Consensus document on the use of antibiotic prophylaxis in dental surgery and procedures

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ABSTRACT

The goal of antibiotic prophylaxis in Odontology is to prevent the onset of infections through the entranceway provided by the therapeutic action, therefore it is indicated providing there is a considerable risk of infection, either because of the characteristics of the operation itself or the patient's local or general condition. Nonetheless, clinical trials with antibiotics in dental pathologies have had scant regard for the required methodological criteria and, in addition, are not sufficiently numerous.

This text presents the results of an expert conference comprising the Presidents of the most representative Scientific Societies in Spain who have analyzed the existing literature and have drawn on their valuable professional experience. It describes the technical circumstances, analyzes the biological and pharmacological foundations and their application to the most representative medical situations. It is concluded that antibiotic prophylaxis in Odontology has certain well-founded, precise indications and offers the international scientific community a practical protocol for action.

Key words: *Prophilaxis, antibiotics, dentistry.*

RESUMEN

La profilaxis antibiótica en Odontología tiene como objetivo prevenir la aparición de infección a partir de la puerta de entrada que produce la actuación terapéutica, por lo que se encuentra indicada siempre que exista un riesgo importante de infección, ya sea por las características mismas de la operación o por las condiciones locales o generales del paciente. Sin embargo, los ensayos clínicos con antibióticos en patologías dentarias responden poco a los criterios metodológicos requeridos, y además no son lo suficientemente numerosos.

Se presentan los resultados de una conferencia de expertos integrada por los Presidentes de Sociedades científicas españolas más representativas que han analizado la bibliografía existente y han aportado sus valiosas experiencias profesionales. Se describen las circunstancias técnicas, se analizan los fundamentos biológicos y farmacológicos y se aplican a las situaciones

médicas más representativas. Se concluye que la profilaxis antibiótica en Odontología cuenta con indicaciones bien fundamentadas y precisas, ofreciendo a la comunidad científica internacional un protocolo práctico de actuación.

Palabras clave: *Profilaxis, antibióticos, odontología.*

CONTENTS

1. INTRODUCTION
2. THEORETICAL BACKGROUND
• Complications to avoid
• Cost-Benefit Balance
• Target Bacterial Population
• Antibiotic administration regimen
• The patient's state of health
• Undesirable effects (economic, biological-resistances, medical-allergic)
• Decision-making (equational empiricism)
3. CLINICAL BASES: :
– What dental procedures require antibiotic prophylaxis?
– What types of patients require antibiotic prophylaxis?
– Selection criteria: Bacterial target, normal flora, adequate selection of the antibiotic, pharmacokinetic and pharmacodynamic aspects
– Value of antiseptics and oro-dental hygiene
4. ANALYSIS OF DENTAL PATHOLOGY
5. ANALYSIS OF ORAL AND MAXILLO-FACIAL SURGICAL PATHOLOGY
6. ANALYSIS OF PERIODONTAL PATHOLOGY
7. ANALYSIS OF PAEDIATRIC PATHOLOGY
8. INFECTIOUS ENDOCARDITIS PROPHYLAXIS
9. CONCLUSIONS

1. INTRODUCTION

Classically, prophylaxis has been considered pre- or perioperative administration of an antibiotic for prevention of a local and/or systemic infectious complication and the corresponding clinical consequences.

The aim of antibiotic prophylaxis in surgery is to prevent the possible appearance of infection in the surgical wound, creating a state of resistance to micro-organisms through antibiotic concentrations in blood that avoid bacterial proliferation and dissemination right from the point of entry that the surgical wound represents.

10% of antibiotic prescriptions made in our country are used for odontogenic infections, and a significant part of them are for prophylaxis in dental surgery and procedures (1). Like recommendations about use of antibiotics in odontogenic infection treatment, antibiotic prophylaxis recommendations cannot be based on clinical trials (nor on Evidence-Based Medicine), since clinical trials with antibiotics in dental pathologies respond little to the required methodological criteria, and furthermore are not sufficiently numerous to establish a line of conduct. Therefore, the general therapeutic or prophylactic antibiotic prescription strategy is based on professional agreement and consensus documents.

The recommendations proposed in this document are based on the consensus of the professionals who participated in developing it.

2. THEORETICAL BACKGROUND

Complications to avoid

Multi-microbial local infections are cutaneous-mucosa, dental or bone infections that are encouraged following invasive dental procedures (2) and they translate clinically into swellings, abscesses, loss of teeth, implants or prosthetic structures. In a study done in our country, it was demonstrated that the complications subsequent to extraction of the third molar are an infection and not exclusively inflammatory, since statistically significant differences were found in the frequency of infectious complications among groups who received preventive treatment (5 days) or pre-operative prophylaxis (single dose) with amoxicillin / clavulanate 2000/125 mg, and the group that received placebo (2.7%, 5.3% and 16% respectively) (3). Rates of infectious complication were higher in the case of osteotomy or longer surgical duration, treatment being clearly better in these cases than prophylaxis or placebo. The infecting innoculant increases as the surgical time extends. Thus, the probability of infection around dental implants depends basically on how traumatic or prolonged the surgery is (4), it being considered that the infrequent precocious losses of the implant (5) are due to contamination during the insertion phase (6).

