

New Prophylaxis Guidelines

Have they gone too far?

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Introduction

- Infective endocarditis (IE) is a low-prevalent pathology with an incidence of 25-50 cases for each 1,000,000 inhabitants/year.
- Neither incidence nor associated mortality have significantly decreased over the last 30 years.
- The guidelines are based almost exclusively on the opinion of experts due to its low incidence, lack of randomized studies, and the few meta-analyses published. Almost all the information available springs from small case-control studies.

In year 2007, the AHA published new prophylaxis guidelines for infective endocarditis.



These had significant changes in comparison to previous ones, restricting the indication of prophylaxis to those patients in high risk, who would have a worse evolution if infective endocarditis appears.

Besides, the indication of prophylaxis for procedures on urinary and gastrointestinal tracts was removed.

Cardiac affections that continue with indication of prophylaxis



- Valve prosthesis.
- History of prior endocarditis.
- Cyanotic congenital heart diseases:
 - ✓ Not repaired.
 - ✓ Repaired with prosthetic material over the last 6 months.
 - ✓ Repaired with residual defects close to the patch.
- Heart transplantation recipients that develop valvulopathies.



Procedures considered risky with indication of prophylaxis

2006

Dental

- Dental extractions, implants, and endodontic therapy
- Periodontal procedures
- Any dental maneuver that may present bleeding or gingival lacerations

Respiratory airways

- Amygdalectomy/adenoidectomy
- Surgery that may affect the respiratory mucosa
- Bronchoscopy with rigid bronchoscope

Digestive tract

- Sclerosis of esophageal varices
- Retrograde cholangiography
- Surgery of biliary tract
- Surgery that affects the intestinal mucosa

2006

Genitourinary tract

- Prostate surgery
- Cystoscopy
- Urethral dilation

Only for patients in high risk

- Bronchoscopy with flexible bronchoscope
- Transesophageal echo
- Digestive endoscopy
- Vaginal hysterectomy
- Vaginal birth



Procedures considered risky with indication of prophylaxis

2007

Dental

- Any dental maneuver manipulating the gingival mucosa or the periapical dental region, or with perforation of oral mucosa.

