CHI DEVE FARE LA PROFILASSI DELL'ENDOCARDITE?

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Sabato 15 giugno 2019

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BUON USO DEGLI ANTIBIOTICI NELL'ERA DELLE RESISTENZE
Come far si che il miracolo continui

La Profilassi

- Etimologia : da greco προφυλάσσω, “difendere” o “prevenire”

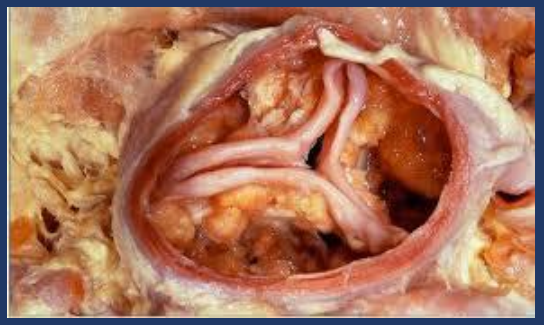
- Definizione: “…le norme e i provvedimenti che si devono adottare, collettivamente o da parte di singoli, per la difesa contro una determinata malattia, e la loro applicazione pratica”.

http://www.treccani.it/enciclopedia

La profilassi in medicina: presupposti

- Patologia con impatto clinico rilevante
- Meccanismo fisiopatologico noto
- Evidenza scientifica che vi sia una correlazione tra l'intervento (profilassi) e lo sviluppo della malattia

