. Staphylococcal IE treatment [4]

Type of IE	Bacteria	No penicillin allergy		Penicillin allergy		Duration
		Antibiotic	Posology	Antibiotic	Posology	
NVE	MSSA	**Oxacillin**[1]	200 mg/kg/24h	**Vancomycin**	30 mg/kg/24h	4-6 weeks
	MRSA	**Vancomycin or Daptomycin**	30 mg/kg/24h 10 mg/kg/24h	**Vancomycin or Daptomycin**	30 mg/kg/24h 10 mg/kg/24h	4-6 weeks 4-6 weeks
PVE	MSSA	**Oxacillin**[1] + **Gentamicin**[2] + **Rifampin**	200 mg/kg/24h 3 mg/kg/24h 15 mg/kg/24h	**Vancomycin**[1] + **Gentamicin**[2] + **Rifampin**	30 mg/kg/24h 3 mg/kg/24h 15 mg/kg/24h	≥ 6 weeks (gentamicin only 2 weeks)
	MRSA	**Vancomycin or Daptomycin** + **Gentamicin**[2] + **Rifampin**[3]	30mg/kg/24h 10mg/kg/24h 3mg/kg/24h 15mg/kg/24h	**Vancomycin or Daptomycin** + **Gentamicin**[2] + **Rifampin**	30 mg/kg/24h 10mg/kg/24h 3mg/kg/24h 15mg/kg/24h	≥ 6 weeks (gentamicin only 2 weeks)

[1] alternative: cefazolin 100mg/kg/24h divided in 3 doses or 30mg/kg loading dose with a duration of 1h, then 100mg/kg/24h in continuous infusion

[2] will be excluded if the strain is gentamicin resistant

[3] if the strain is rifampin resistant, the addition of one or two antibiotics will be taken into consideration, based on the antibiogram results

Enterococcal Infective Endocarditis

As is the case with Streptococcus and Staphylococcus spp, it is important to know whether Enterococci are sensitive or resistant to beta-lactams.

The suggested regimens for beta-lactam-sensitive strains include Amoxicillin (200mg/kg/24h) in combination with gentamicin (3mg/kg/24h) for 4-6 weeks (gentamicin only for 2 weeks). The recommended antibiotics for individuals who are allergic to beta-lactams are vancomycin (30mg/kg/24h) or teicoplanin (6mg/kg/24h) in combination with gentamicin, with the same therapy period. For gentamicin resistant, beta-lactam-sensitive strains, amoxicillin is associated with ceftriaxone 2g bid – for patients who are allergic to penicillins, vancomycin or teicoplanin are preferred, in monotherapy, and the course of treatment is longer than 6 weeks [4].

For beta-lactam and gentamicin-sensitive strains, AHA (American Heart Association) additionally recommends penicillin G (18-30MU/24h). For NVE, the course of treatment lasts 4 to 6 weeks; for PVE, it lasts longer than 3 months. For gentamicin-resistant strains, AHA (American Heart Association) recommends in addition to what was written above, penicillin G (18-30 MU/24h) plus streptomycin 15mg/kg/24h divided in two doses. For penicillin-resistant, gentamicin and vancomycin-sensitive strains, the preferred regimens are vancomycin (30mg/kg/24h divided in two doses) plus gentamicin (3mg/kg/24h) for 6 weeks. Last but not least, for penicillin, gentamicin and vancomycin resistant strains, IV Linezolid (600mg bid) or daptomycin (10-12 mg/kg/dose) are preferred, for more than 6 weeks, with monitorisation of CBC [4].

HACEK group Infective Endocarditis

AHA (American Heart Association) recommends ceftriaxone (2g/day) or ampicillin (2g every 4h) or ciprofloxacin (1g/24h PO or 800 mg/24h IV divided in two doses) – the duration of treatment is 4 weeks for NVE and 6 weeks for PVE [6].

Culture negative Infective Endocarditis with identification of the etiologic agent (Table 8)

3. Infective Endocarditis prophylaxis

Today, IE prophylaxis is based on four principles:

- Evidence that IE antibiotic prophylaxis is effective is insufficient to account for the widespread use of antibiotics for this purpose;
- Antibiotic prophylaxis must be limited only to **high-risk patients** (patients with a high risk of acquiring iE/post IE complications);
- Antibiotic prophylaxis must be limited only to **high-risk procedures**, that are known to cause bacteremia with germs usually incriminated in IE;
- Maintaining good oral hygiene is probably as efficacious as antibiotic prophylaxis.