Respiratory airways

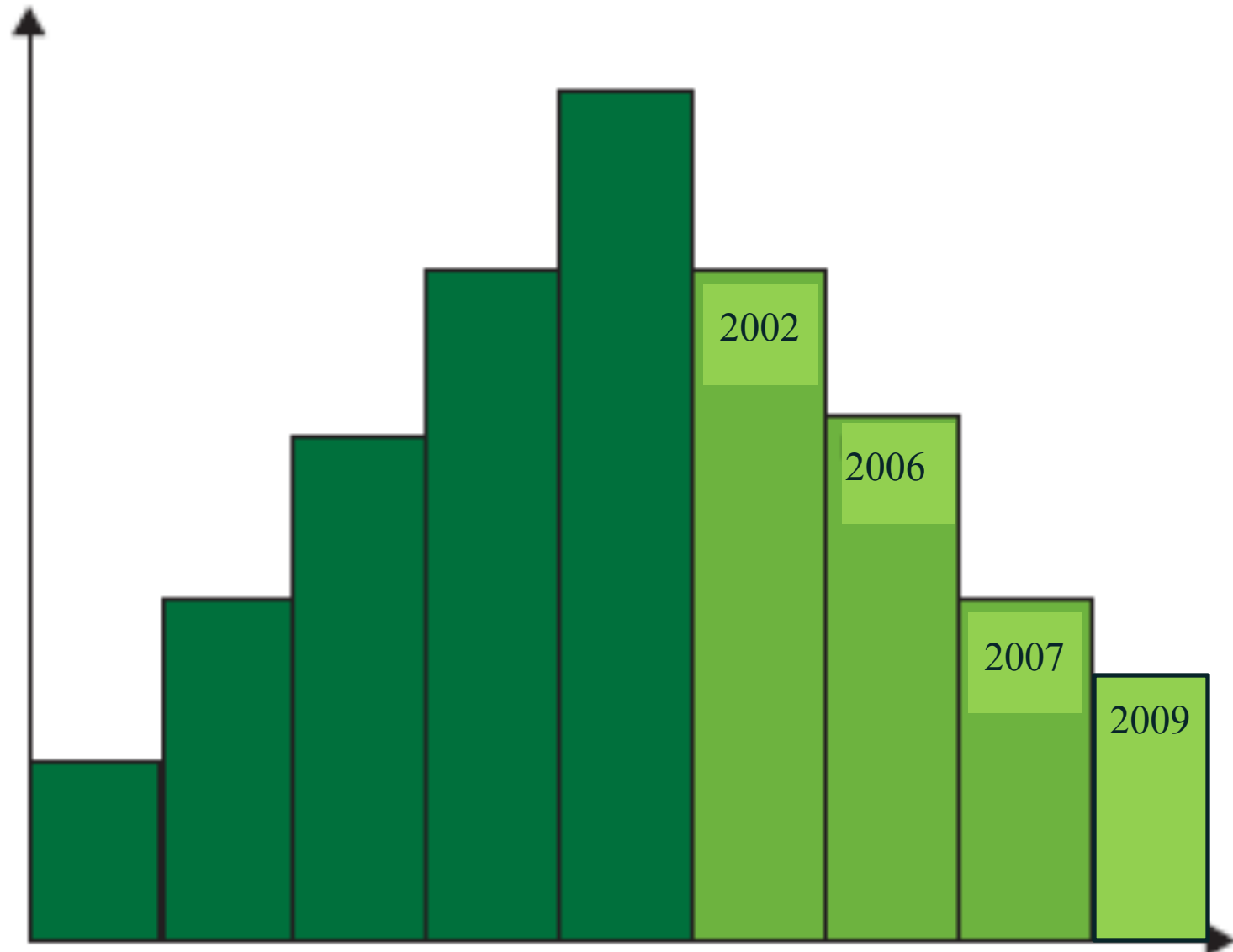
- Maneuvers that entail incision or biopsy of respiratory mucosa.

Skin

- Procedures that act on the infected skin or skin structures

French guidelines 2002	They suggest prophylaxis only for patients in high risk of IE and with a potential worse evolution . Prior IE, prosthesis, and conduits or prosthetic shunts. It leaves prophylaxis for the rest as “optional”, highlighting the importance of oral hygiene and health
Guidelines from the British Society for Antimicrobial Chemotherapy 2006	Antibiotic prophylaxis only for the patients in the highest risk. Prior IE, prosthesis, conduits, and prosthetic shunts
American Heart Association (AHA) 2007	It withdraws prophylaxis for native valves and for procedures on the genitourinary (GU) and gastrointestinal (GI) tracts.
British National Institute for Health and Clinical Excellence 2008	They suggest withdrawing all prophylaxis except procedures on the GU and GI tracts when there is suspicion of pre-existing infection
European Society of Cardiology 2009	The indications are similar to those of the AHA, but excluding heart transplantation recipients with valvulopathies. They limit the prophylaxis to odontological procedures.

Indications of antibiotic prophylaxis in the world in the last few years



Modified from Duval X et al. *Lancet Infect Dis* 2008; 8: 225



Rationale

- **Not** based on new evidence, but on the **absence** of it.
- Although at times contradictory, the series published to date of observational studies do not support routine use of antibiotic prophylaxis.

Rationale



- It would be more likely for an IE to occur associated to episodes of bacteriemias that occur daily, associated to daily activities, than to a medical procedure.
- Prophylaxis would prevent a very small number of cases of IE associated to procedures.
- The risk of complications associated to antibiotic therapy would exceed the potential benefit of it.
- Maintenance of hygiene and oral health would reduce the incidence of daily bacteriemias, being more important to prevent IE than the antibiotic prophylaxis of an odontological procedure.