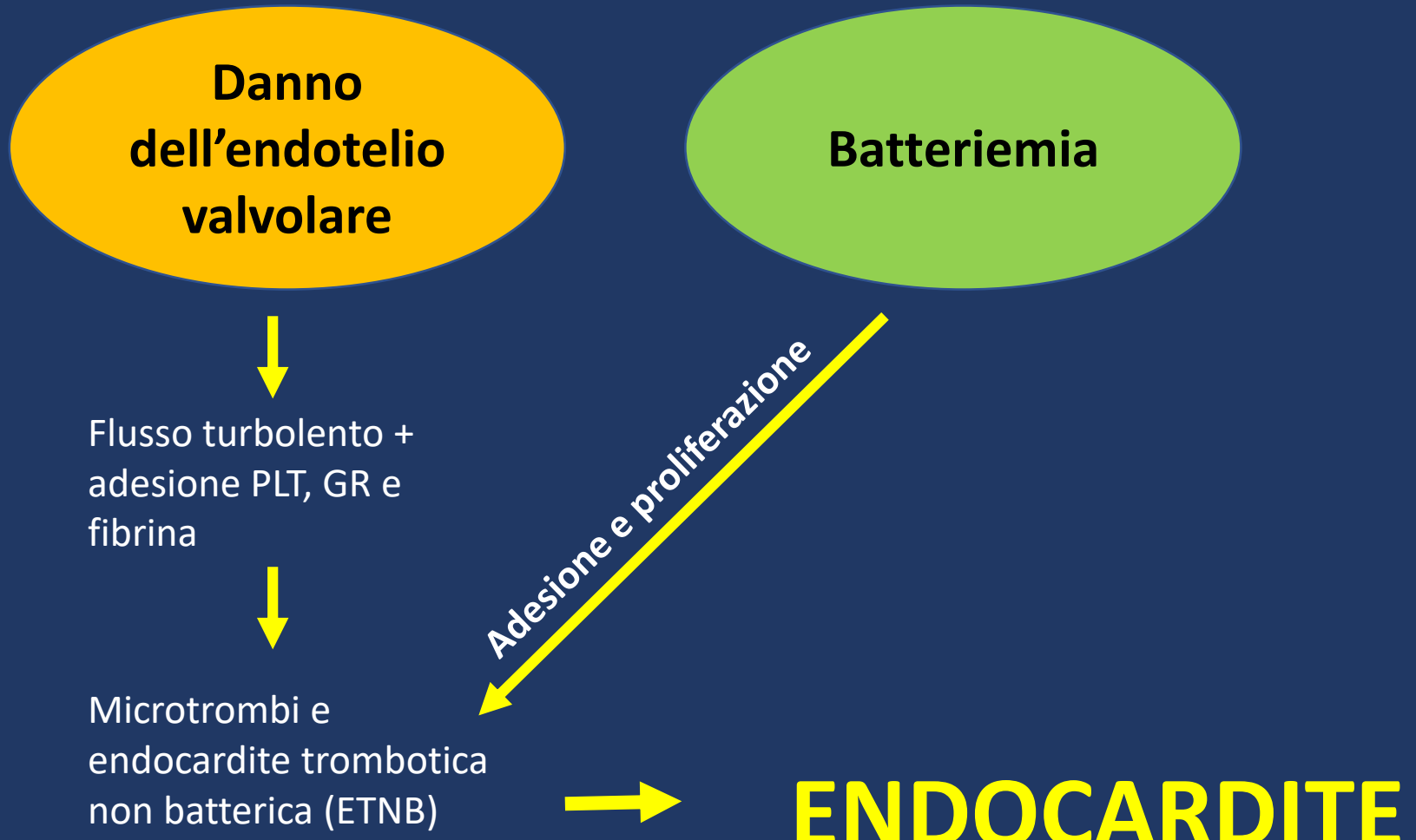
Endocardite:epidemiologia



- Malattia frequente (3-9 casi/100.000 persone/anno nei Paesi industrializzati)
- Mortalità intraospedaliera 15-22%; mortalità a 5 anni 40%
- 50% di casi in pazienti con malattia valvolare cardiaca sottostante
- 1/3 dei casi associata alle pratiche assistenziali (HCA o HA)

Hoen et al. NEMJ 2013

Endocardite batterica: fisiopatologia



The remarks which follow are based upon 150 cases, of admitted to St. Bartholomew's Hospital, 23 to the Great Northern Hospital, ai 12 were seen privately. All these cases have occurred during the past eight years.

ii. *Nomenclature.* Until the last ten years or so it was customary distinguish two kinds of endocarditis—a 'simple' or non-infective kind, most

1909

commonest, and the second is the least frequent. In the majority of cases the patient is known to be suffering from, or possesses in a latent form, some valvular defect which is a sequel to rheumatic fever. Usually the interval

v. *Relation to preceding Valvular Disease.* This is discussed under paragraph xii, p. 305, dealing with the signs of infective endocarditis.

vi. *Influence of Congenital Defects.* There seems little doubt that a congenital defect in the heart predisposes it in some measure to infection. This

and run a rapid course, it may be said that infective endocarditis is due to the operation of streptococci of low virulence, of the types found in normal faeces and in normal saliva. They are for the most part short chained

QUARTERLY JOURNAL OF MEDICINE, April, 1909

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In cases of the primary form, where no previous valvular lesion has been present, no such prophylactic measures would be possible. But in the secondary form of the disease, where the infection is grafted upon a previously sclerosed endocardium, and which, as already said, includes by far the majority of the cases, it is possible to do something to prevent the development of the mischief.

QUARTERLY JOURNAL OF MEDICINE, April, 1909

Profilassi dell'endocardite: le prime raccomnadazioni

Treatment of Streptococcal Infections in the General Population

Following epidemics and in certain population groups, it has been found that about 3 per cent of untreated streptococcal infections are followed by rheumatic fever. Adequate and early penicillin treatment, however, will eliminate streptococci from the throat and prevent most attacks of rheumatic fever.

Headache—common.

Fever—variable, but generally from 101 t 104F.

Abdominal pain—common, especially in chi dren; less common in adults.

Nausea and vomiting—common, especiall in children.

1957

Common Signs

Prophylaxis Against Bacterial Endocarditis

In individuals who have rheumatic or congenital heart disease, bacteria may lodge on the heart valves or other parts of the endocardium, producing bacterial endocarditis. Transient bacteremia which may lead to bacterial endocarditis is known to occur following various surgical procedures including dental extractions and other dental manipulations which disturb the gums, the removal of tonsils and adenoids, giving birth, and operations on the gastrointestinal or urinary tracts. It is good medical and dental practice to protect patients with rheumatic or congenital heart disease by prophylactic measures.