High-risk cardiopathies for which antibiotic prophylaxis is recommended in case of high-risk procedures are the following:

- Patients with prosthetic heart valves;
- Patients with a history of IE;
- Patients with unrepaired cyanogenic congenital heart defects or residual shunt.

TABLE 8. Culture negative IE with identification of etiologic agent [4]

Pathogen	Therapy	Comments
Coxiella burnetii	**Doxycycline** 200mg/24h, PO + **Hydroxychloroquine** 600mg/24h PO Alternative (if hydroxychloroquine CI): **Doxycycline** 200mg/24h, PO + **Ofloxacin** 400mg/12h PO	Duration of treatment – minimum 18 months for NVE and 24 months for PVE. The main objective of treatment is the lowering with 2 dilutions of the phase I IgA and IgG antibody titer after one year and the disparition of phase II IgM antibodies after one year
Bartonella	**Ceftriaxone** 2g/24h IV or **Amoxicillin** 200 mg/kg/24h[1] IV or **Doxycycline** 200mg/24h PO + **Gentamicin** 3 mg/kg/24h IV	Duration of treatment is 6 weeks (Gentamicin only for 3 weeks)
Tropheryma whipplei	**Doxycycline** 200mg/24h, PO + **Hydroxychloroquine** 600mg/day PO	Optimal duration of treatment not known (>12 months)
Brucella	**Doxycycline** 200mg/24h, PO + **Trimethoprim-Sulfamethoxazole** 800/160mg/12h PO + **Rifampin** 10mg/kg/12h PO	Minimum duration of treatment – 3 months Treatment objective is a lowering of antibody titer below 60

CI = contraindicated

For other valve defects or congenital heart defects antibiotic prophylaxis in case of high-risk procedures is not recommended.

High-risk procedures for which antibiotic prophylaxis is recommended in case they are done on IE high-risk patients are the following: dental extractions, subgingival scaling, manipulation of the gingival tissue, periapical region of teeth, or the oral mucosa.

Antibiotic prophylaxis is not recommended in: anesthetic injections in uninfected tissue, suture ablation, retroalveolar X-ray, implantation or adjustment of orthodontic devices or detachable prostheses, or dental or gingival trauma.

Also, antibiotic prophylaxis is not recommended in case of procedures undertaken on the respiratory tract, such as: laryngoscopy, bronchoscopy, endotracheal intubation, nor in case of gastroscopy, TOE, colonoscopy, cystoscopy [4,8].

Recommendations on prophylaxis before abscess incision and drainage are not yet clarified. According to research, simple abscesses seldom cause bacteremia after being punctured and drained. However, MRSA, which is usually implicated in IE, is the pathogen most frequently responsible for oral abscesses. For patients with high-risk conditions undergoing routine incision and drainage of a simple abscess, it is prudent to administer clindamycin (600 mg IM/IV) or vancomycin (20 mg/kg) 30 to 60 minutes before to the procedure [9].

TABLE 9. Antibiotic prophylaxis in IE [4]

Beta-lactam allergy	Antibiotic	Posology One dose administered 1-2 hours before the procedure
No beta-lactam allergy	Amoxicillin PO/IV	Adult: 2g Children: 50-75 mg/kg
Beta-lactam allergy	Clindamicin PO/IV	Adult: 600mg Children: 15-20 mg/kg

4. Anticoagulant therapy

Anticoagulant and antiaggregant treatment are contraindicated in IE because they increase the risk of bleeding (particularly in the CNS) while having no effect on stroke risk. If IE affects a person who is currently receiving anticoagulant therapy, the therapy should only be continued if it is absolutely necessary (for example, in the case of patients who have mechanical valvular prostheses). Unfractionated heparin can be used as an alternative to oral anticoagulant treatment for two weeks if necessary [4,10].

CONCLUSIONS

Infective endocarditis, although uncommon, can be a life-threatening illness. The epidemiology and microbiology of this condition have undergone significant changes in recent decades. Despite improvements in diagnosis and treatment, mortality rates remain high.

The clinical manifestations of infective endocarditis often involve multiple body systems, leading individuals to seek initial care from various medical professionals who may have varying levels of knowledge about the disease. However, given the prognostic implications, early and accurate diagnosis is crucial. Treatment guidelines have remained relatively stable over the past decade.

The issue of antibiotic prophylaxis for high-risk individuals undergoing dental procedures in relation to infective endocarditis is controversial, and further research is needed to establish a consensus.

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