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- Common daily activities such as brushing your teeth and even chewing, are associated to a frequency of transient bacteriemias from a 10 to a 70% according to different authors.
- An average person has 154,000 times more chances of being exposed to a bacteriemia in a year brushing twice a day his/her teeth than in a dental extraction; the bacteria going through the heart associated to the former would exceed in almost 6,000,000 those going through after an odontological procedure.

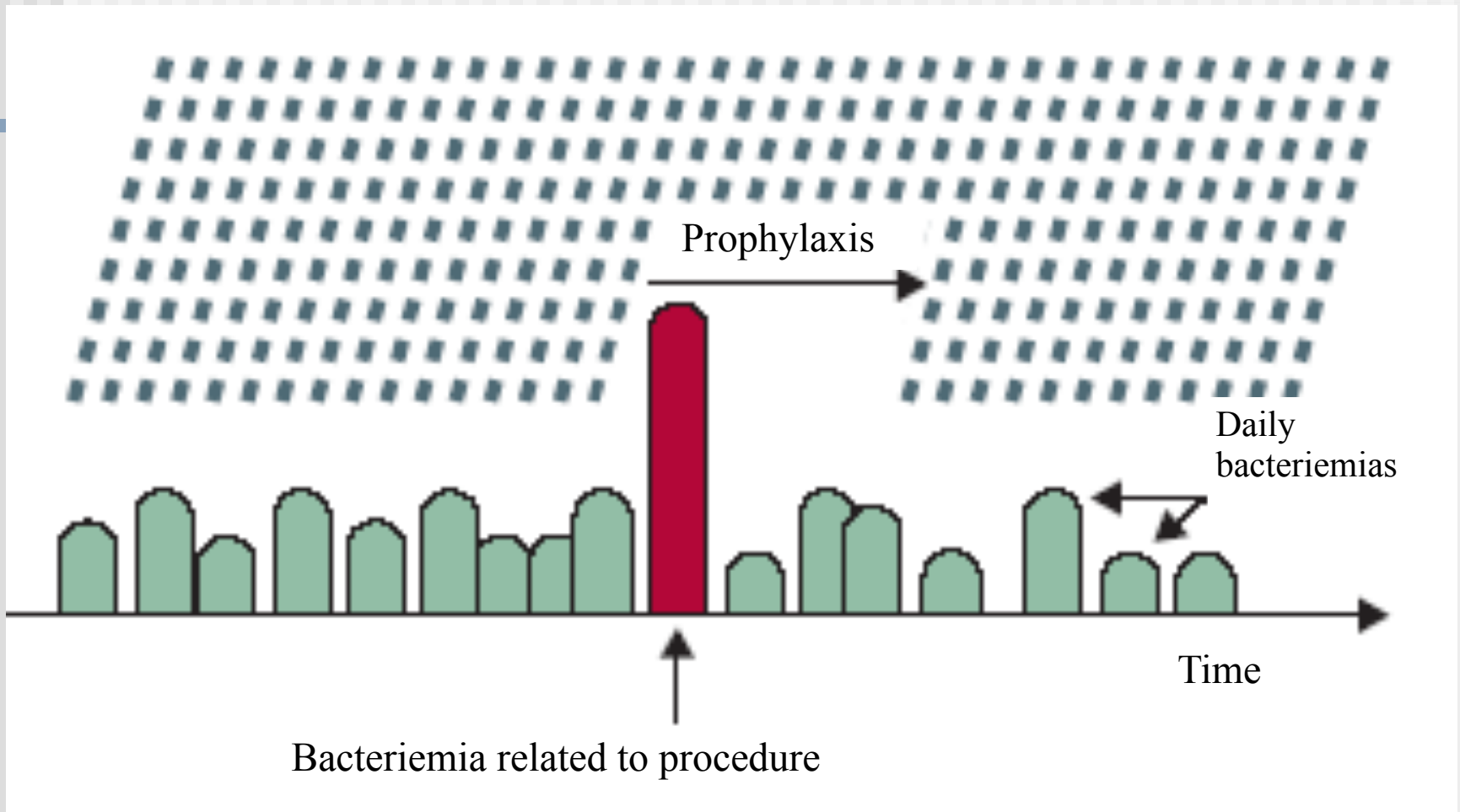
Roberts GJ. *Pediatr Cardiol* 1999; 20: 317
Seymour RA et al. *Br Dent J* 2000; 189: 610
Lucas V, Roberts GJ *Pediatr Dent* 2000; 22: 96