Recommended Prophylactic Methods

Penicillin is the drug of choice for administration to patients with rheumatic or congenital heart disease undergoing dental manipulations, or surgical procedures in the oral cavity.

Although the exact dosage and duration of therapy are somewhat empirical, there is some evidence that for effective prophylaxis reasonably high concentrations of penicillin must be present at the time of the dental procedure.

	Recommended drug	Prophylaxis for adults
AHA (1972)[64]	Penicillin	600 000 units procaine penicillin G with 200 000 units crystalline penicillin G IM 1 h before procedure and once daily for 2 days after the procedure
AHA (1977)[65]	Penicillin	Aqueous crystalline penicillin G (1×10^6 units IM) with procaine penicillin G (600 000 units IM), 30 min to 1 h before the procedure and then penicillin V 500 mg orally every 6 h for two doses
BSAC (1982)[66]	Amoxicillin	3 g 1 h before procedure
AHA (1984)[67]	Penicillin V	2 g orally 30 min to 1 h before procedure; then 1 g 6 h after initial dose
BSAC (1986)[68,69]	Amoxicillin	3 g 1 h before procedure
AHA (1990)[70]	Amoxicillin	3 g orally 1 h before procedure; then 1·5 mg 6 h after initial dose
BSAC (1990)[71]	Amoxicillin	3 g 1 h before procedure
BSAC (1992)[72,73]	Amoxicillin	3 g 1 h before procedure
France (1992)[74]	Amoxicillin	3 g 1 h before procedure
European Infectious Diseases Society consensus (1995)[75]	Amoxicillin	3 g 1 h before procedure
AHA (1997)[8]	Amoxicillin	2 g 1 h before procedure
New Zealand (1999)[76]	Amoxicillin	2 g 1 h before procedure; then 1 g 6 h after initial dose
Switzerland (2000)[34]	Amoxicillin	2·25 g (3×750 mg) 1 h before procedure then 750 mg 6 h after initial dose
France (2002)[33]	Amoxicillin	3 g or 2 g (if weight <60 kg) 1 h before procedure
European Society of Cardiology consensus (2004)[77]	Amoxicillin	2 g 1 h before procedure

Profilassi dell'endocardite: la storia 1990

define when prophylaxis is recommended for patients with mitral valve prolapse, (5) for oral or dental procedures the initial amoxicillin dose is reduced to 2 g, a follow-up antibiotic dose is no longer recommended, erythromycin is no longer recommended for penicillin-allergic individuals, but clindamycin and other alternatives are offered; and (6) for gastrointestinal or genitourinary procedures, the prophylactic regimens have been simplified. These changes were instituted to more clearly define when prophylaxis is or is not recommended, improve practitioner and patient

will develop this infecti
particular procedure wil
sible.

There are currently no ra
carefully controlled humar
tients with underlying str
disease to definitively e

Gallbladder surgery
Cystoscopy
Urethral dilatation
Urethral catheterization if urinary tract infection is present†
Urinary tract surgery if urinary tract infection is present†
Prostatic surgery
Incision and drainage of infected tissue†
Vaginal hysterectomy
Vaginal delivery in the presence of infection†

Endocarditis Prophylaxis Not Recommended‡

Dental procedures not likely to induce gingival bleeding, such as simple adjustment of orthodontic appliances or fillings above the gum line
Injection of local intraoral anesthetic (except intraligamentary injections)
Shedding of primary teeth
Tympanostomy tube insertion
Endotracheal intubation
Bronchoscopy with a flexible bronchoscope, with or without biopsy
Cardiac catheterization
Endoscopy with or without gastrointestinal biopsy
Cesarean section
In the absence of infection for urethral catheterization,

Previous coronary artery bypass graft surgery
Mitral valve prolapse without valvular regurgitation†
Physiologic, functional, or innocent heart murmurs
Previous Kawasaki disease without valvular dysfunction
Previous rheumatic fever without valvular dysfunction
Cardiac pacemakers and implanted defibrillators

*This table lists selected conditions but is not meant to be all-inclusive.

