# INFECTIVE ENDOCARDITIS: WHAT IS CHANGED IN EPIDEMIOLOGY AND PROPHYLAXIS

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*[L'endocardite infettiva: cosa è cambiato nella epidemiologia e nella profilassi]*

**ABSTRACT**

This article shows the most recent opinions in the literature, concerning the epidemiology and prophylaxis of infective endocarditis (I.E.). They are also defined the basic principles of the previous guidelines and the reasons for their comprehensive reformulation. The article finally illustrates the new recommendations for prophylaxis of IE.

**Key words:** Infective Endocarditis (I.E.), Epidemiology (I.E.), Prophylaxis (I.E.), Guidelines (I.E.)

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## Introduction

Infective endocarditis (IE) is a not very common disease but still, at present, with high morbidity and mortality, which consists in the infection of the endocardial surface of the heart, including large intra thoracic vessels, native heart valves, prosthetic valves, most often on the left side, less frequently (10 to 20% of cases) on right heart or endocardial leads, caused predominantly by streptococcus, staphylococcus or other bacteria, less commonly by fungi. It causes fever, heart murmurs, petechiae, anemia, embolic phenomena, and endocardial vegetations. Vegetations may result in valvular incompetence or obstruction, myocardial abscess, or mycotic aneurysm. Diagnosis requires demonstration of microorganisms in blood and usually echocardiography. Treatment consists of prolonged antimicrobial treatment and sometimes surgery.

## Epidemiology

Epidemiology of infective endocarditis (IE) is continuously changing in the last decades, with new high risk patients and new microorganisms, with more intracardiac device infections, with intravenous (IV) drug abusers, and increasing nosocomial infections. IE can occur at any age. Men are affected about twice as often than women. IV drug abusers and immunocompromised patients are at highest risk[1-3].

The incidence of IE varies from 3 to 10 episodes/100.000 persons/year and mortality reaches 20% in the last 30 years. Moreover, despite advances in diagnosis and treatment, incidence and mortality of the disease did not decreased[1-3].

Furthermore the epidemiological profile profoundly changed. The mean age of patients with IE has gradually increased in the antibiotic era.

While in the past IE struck young adults with predominantly rheumatic valvular disease, it has become at present a disease that affects patients in more advanced age, often after therapeutic procedures, medical or nursing (introduction and manipulation of venous catheters, IV therapy, hemodialysis, chemotherapy, etc.), or carriers of prosthetic valves, or valvular diseases not previously known[3-5].

Moreover IE is more frequent in debilitated, diabetic, uremic patients and alcoholics. In the latest case studies, the incidence is low among young people, increases with age, and reaches a peak incidence of 14.5 episodes/100.000 patients per year between 70-80 years of age[3-5].

Many factors are related to this shift in age distribution: the age of the population has been increasing steadily; people with rheumatic or congenital heart disease are surviving longer; increased incidence of IE on degenerative valvular disease in the elderly; more frequent prosthetic valve surgery; new at-risk groups has emerged, including IV drug users, patients with intracardiac devices, and those exposed to health care associated bacteroemia (e.g., intravenous catheters)[3-5].

Male sex appears to be more frequent involved than female in all epidemiological studies, with a male/female ratio that can exceed 2:1 with a range of 1 to 3:1 in 18 large series. Despite increased male incidence, female are prone to a worse prognosis[6].

Given the complexity of therapy and poor prognosis of IE, for over 50 years have been developed, by international scientific societies, protocols and guidelines for prevention. During this period of time the guidelines have undergone a long evolutionary process, while remaining based on experts opinions, because of the low incidence of the disease, the absence of randomized trials and for the limited number of meta-analysis[7]. Since 2006, with the publication of the guidelines of the British Society for Antimicrobial Chemotherapy (BSAC), and later the American Heart Association (AHA) in 2007, the National Institute for Health and Clinical Excellence (NICE) in 2008 and of the European Society of Cardiology (ESC) in 2009, the recommendations on prophylaxis of IE have undergone a radical change[8-11].