- Both the episodes of bacteriemia associated to odontological procedures and those produced by daily activities are associated to a number of circulating bacteria ($< 10^4$ CFU/ml) much less than necessary to produce IE in animal models (10^{6-8} CFU/ml)

Roberts GJ et al *Heart*. 2006;92:1274

Lucas VS et al. *Br J Exp Pathol*. 1972;53: 50





- Beyond the abovementioned data in our center, from 142 patients analyzed over the last 15 years with IE, the background of instrumental maneuvers in the 3 months prior to diagnosis were above 16%
- These values in the different series are between 2.7 and 5%.

Kazelian et al. *Rev Arg Cardiol* 2009; 77 Vol 2: 184
Duval X et al *Clin Infect Dis* 2006; 42: e102
Van der Meer JT et al. *Arch Intern Med* 1992; 152: 1869
Strom BL et al. *Ann Intern Med* 1998; 129: 761



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- The risk of IE after an odontological procedure is:
- ✓ 1 in 14 million dental procedures in the general population.
- ✓ 1 in 1.1 million procedures in patients with mitral valve prolapse (MVP).
- ✓ 1 in 54,000 and 142,000 in other acquired valvulopathies (including rheumatic).
- ✓ 1 in 11,000 and 114,000 procedures in patients with valve prosthesis.
- ✓ 1 in 95,000 in patients with prior IE.