†Individuals who have a mitral valve prolapse associated with thickening and/or redundancy of the valve leaflets may be at increased risk for bacterial endocarditis, particularly men who are 45 years of age or older.

Table 2.—Dental or Surgical Procedures*

Endocarditis Prophylaxis Recommended

Dental procedures known to induce gingival or mucosal bleeding, including professional cleaning
Tonsillectomy and/or adenoidectomy

Dajani AS et al. JAMA, December 1990

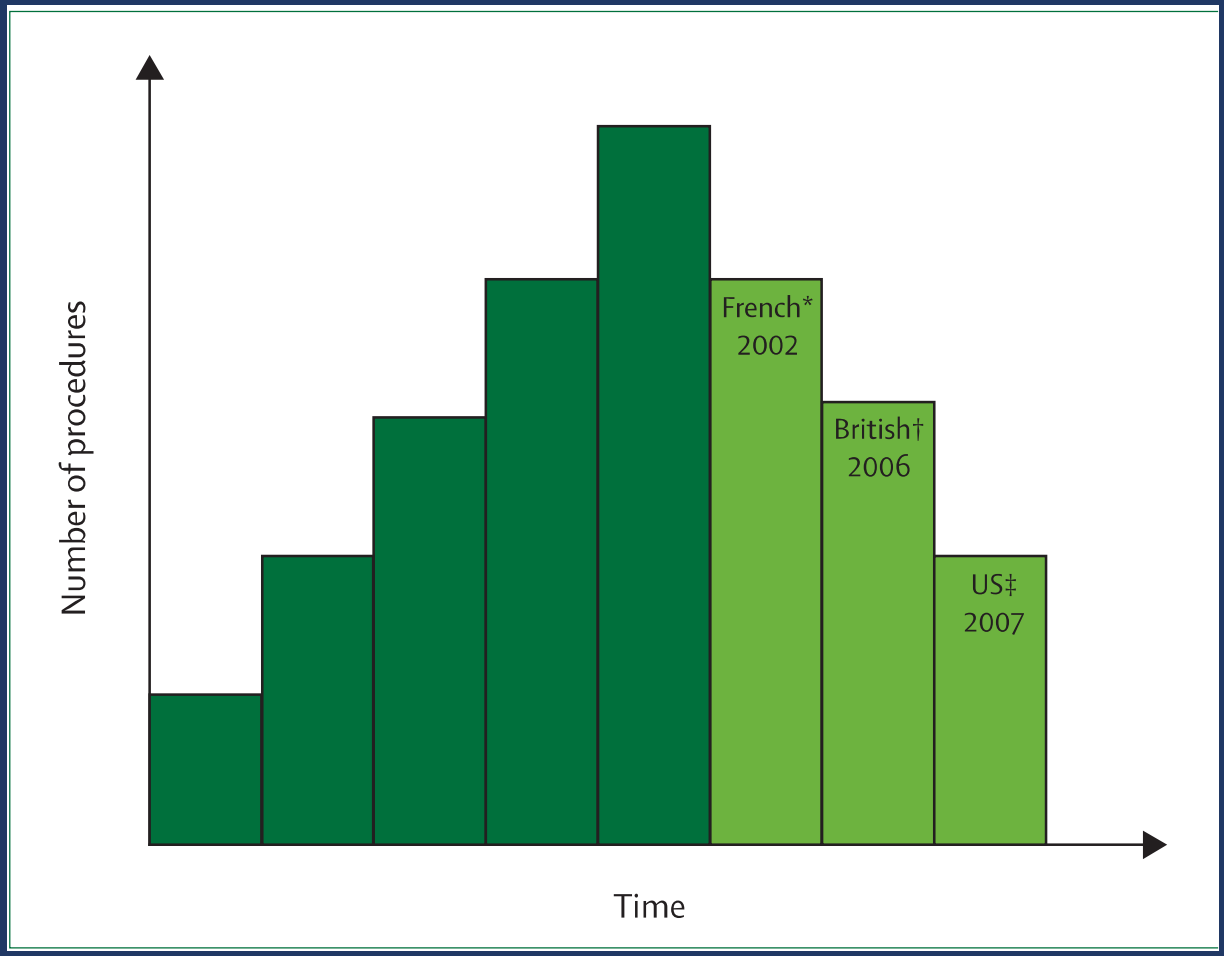
Gli anni ’90 e 2000: il dibattito scientifico