## Etio-pathogenesis of infective endocarditis

The normal heart is relatively resistant to infection. Bacteria and fungi do not easily adhere to the endocardial surface, and constant blood flow helps prevent them from settling on endocardial structures. Thus, *two factors* are generally required for endocarditis: *endocardial factors*, consisting in a predisposing abnormality of the endocardium, and *microorganisms in the bloodstream* (*bacteroemia*)[1,2]. Rarely, massive bacteroemia or particularly virulent *microorganisms* cause endocarditis on normal valves[1,2].

*Endocardial factors*: Endocarditis usually involves the heart valves. Major predisposing factors are congenital heart defects, rheumatic valvular disease, bicuspid or calcified aortic valves, mitral valve prolapse, and hypertrophic cardiomyopathy. Prosthetic valves are a particular risk. Occasionally, mural thrombi, ventricular-septal defects, and patent ductus arteriosus sites become infected. The actual nidus for infection is usually a sterile fibrin-platelet vegetation formed when damaged endothelial cells (shear stress) release tissue factor. Infective endocarditis occurs most often on the left side (i.e., mitral or aortic valve). About 10 to 20% of cases are right-sided (tricuspid or pulmonic valve). IV drug abusers have a much higher incidence of right-sided endocarditis (about 30 to 70%)[1,2].

*Microorganisms*: Microorganisms that infect the endocardium may reach heart structures, through a bacteraemia, from distant infected sites (i.e., cutaneous or oral abscess or infection as pyoderma, stomatitis, inflamed or infected gums, urinary tract infections) or have obvious portals of entry such as a central venous catheter or a drug injection site. Almost any implanted foreign material (i.e., ventricular or peritoneal shunt, prosthetic device) is at risk of bacterial colonization, thus becoming a source of bacteroemia and hence endocarditis. Endocarditis also may result from asymptomatic bacteroemia, such as typically occurs during invasive dental, medical, or surgical procedures. Even tooth brushing and chewing can cause bacteroemia (usually due to Viridans Streptococci) in patients with gingivitis. Also trauma to the mucous membranes (oral, gastrointestinal, urethral, etc..) can cause transient bacteraemia. Causative microorganisms vary by site of infection, source of bacteroemia, and host risk factors (i.e., IV drug abuse), but overall, Streptococci and Staphylococcus Aureus cause 80 to 90% of cases. Enterococci, gram-negative bacilli, HACEK organisms (Haemophilus spp, Aggregatibacter Actinomycetemcomitans, Cardiobacterium

Hominis, Eikenella Corrodens, and Kingella Kingae), and fungi cause most of the rest. Why streptococci and staphylococci frequently adhere to vegetations and why gram-negative aerobic bacilli seldom adhere is unclear. However, the ability of Staphylococcus Aureus to adhere to fibronectin may play a role, as may dextran production by Viridans Streptococci. After colonizing of vegetations, the microorganisms are covered by a layer of fibrin and platelets, which prevents access by neutrophils, Ig, and complement and thus blocks host defenses[1,2].

The pathogenesis of IE is a complex interaction between the pathogen circulating in the blood stream with the matrix and platelets at the site of endocardial cell damage. Many clinical manifestations result from the host's immune response to the infecting organism.

The sequence of events that leads with IE includes:

1) formation of thrombotic not-bacterial endocarditis (TNBE) on valves surface or damaged endothelium in other areas of the heart,

2) bacteremia,

3) adhesion of bacteria circulating to TNBE,

4) proliferation of bacteria in the vegetation[1,2].

Generally the endocardial damage occurs when a current of blood very rapidly passes from an high pressure chamber (ventricle), to a low pressure chamber (atrium), because of a pressure gradient, as in some congenital heart diseases or through a restricted orifice (i.e., a stenotic valve). In both conditions there is the formation of a turbulent blood flow causing, on close endocardial surfaces, the augmentation of the endothelial *shear stress*[1,2]. This condition predisposes the endothelial surface to the deposition of platelets and fibrin, which favors the TNBE. Moreover immediately downstream of the orifice, there is the decrease in lateral blood pressure (Venturi effect) and, consequently, decrease endocardium nutrition. The flow, here, favors both the endocardial damage that the deposition of germs. Another area affected by hemodynamic stress is the margin of valve closure[1,2].