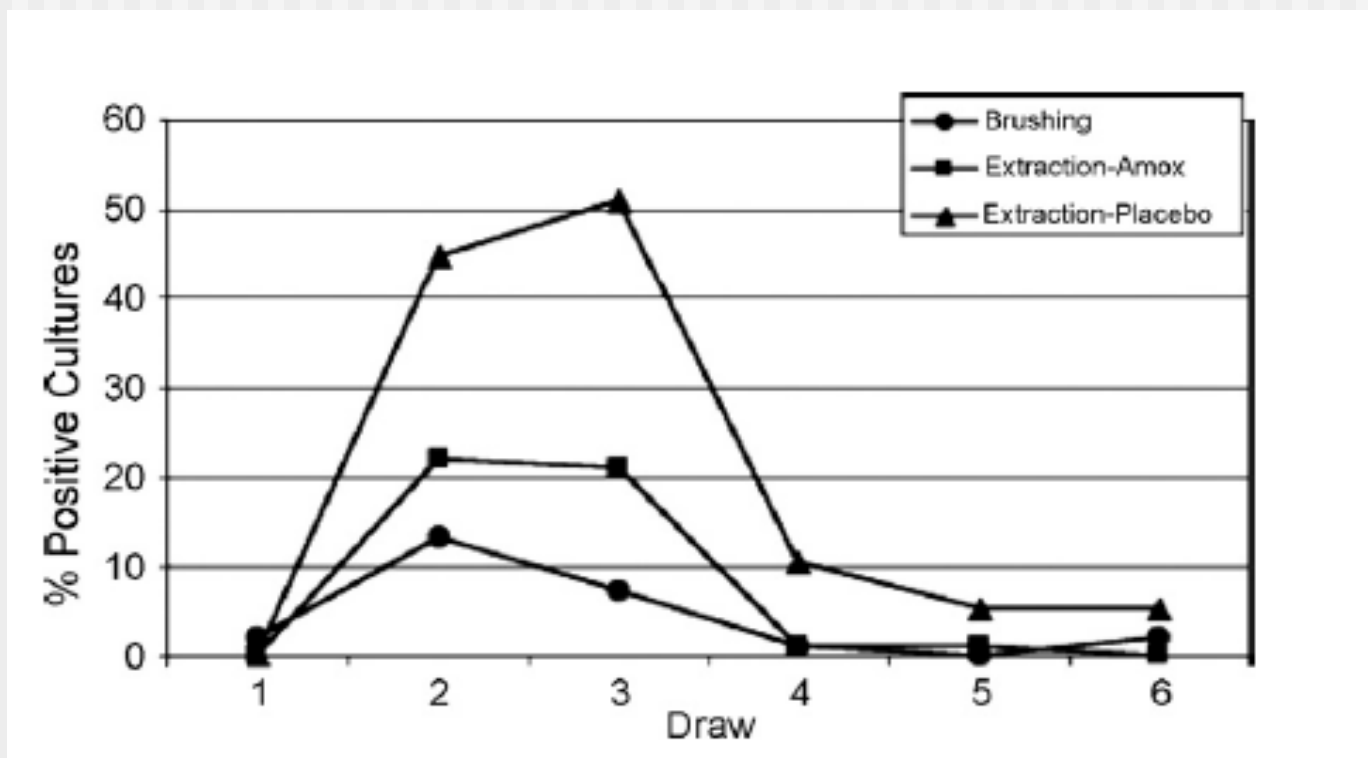


- A large number of patients should be treated to prevent an event, even if we were to consider the effectiveness of antibiotic prophylaxis as being 100%.
- Van Der Meer et al, in a prospective study of case-control study at 2 years, found 8 cases of IE, out of which 5 had received prophylaxis.
- Imperiale et tal, in a retrospective case-control study of patients with cardiac lesions of high risk that developed IE within 8 weeks of an odontological procedure, found that 1 patient (13%) had received prophylaxis against 15 controls (63%) .

Van der Meer JT et al. *Lancet* 1992; 339: 135
Imperiale TF, et al. *Am J Med* 1990; 88: 131



Incidence of positive hemocultures





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Anaphylaxis

- Guidelines suggest that although infrequent, cases of fatal anaphylaxis associated to the use of penicillin (10-30/million treated) should be taken into account, due to the high number of patients to be treated to prevent a case.
- Since 1990 the indication of first choice is amoxicillin.

The cases of anaphylaxis reported in the United Kingdom between 1963 and 2008 were 273 with 12 fatal cases.

According to the medication regulatory agency in the United Kingdom, between 2002 and 2007, 100 million treatments were indicated.

Ahlstedt S. *Allergy* 1984; 39: 151

Lin RY. *Arch Intern Med* 1992; 152: 930

Bacterial resistance



- It is not known for certain, what is the impact of a single dose of amoxicillin on the selection of resistant bacteria.
- There seems to be an established relationship with macrolides.



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Characteristics of high risk of patients

- It would seem reasonable to take into account besides the mentioned heart diseases as being a high risk, also co-morbidities of the patient such as age, diabetes, and immunodeficiencies among others (only taken into account in the French guidelines from 2002) at the time of indicating prophylaxis due to the poor evolution that an IE would have in such patients.



- In the Italian registry of IE (RIEI), from 267 cases of IE, 6.7% had a history of an odontological procedure, 44% of them had received antibiotic prophylaxis; 15% had other non-odontological procedures with antibiotic prophylaxis in 46%.



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- Since these guidelines are based on **absence of evidence** instead of on absence of benefits, each case should be evaluated individually and discussed with the patient before making decisions on the indication or antibiotic prophylaxis in the cases from moderate to high risk.



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- “Absence of evidence does not necessarily imply absence of benefit.”
 - IE is a severe pathology in any context, so if there was no benefit from the antibiotic therapy, it should not be indicated in any patient, and if there is, even if minimal, it should be indicated in all risk patients.