- Expert opinion, non studi randomizzati controllati
- Efficacia della profilassi per prevenire EI dimostrata solo in modelli murini
- Burden di batteriemie transitorie > nella vita quotidiana che dopo procedura invasiva
- Possibili effetti negativi della profilassi: anafilassi, selezione di germi resistenti
- Pochi dati sulle batteriemie successive a procedure non-dentarie

- Endocardite = malattia grave
- Basso rischio di effetti avversi della profilassi
- Difficile fare un RCT (bassa incidenza, problemi etici)

Duval X et al. *LancetInfectDis*2008; 8: 225–32

Rappresentazione del numero di procedure per le quali è raccomandata l'AP: Evoluzione delle LG negli anni



Duval X et al. *LancetInfectDis*2008; 8: 225–32

Prevention of Infective Endocarditis

Guidelines From the American Heart Association **2007**

A Guideline 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

-- in assenza di dati scientifici sufficienti, la profilassi andrebbe riservata ai pazienti con malattie cardiache sottostanti che lo pongono al **alto rischio di outcome sfavorevole** in caso di insorgenza di EI (protesi cardiache; pregressa EI; cardiopatie congenite in casi selezionati; valvulopatie post-Tx di cuore)

-- in tale setting, è ragionevole la somministrazione della profilassi **prima delle procedure dentali invasive**

-- profilassi non raccomandata per procedure GU o GI

Wilson et al. Circulation 2007

Le linee guida attuali

European Heart Journal Advance Access published August 29, 2015

European Heart Journal
doi:10.1093/eurheartj/ehv319

ESC GUIDELINES

2015 ESC Guidelines for the management of infective endocarditis

The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC)

Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM)

Authors/Task Force Members: Gilbert Habib* (Chairperson) (France), Patrizio Lancellotti* (co-Chairperson) (Belgium), Manuel J. Antunes (Portugal), Maria Grazia Bongiorni (Italy), Jean-Paul Casalta (France), Francesco Del Zotti (Italy), Raluca Dulgheru (Belgium), Gebrine El Khoury (Belgium), Paola Anna Erba[a] (Italy), Bernard Iung (France), Jose M. Miro[b] (Spain), Barbara J. Mulder (The Netherlands), Edyta Plonska-Gosciniak (Poland), Susanna Price (UK), Jolien Roos-Hesselink (The Netherlands), Ulrika Snygg-Martin (Sweden), Franck Thuny (France), Pilar Tornos Mas (Spain), Isidre Vilacosta (Spain), and Jose Luis Zamorano (Spain)

ESC guidelines, 2015

Le categorie a rischio

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

ESC guidelines, 2015

Le procedure dentarie a rischio

Recommendations	Class[a]	Level[b]
A. Dental procedures		
• Antibiotic prophylaxis should only be considered for dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa	IIa	C
• Antibiotic prophylaxis is not recommended for local anaesthetic injections in non-infected tissues, treatment of superficial caries, removal of sutures, dental X-rays, placement or adjustment of removable prosthodontic or orthodontic appliances or braces or following the shedding of deciduous teeth or trauma to the lips and oral mucosa	III	C

ESC guidelines, 2015

ANTIBIOTICOPROFILASSI PERIOPERATORIA NELL'ADULTO

Redazione:		Verifica:	Approvazione:
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Firma		*Firma*	*Firma*

Documento precedente	Versione attuale	Data	Descrizione della modifica
PCI_PRO_03 del 02/09/2009	02	30/06/2013	*Aggiornamento del documento nel nuovo formato aziendale*

Parola chiave 1	Parola chiave 2	Parola chiave 3
Prevenzione e controllo infezioni	*Profilassi perioperatoria*	*Antibiotici*