Different bacterial species can adhere to the endothelium through specific mediators that act as virulence factors in the pathogenesis of IE. This is the *Fim A protein* of some groups of *Streptococcus Viridans* which acts as adhesin for the matrix of fibrin and platelets of TNBE, and staphylococcal adhesins for proteins of the extracellular matrix, with possible formation of *biofilms* also of implantable medical devices. The use of vaccines against these adhesins showed protective effects of experimental endocarditis and offers interesting perspectives for their use in humans[12].The microorganisms that adhere to vegetations stimulate further deposition of fibrin and platelets on the surface and they rapidly proliferate, reaching the density of $10^8$-$10^{11}$colony forming units (CFU) / gram of vegetation in the left heart. The vegetations of the right heart have less bacterial density, probably for a bigger activity of host defense at this level. In mature vegetations, over 90% of the microorganisms is metabolically inactive and responds poorly to antibiotics bactericidal activity[13].

## Pathophysiology

### *Endocarditis has local and systemic consequences[1,2]*

*Local consequences*

The main feature of IE is formation of infected vegetations with crumbly texture composed of thrombotic debris, associated often with destruction of the underlying cardiac tissue. Inside the thrombus bacteria replicate giving rise to bacterial colonies that can be found both on the surface and in depth of the thrombus. If a septic clot passes through the coronary arteries, it can establish a condition of infectious myocarditis. The presence of bacterial colonies on sub valvular apparatus can determine colonization of chordae tendineae and breakage. Local consequences include formation of myocardial abscesses with tissue destruction and sometimes conduction system abnormalities (usually with low septal abscesses). Severe valvular regurgitation may develop suddenly, causing heart failure and death (usually due to mitral or aortic valve lesions). Aortitis may result from infection contiguous spread. Prosthetic valve infections are particularly likely to involve valve ring abscesses, obstructing vegetations, myocardial abscesses, and mycotic aneurysms manifested by valve obstruction, dehiscence, and conduction disturbances.

*Systemic consequences*

A major complication of IE are primarily the clots colonized by the microorganisms, that, due to the nature of the crumbly vegetations, may embolize and result in ischemia and/or abscesses of different organs and can cause widespread sepsis.

Therefore, consequences of IE are primarily

due to embolization of infected material from the heart valve and, especially in chronic infection, immune-mediated phenomena. Lesions of the left side, more common than those of the right side, may embolize to any tissue, particularly the kidneys, spleen, and central nervous system (CNS). Mycotic aneurysms can form in any major artery. Cutaneous and retinal emboli are common. Diffuse glomerulonephritis may result from immune complex deposition. Right-sided lesions typically produce septic pulmonary emboli, which may result in pulmonary infarction, pneumonia, or empyema.

## Clinical forms of infective endocarditis with their microbiological etiologic agents

### Acute bacterial endocarditis (ABE)

It is characterized by very virulent strains of bacteria; as etiologic agents. Usually progresses rapidly (*i.e., over days*) and has, in general, tumultuous and destructive character. It has a duration less than six weeks. It may have a *fulminant* course with greater potential for acute heart failure. Has abrupt onset and often a source of infection or portal of entry is frequently evident or is preceded by suppurative infections (meningitis or pneumonia staphylococcal abscesses). When bacteria are virulent or bacterial exposure is massive, ABE can affect normal valves. Furthermore cardiac injuries are widely destructive and there may be necrosis of cardiac tissue (necrotizing type).

Moreover the vegetation can cause erosion or ulceration of the valve leaflets and form abscess cavities, and this is called vegetative-ulcerative endocarditis. Fast progression of valve disease causes a sharp and changeable murmur, for the rapid variation of lesion, differently from stable chronic valvular defects[1-6].

*The involved germs are:*

- Staphylococcus Aureus (70%),
- Streptococcus pyogene,
- Streptococcus Pneumoniae,
- Alpha-hemolytic Streptococci,
- Pseudomonas Aeruginosa,
- Brucella spp,
- Neisseria Gonorrhoeae, Neisseria Meningitidis.