Mono-microbial systemic infections are infections that take root in patients with infection-susceptible focal point (endocardial alterations, bone or joint prostheses), in patients with higher susceptibility to systemic infection by certain micro-organisms (splenectomized patients or those with infection by encapsulated bacteria of the *Streptococcus* or *Haemophilus* genera), or in patients with generalized alterations of the immune system that facilitate septicaemia (immunodepressed, immuno-compromised and malnourished). Generally, the first step tends to be bacteraemia, which is produced after an invasive procedure. This bacteraemia is well studied in very prevalent periodontal disease (periodontitis) due to the permeability of the epithelium that surrounds the tool-tissue interface, and the levels of prostaglandin in the local circulation that increase the number of leukocytes and fibrinogen levels, slowing down circulation in these cases, thus favouring the passage of bacteria to the blood (7). Thus, in animal models, endocarditis subsequent to bacteraemia is 48% in rats with periodontal diseases versus 6% in healthy rats (8). In humans, bacteraemia subsequent to invasive

procedures is around 51-55% (9).

Cost-Benefit balance

The physician's criterion for choosing antibiotic prophylaxis or not must be based on the benefit and the cost of the risk. The economic cost of prophylactic operations (usually short-term) is acceptable when compared with the total cost of dental treatment. Obviously, the benefit is the prevention, by the antibiotic, of the infectious complications subsequent to surgery and/or procedures. Lastly, the risk of antibiotic prophylaxis is the appearance of adverse reactions (fundamentally allergic) and the selection of resistances.

Target bacterial population

The target bacterial population depends on the location of the infectious complication to be covered. Thus, local infections following odontogenic procedures are habitually multimicrobial, since many of the species isolated tend to go in pairs (*Bacteroides* sp and *Fusobacterium; Peptostreptococcus* sp. and *Prevotella* sp.*; Prevotella* sp. and *Eubacterium* sp.) (10,11) with a strong aerobic/anaerobic component (12-14), and to a much lesser degree, a micro-aerophil component, corresponding to the possible contamination/infection during surgery by a normal microbiote of the mouth and saliva, as well as by odontopathogens of periodontal disease, which has very high prevalence (50% of the adult population has gingivitis and 30% periodontitis) (15).

The systemic infections to be prevented in patients with underlying disease are those subsequent to post-dental manipulation bacteraemia that generally occur after invasive procedures. This bacteraemia is generally mono-microbial, and is originated by contamination/infection by a normal microbiote or odontopathogen during surgery. We have known since the 1930s that, following dental manipulation, the number of blood cultures positive for Streptococcus is 75% in individuals with caries, gingivitis and periodontitis, versus 30% in healthy subjects (16,17).

The micro-organisms most frequently involved are *Streptococcus* of the *viridans* group, followed by coagulase-negative (*epidermidis*) and coagulase-positive (*aureus,* and perhaps *lugdunensis*) species of the genus *Staphylococcus*, of oral origin (18), and lastly in 4-7% of cases, Gram-negative bacilli of the HACEK group (*Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella*), several of which are considered odontopathogens (19). Nor must we forget the high percentage of bacteraemias by anaerobes (*Eubacterium, Peptostreptococcus, Propionibacterium, Lactobacillus*) that are detected when the proper methods are used (blood cultures for anaerobes) (20,21). Table 1 shows the most frequent odontogenic pathogens.

Antibiotic administration regimen

The main goal of antibiotic prophylaxis is to attain elevated levels of antibiotic in serum during the surgical process, and for some hours after the incision is closed. In this sense, the dose used must be high, never lower than that used as treatment. Administration prior to surgical intervention or the procedure may be sufficient in most interventions. Only in those cases in which the half-life of the antibiotic is less than one hour and the duration of the intervention 2-3 hours, or more than twice the half-life of the antibiotic, would it be necessary to repeat the dose. Similarly, if there is more than 1-2 L of blood loss during the procedure, administration of an additional dose of antibiotic should be considered (22-25).

AEROBIC	**N=**	**ANAEROBIC**	**N=**
Streptococcus, viridans group	139	*Peptostreptococcus*	105
Staphylococcus	9	*Prevotella pigmentata*	93
Corynebacterium	9	*Fusobacterium*	90
Campylobacter	9	*Prevotella no pigmentata*	56
Neisseria	8	*Gemella*	36
Actinomyces	7	*Porphyromonas*	35
Lactobacillus	6	*Bacteroides*	14
Others	13	Others	35
TOTAL	200	TOTAL	464

Table 1. Pathogen isolates of patients with odontogenic infection.

The patient's state of health

Invasive oral dental procedures (intraligamentary local anaesthesias, endodontia procedures, curettage, placement of probes, single and multiple dental extraction, transplants/re-implants; and periapical, periodontal, bone and implant surgery or surgery of the mucosa as well as biopsy of the salivary glands, etc.) entail a risk of infection in healthy subjects in some cases, and always in individuals at risk for local and/or general infection (individuals with transplants, implants, immuno-depressed, or suffering from malnourishment or uncontrolled associated pathology, etc.) (2,26).