Procedure per le qualî RACCOMANDATA la profilassi dell'EI

A) Procedure odontoiatriche: procedure che prevedono la manipolazione dei tessuti gengivali o della regione periapicale dei denti o la perforazione della mucosa orale (ad eccezione dell'infiltrazione di anestetico locale attraverso mucosa non infetta):

- estrazioni dentarie ed altri interventi di chirurgia orale
- procedure parodontali, inclusi sondaggio, ablazione tartaro, scaling e root planing, chirurgia parodontale
- impianti endoossei o reimpianti di denti avulsi
- terapie canalari con strumentazione oltreapice
- chirurgia endodontica (apicectomie)
- posizionamento sottogengivale di dispositivi medicati
- utilizzo di matrici e cunei interdentali
- iniezioni anestetiche intraligamentose-
- biopsie o altri prelievi di tessuto

Le procedure non dentarie

Recommendations	Class[a]	Level[b]
B. Respiratory tract procedures[c]		
• Antibiotic prophylaxis is not recommended for respiratory tract procedures, including bronchoscopy or laryngoscopy, or transnasal or endotracheal intubation	III	C
C. Gastrointestinal or urogenital procedures or TOE[c]		
• Antibiotic prophylaxis is not recommended for gastroscopy, colonoscopy, cystoscopy, vaginal or caesarean delivery or TOE	III	C
D. Skin and soft tissue procedures[c]		
• Antibiotic prophylaxis is not recommended for any procedure	III	C

Systematic antibiotic prophylaxis is not recommended for non- dental procedures. Antibiotic therapy is only needed when invasive procedures are performed in the context of infection.

ESC guidelines, 2015

Misure di prevenzione non specifiche nei pazienti a alto rischio

These measures should ideally be applied to the general population and particularly reinforced in high-risk patients:
• Strict dental and cutaneous hygiene. Dental follow-up should be performed twice a year in high-risk patients and yearly in the others.
• Disinfection of wounds.
• Eradication or decrease of chronic bacterial carriage: skin, urine.
• Curative antibiotics for any focus of bacterial infection.
• No self-medication with antibiotics.
• Strict infection control measures for any at-risk procedure.
• Discourage piercing and tattooing.
• Limit the use of infusion catheters and invasive procedure when possible. Favour peripheral over central catheters, and systematic replacement of the peripheral catheter every 3–4 days. Strict adherence to care bundles for central and peripheral cannulae should be performed.

ESC guidelines, 2015

Regimi di profilassi raccomandati

Situation	Antibiotic	Single-dose 30–60 minutes before procedure	
		Adults	Children
No allergy to penicillin or ampicillin	Amoxicillin or ampicillin[a]	2 g orally or i.v.	50 mg/kg orally or i.v.
Allergy to penicillin or ampicillin	Clindamycin	600 mg orally or i.v.	20 mg/kg orally or i.v.

Alternatively, cephalexin 2 g i.v. for adults or 50 mg/kg i.v. for children, cefazolin or ceftriaxone 1 g i.v. for adults or 50 mg/kg i.v. for children.

NO FQ e GLICOPEPTIDI →

- **non chiara efficacia**
- **rischio di selezione di resistenze**

Timing della profilassi dell'EI

30-60 minuti prima della procedura chirurgica

...e il futuro?

Current practice in prophylaxis of endocarditis: are we running into trouble?

Johannes M. Albes *

Antibiotic Prophylaxis Against Infective Endocarditis

Widening the Net?*

John B. Chambers, MA, MD

J Am Coll Cardiol. 2018 Nov 13;72(20):2455-2456. doi: 10.1016/j.jacc.2018.09.025. Epub 2018

Preventing Endocarditis: No Rest for the Worrier.

Bolger AF[1].

Conclusioni:

- Attuali LG raccomandano AP nei pazienti ad alto rischio in occasione di procedure dentistiche invasive
- Importanza delle misure igienico-sanitarie non specifiche di prevenzione
- Dibattito aperto in merito a potenziali nuove categorie di pazienti a rischio e di procedure da considerarsi a rischio