### Subacute bacterial endocarditis (SBE)

In the SBE *the infection is supported by low virulence strains*. Although aggressive, usually develops insidiously and progresses slowly (*i.e., over weeks to months*). Has insidious course characterized by fever, malaise, asthenia, fatigue, arthralgia and neurological disorders. Has a duration more than six weeks. Often, no source of infection or portal of entry is evident. SBE frequently develops upon already diseased valves after asymptomatic bacteroemia due to periodontal, gastrointestinal, or genitor-urinary infections. Therefore the pre-existing lesion is site of clots formation that work as a trap for bacteria. The lesions are, in general, less destructive than those that occur in acute bacterial endocarditis and they may turn towards healing[1-6].

*The involved germs are:*

Most commonly *Streptococci as*:

*Streptococcus Viridans to 70%,*

*Staphilococcus Epidermidis,*

*Enterococci, non-enterococcal group D, anaerobic or microaerophilic*,

Less commonly *Staphilococcus Aureus, Staphylococcus epidermidis, Gemella morbillorum, Abiotrophia defectiva, Granulicatella spp, and Haemophilus spp*[1-6].

### Prosthetic valvular endocarditis (PVE)

Develops *from 2 to 3% of patients within the first year after valve replacement and in 0.5% year thereafter*. It is more common after aortic than after mitral valve replacement and affects mechanical and bioprosthetic valves equally. Early-onset infections are caused mainly by contamination during surgery with antimicrobial-resistant bacteria (i.e, *Staphilococcus Epidermidis, diphtheroids, coliform bacilli, Candida spp, Aspergillus spp*). *Late-onset infections (more than two months after surgery)* are caused mainly by contamination with low-virulence organisms during surgery or by transient asymptomatic bacteremias, most often with streptococci; *Staphilococcus Epidermidis, Diphtheroids*, and the fastidious *gram-negative bacilli, HACEK organisms (Haemophilus spp, Aggregatibacter actinomycetemcomitans, Cardiobacterium Hominis, Eikenella Corrodens, and Kingella Kingae)*[1-6].

## Rationale of prophylaxis against infective endocarditis

*Prophylaxis against IE is based on the following points:*

- IE is preceded by bacteremia;
- Some dental, gastrointestinal, genitourinary

procedures could cause bacteremia with organisms, especially in patients with predisposing heart disease, which might determine IE;

• These bacteria are susceptible to antibiotics. It follows that antibiotics should be administered to patients with predisposing heart disease before procedures that may cause bacteremia.

*In order to reach a reliable prophylaxis, the following requirements must be met:*

• Identification of patients at risk;

• Identification of the procedures cause of bacteremia;

• Choice of appropriate treatment, with the best balance between the risk of side effects and risk of developing IE.

## A Brief history of the guidelines on the prevention of IE

In 1955 published on *Circulation* the first document of the AHA on the prevention of bacterial endocarditis[14]. Other AHA 8 documents up to 1997 are supplemented and enriched the initial recommendations, identifying pathogens, the most appropriate antibiotic regimens, procedures at risk, hygiene rules to be observed, predisposing heart disease, risk profiles[9].

In the 1997 guidelines, in particular, were identified categories of patients at high risk, moderate and low, and it was also recognized that the majority of IE is not attributable to invasive procedures, but *random* bacteremia during ordinary activities, such as cleaning of the teeth and chewing, and that the antimicrobial prophylaxis may fail[15].

These guidelines were based on the fundamental principles summarized in the preceding paragraph, as well as on the experimental demonstration of the effectiveness of antimicrobial prophylaxis in the prevention of EI in animals and in humans on the assumption of effectiveness of prevention by EI associated with dental, gastrointestinal and genitourinary procedures.

The evidence relevant to the formulation of the guidelines consisted of expert opinion, clinical experience, few case-control studies and descriptive studies with surrogate measures of risk.

Thus the class of attributable recommendation is IIb and the level of evidence is C (Table 1)[9].

| ***Classes of recommendation* and *the Level of evidence* in guidelines** | |
|---|---|
| ***Classification of recommendations*** | ***Class I***: Evidence or general agreement of usefulness/efficacy<br><br>***Class II***: Evidence or conflicting opinions to usefulness/effectiveness<br>**a)**: Existence of, or opinions in favor of usefulness/efficacy<br>***b)***:Usefulness/efficacy less well-defined<br><br>***Class III***: Absence of usefulness/effectiveness, in some cases harmful |
| **Level of evidence** | **A)** Randomized trials or meta-analysis of multiple<br><br>**B)** Single randomized study or non randomized studies<br><br>**C)** Consensus of experts |

**Table 1:**

## Reasons for change

The incidence of transient bacteremia after dental procedures presents a wide variation, from 10 to 100%, in contrast, a transient bacteraemia occurs frequently during daily activities such as brushing teeth and chewing. It is estimated that clean the teeth with the toothbrush 2 times per day for 1 year would entail a risk of exposure to bacteremia 154,000 times greater than a single tooth extraction[16]. Brush your teeth with a toothbrush cause bacteremia than 200 times per year compared to 1-2 times a year for visits to the dentist[17]. Therefore it is plausible that a large share of IE may result from this type of daily activities[16,18]. On the other hand a poor oral hygiene can cause bacteremia regardless of procedures on teeth and is responsible for a higher frequency of bacteremia after these procedures.

Prophylaxis seems to prevent a very small number, if any, cases of IE after procedures at risk, and the risk of adverse events from antibiotics may exceed the benefit of prevention.

Risk (procedure) related to dental procedures is 1:14,000,000 in the general population and 1:95,000 in patients with previous IE. Duval et al. have estimated a reduction of the risk of infection related to the dental procedure attributable to the antibiotic prophylaxis: from 1/46,000 to 1/54,300 for the native valves and from 1/10,700 a1/149,000 for the valve prosthesis[19].

Should therefore deal with a huge number of patients to prevent a single case of IE, but even if antibiotic prophylaxis was effective, prescribed and taken correctly, it should serve to protect only a small percentage of patients. In most patients with a first diagnosis of IE, in fact, you cannot identify a previous related procedure and responsible bacteremia is obviously of different origin[20]. The use of antibiotics on a large scale, also, is not without risks, not only for the possible side effects but especially for the emergence of resistant microorganisms[17]. The assumption of efficacy in humans of antimicrobial prophylaxis for IE associated with procedures at risk, has never been satisfactorily proved. This is a crucial point for the thorough revision of the guidelines[9]. Studies on the effectiveness of antibiotic prophylaxis in preventing or reducing bacteremia in humans after dental procedures are in fact contradictory[17]

To date, also there are no data demonstrating that reduce the duration and frequency of bacteremia after a medical procedure leads to a reduction of the risk of IE related to the procedure. The few published case-control studies are not sufficient to support the practice of antibiotic prophylaxis[21, 22]. The strict observance of traditional protocols would have little impact on the total number of IE in general population. No prospective randomized controlled trial has ever tested the hypothesis of effectiveness of antibiotic prophylaxis. Based on these assessments, the expert committee of three scientific societies BSAC, AHA, ESC and NICE, between 2006 and 2009, have made a substantial revision of the guidelines for IE prophylaxis[8-11].

*The essential points of the recent revision of the guidelines can be summarized as follows:*

• Extensive use of antibiotic prophylaxis recommended in previous guidelines is no longer sustainable, based on available evidence;

• Prophylaxis should be limited to patients at higher risk, that is, with greater probability of developing EI and / or with greater risk of unfavorable evolution of IE;

• The maintenance of an optimal oral hygiene reduces the incidence of bacteremia associated with daily activities and is the most important of antibiotic prophylaxis after dental procedures to reduce the risk of IE.

The indications for antibiotic prophylaxis of IE are, therefore, significantly decreased compared to the previous recommendations.

**The new criteria for the prophylaxis of infective endocarditis**

The more recent guidelines, based on the essential points of the change mentioned in the previous paragraph, provides recommendations ranging from a strong limitation of antibiotic prophylaxis to those patients at higher risk, BSAC guidelines, AHA and ESC[8,9,11,23], until its complete abolition, in the NICE guidelines[10].

Any guideline you want to take, the first concrete consequence results from the violation of clinical behaviors force for many years, which may explain the reluctance to change on the part of some physicians, that adds other arguments to support the view that no evidence of benefit is not the same-thing as the evidence of absence, as they may lack adequate trials. Some cases of IE may still be caused by procedures, and could be prevented with prophylaxis. That is because the IE is a serious disease with high mortality.

We think, however, that the recent guidelines, based on solid argumentations, shared by members of the dedicated task forces of the AHA and other prestigious scientific institutions, such as ESC, NICE and the BSAC, should lead to overcome these reservations and change clinical practice, although established for over 50 years.

It seems reasonable also, following these considerations, transpose the message to maintain antibiotic prophylaxis in patients at higher risk, as suggested by BSAC, AHA and ESC[8,9,11,23], rather than abolish it as indicated by NICE[10].

For the reasons discussed in the previous paragraphs, in the most recent guidelines do not exist more class I recommendations for the prophylaxis of IE[11,23]. The class I recommendations of previous guidelines have become of class IIa, for patients at higher risk and for higher risk procedures, which are discussed in the following paragraphs, and for all other cases of class III.

**Major risk patient population**

Only in patients at increased risk of developing IE and / or increased risk of unfavorable evolution of IE is currently indicated as prophylaxis.

*There are three categories of patients:*

• With prosthetic cardiac valves or prosthetic material used for valve repair;

• Those who have contracted previously IE;

• Patients with complex cyanotic congenital

heart disease and postoperative palliative shunt or other prosthetic materials.

After complete surgical repair with prosthetic material in the first 6 months after the procedure until completion of the endothelialization, prophylaxis is indicated[11,23].

In the most recent AHA guidelines prophylaxis is recommended in patients with heart transplant who develop a structural valvular regurgitation[23], otherwise in the ESC guidelines these patients are excluded from prophylaxis because, despite the risk of unfavorable evolution of IE is high, the probability of occurrence of an IE which origins from the teeth is minimum[11].

The most important message, common to all guidelines since 2006 until present, is that prophylaxis is no longer recommended for any form of valvular disease on native valves, with specific reference to mitral valve prolapse, the bicuspid aortic valve and aortic calcification[8-11,23]. Prophylaxis is also not indicated in heart disease already assessed as low risk in previous guidelines: isolated *ostium secundum* atrial septal defect, and 6 months after surgical or percutaneous repair of an atrial or interventricular septal defect, or a patent ductus arteriosus, echocardiographic findings of mitral, tricuspid or pulmonary regurgitation, in the absence of alterations, structural aortic valve sclerosis with peak velocity speed <2 ml sec.

**Procedures at greater risk**

Are considered at higher risk dental procedures that involve manipulation of gingival or periapical region or perforation of the oral mucosa and that include periodontal and endodontic treatments. Only for these procedures is currently indicated antibiotic prophylaxis.

The other dental procedures for which it is not indicated as prophylaxis include: the injections of local anesthetics in uninfected tissues, x-rays, the orthodontic applications, the removal of deciduous teeth or trauma to the lips or to the oral mucosa.

For gastrointestinal, genitourinary and respiratory tract procedures, such as gastroscopy, colonoscopy, cystoscopy, transesophageal echo, laryngoscopy, bronchoscopy, endotracheal intubation or trans nasal, as well as the musculoskeletal and dermatological procedures, antibiotic prophylaxis of IE is not recommended, because it there is no evidence that the related transient bacteraemia can cause IE[11, 23].

Otherwise, if an infectious disease coexists in the region covered by the procedure, is necessary to use antibiotics targeted against the germs most likely responsible for the infection. For the gastrointestinal or genitourinary tract are recommended agents active against enterococci, such as ampicillin and amoxicillin or, in case of intolerance to beta lactams, vancomycin. For procedures regarding respiratory tract recommended agents active against staphylococci, such as penicillin or cefalosporine, vancomycin should be used in patients who are intolerant to beta-lactam antibiotics. For musculoskeletal or dermatological procedures you should use agents active against staphylococci and beta-hemolytic streptococci, such as penicillin or cephalosporins. Vancomycin or clindamycin should be used in case of intolerance or in the presence of resistant strains[11,23].

A further problem is the increasing popularity of body piercing and tattoos. Cases of IE seen after these practices are increasing, particularly in the tongue piercing. Both the piercing and the tattoo should be strongly discouraged in patients at risk of IE. If made, sterility during the procedure must be rigorous.

Finally, invasive therapeutic procedures represent a cause growth of EI, having achieved in recent years on 30% of all cases of EI. Although antimicrobial prophylaxis is not routinely indicated in most of these procedures, it is necessary to optimize the aseptic precautions to be taken during the insertion and manipulation of venous catheters and during any invasive procedure[11,23].

**Antibiotic prophylaxis before dental procedures at risk**

In Table 2 are presented the antibiotics that may be administered as a single dose from 30 to 60 minutes before the dental procedures at risk. The main target and consists of the oral streptococci, although it remains unclear the impact of the increasing resistance of these bacteria on the effectiveness of antibiotic prophylaxis. In the absence of allergy medications, first choice drugs are amoxicillin or ampicillin.In case of allergy is recommended the use of clindamycin. As an alternative to amoxicillin or ampicillin can be used cephalexin 2 g intravenously in adults 0.50 mg / kg in children, cefazolin or ceftriaxon 1 g intravenously in adults or 50 mg / kg in children. Fluoroquinolons and glycopeptides are not recommended for their uncertain

effectiveness and for the possible induction of resistance[11,23].

| **Recommended antibiotic prophylaxis before dental procedures at risk** | | | |
|---|---|---|---|
| **In single dose 30-60 min before the procedure** | | | |
| *Patients* | *Antibiotic* | *Adults* | *Children* |
| Not allergic to penicillin | amoxicillin or ampicillin | 2 g orally or iv | 50 mg / kg orally or iv |
| Allergic to penicillin | clindamycin | 600 mg orally or iv | 20 mg / kg orally or iv |

**Table 2:**

## Conclusion

The antibiotic prophylaxis of IE is currently only recommended in patients at higher risk who are undergoing dental procedures at greater risk. In clinical practice, given the radical change of behavior established for decades, should be assessed individually the risk / benefit ratio and clearly inform the patient, involving him in the decision.

## References


1) Karchmer AW. *Infective Endocarditis*. In: Bonow RO, Mann DL, Zipes D P, Libby P, eds. In: Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 9th Ed. Philadelphia; Elsevier Saunders 2012: *1540-1558*.
2) Moreillon B, Que YA. *Infective endocarditis*. Lancet 2004, 363: *139-49*.
3) Hoen B, Alla F, Selton Suty C, Beguinot I, Bouvet A, Briancon S, et al. *Changing profile of infective endocarditis: results of a 1-year survey in France*. JAMA 2002; 288: *75-81*.
4) Hill EE, Herijgers P, Claus P, S Vanderschueren, Herregods MC, Peetermans WE. *Infective endocarditis: changing epidemiology and predictors of 6-month mortality: a prospective cohort study*. Eur Heart J 2007, 28: *196-203*.
5) Tleyjeh IM, Abdel-Latif A, Rahbi H, Scott CG, Bailey KR, Steckelberg IM, et al. *A systematic review of population based studies of infective endocarditis*. Chest; 2007, 132: *1025-35*.
6) Aksoy O, Meyer LT, Cabell CH, Kourany WM, Pappas PA, Sexton DJ. *Gender differences in infective endocarditis: pre-and co-morbid conditions lead to different management and outcomes in female patients*. Scand J Infect Dis 2007; 39: *101-7*.
7) Naber CK, Erbel R, Baddour LM, D. Horstkotte. *New guidelines for infective endocarditis: a call for collaborative research*. Int J Antimicrob Agents 2007, 29: *615-6*.
8) Gould FK, Elliott TS, Foweraker J, Fowler VG Jr, AE Bolger AF, Levison ME, et al. *Working Party of the British Society for Antimicrobial C. Guidelines for the prevention of endocarditis. Report of the Working Party of the British Society for Antimicrobial Chemotherapy*. J Antimicrob Chemother 2006 I; 57: *1035-42*.
9) Wilson W, Taubert KA, Gewitz M, Lockhart PB, Baddour LM, Levison M, et al. *Prevention of infective endocarditis: guidelines from the American Heart Association: a guide line from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee*, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation 2007, 116: *1736-54*.
10) Richey R, Wray D, Stokes T. *Prophylaxis against infective endocarditis: summary of NICE guidance*. BMJ 2008; 336: *770-1*.
11) Habib G, Hoen B, Tornos P, Thuny F, Prendergast B, Vilacosta I, et al. *Guidelines on prevention, diagnosis and treatment of infective endocarditis executive summary, the task force on infective endocarditis of the European Society of Cardiology*. Eur Heart J 2009, 30: *2369-2413*.
12) Kitten T, Munro CL, Wang A, Macrina FL. *Vaccination with FimA from Streptococcus parasanguis protects rats from endocarditis caused by other viridans streptococci*. Infect Immun 2002; 70: *422-5*.
13) Durack DT Beeson PB. *Experimental bacterial endocarditis, II: survival of a bacteria in endocardial vegetations*. Br J Exp Pathol 1972; 53: *50-3*.
14) Jones TD, Baumgartner L, Bellows MT, Breese BB, Kuttner AG, McCarty M, et al. *(Committee on Prevention of Rheumatic Fever and Bacterial Endocarditis, American Heart Association). Prevention of rheumatic fever and bacterial endocarditis through control of streptococcal infections*. Circulation 1955; 11: *317-20*.
15) Dajani AS, Taubert KA, Wilson W, Bolger AF, Bayer A, Ferrieri H et al. *Prevention of bacterial endocarditis: recommendations by the American Heart Association*. JAMA 1997; 277: *1794-801*.
16) Roberts GJ. *Dentists are innocent! 'Everyday' bacteremia is the real culprit: a review and assessment of the evidence that dental surgical procedures are a principal cause of bacterial endocarditis in children*. Pediatr Cardiol 1999; 20: *317-25*.
17) Lockhart PB, Brennan MT, Sasser HC, Fox PC, Paster BJ, Bahrani-Mougeot FK. *Bacteremia associated with toothbrushing and dental extraction*. Circulation 2008; 117: *3118-25*.
18) Duval DL, Leport C. *Prophylaxis of infective endocarditis: current tendencies, continuing controversies*. Lancet Infect Dis 2008; 8: *225-32*.
19) Duval X, Alla F Hoen B, Danielou F, Larrieu S, Delahaye F et al. *Estimated risk of endocarditis in adults with predisposing cardiac conditions undergoing dental procedures with or without antibiotic prophylax-*

*is*. Clin Infect Dis 2006; 42: *102-7*.

20) van der Meer JT, Thompson J, Valkenburg HA, Michel MF. *Epidemiology of bacterial endocarditis in The Netherlands I. Patient characteristics*. Arch Intern Med 1992; 152: *1863-8*.

21) Strom BL, Abrutyn E, Berlin JA, Kinman JL, Feldman RS, Stolley PD, et al. *Dental and cardiac risk factors for infective endocarditis. A population based, case-control study*. Ann Intern Med 1998, 129: *761-9*.

22) Lacassin F, Hoen B, Leport C, Selton-Suty C, Delahaye F, Goulet V, et al. *Procedures associated with infective endocarditis in adults. A case control study*. Eur Heart J 1995;16: *1968-74*.

23) Nishimura RA, Carabello BA, Faxon DP, Freed MD, Lytle BW, O'Gara PT, et al. *ACC/AHA 2008 Guideline Update on valvular heart disease: focused update on infective endocarditis. A report of the American College of Cardiology / American Heart Association Task Force on Practice Guidelines*. Circulation 2008, 118: *887-96*.

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