Non-invasive oral-dental procedures (application of fluoride or sealing of fissures, blood-free prosthetic care, post-surgical suture removal, orthodontia, radiology and non-intraligamentary anaesthesia) do not present risk of infection either in healthy subjects or in those at risk, and therefore they are never candidates for antibiotic prophylaxis (2,26).

In the case of subjects with risk of systemic infection (individuals with risk of endocarditis and those with joint prostheses), prophylaxis will be indicated for invasive procedures, and will be true pre-operative prophylaxis (the concept of preventive treatment is not applicable in this case) (2,26), and generally in a single dose. It is in these latter cases that medical and legal implications are discussed most, as legal disputes have arisen due to the absence of prophylaxis or due to the administration of incorrect antibiotics or at incorrect times in the prevention of bacterial endocarditis (27).

Undesirable effects (economic, biological resistance, medical and allergic)

Due to the exclusive action of antibiotics on bacterial structures, the adverse effects are not frequent when compared to other types of drug.

Generally speaking, the incidence of adverse effects of antibiotics or idiosyncratic reactions to them is low. This allows, e.g. for prophylaxis in situations such as bacterial endocarditis in patients with no history of penicillin allergy, the use of a single dose of amoxicillin 2 g without fear of encountering anaphylactic reactions (28).

Selection of resistance in normal flora (pharyngeal or intestinal) depends on the type of antibiotic used, since the resistance selection capacity is different for each compound (29,30) and less with short periods at high prophylaxis or treatment doses (31

Decision making (equational empiricism)

In the last instance, the decision prophylaxis is up to the physician, who will use the equation: *risk = degree of damage x probability of suffering it.* This approach is subjective. Faced with the probability, even remote, of irreparable damages, the prevention of systemic infectious complications (for ex. infectious endocarditis, late-onset infection of a joint prosthesis) must be seen as important by the specialists treating them (cardiologists, traumatologists, infectologists, …). Given the scarcity of adequate clinical trials, the prevention of local complications (for ex. peri-implantitis) as a result of dental manipulations will continue to be at the discretion of the specialist in question.

3. CLINICAL BASES

The appearance of a continuity solution in the skin, mucosa or hard tissues of the mouth consequent to surgical or procedural trauma leads to the alteration of the main barrier that stops invasion by micro-organisms. This is how pathogens enter and can colonize and infect deep tissues. This means that, depending on the bacterial inoculate, the possibility of infection increases depending on whether the procedure or surgery is clean, clean-contaminated, contaminated or dirty. The greater the degree of contamination, the greater the risk of post-surgical infection.

The risk of contamination of the surgical field increases with exposure time and complexity of the continuity edge involved, and is minimized with proper surgical technique and the good condition of the patient. However, antibiotic prophylaxis has been shown to be a more critical factor and a subject for discussion.

The control measures in the surgical technique to minimize the risk of infection are: clean incisions; tear-free mucoperiostial examinations; irrigation as a method for cooling and removing drilled alveolar-bone particles; constant aspiration and careful haemostasis. If local anaesthesia is used, avoid possible tissue tearing with the needle and ensure slow administration of the anaesthesia. Detailed care must also be taken with dividers, retractors and tongue depressors on the lips, flaps and tissues. If drains and compression dressings have to be put in place, do so in the right position. Lastly, we have to remember that some of the sutures made bring edges together and there is therefore a transfer of both the moist environment of the oral cavity itself as well as food residues, and it is consequently recommended that antiseptic or normal saline rinses be started 24 hours after the surgery.

As a general rule, prophylaxis is always indicated when there is an important risk of infection, either because of the characteristics of the operation or because of the patient's local or general conditions. Among the factors that will determine the possible appearance of infection are notably the type and duration of surgery and the surgical risk of the patient due to co-morbidity (assessable in terms of anaesthetic risk or ASA class): diabetes, kidney disease, liver disease (cirrhosis), cardiopathies and therapeutic immunosuppressants (corticoids, radiotherapy, chemotherapy, prior infections with antibiotic therapy either not well-known or not rationalized). Minor interventions in healthy patients do not generally require prophylaxis.

What types of patient require antibiotic prophylaxis?

Using antibiotic prophylaxis or not in dental surgical procedures and techniques will depend on the type of patient and the type of procedure performed. Certain patients are candidates for prophylaxis in invasive procedures. And in contrast, non-invasive procedures do not require prophylaxis in any case.

To that end, patients could be classified as: a) healthy patients, b) patients with local or systemic infection risk factors, and c) patients with post-bacteraemia focal infection risk factors.

In the healthy individual, prophylaxis is based exclusively on the risk of the procedure (26) with transplants, re-implants, grafts, tumour/bone surgery (as with orthopaedic and trauma surgery) having a high risk, and also periapical surgery and dental inclusions, where the co-existence of prior infection is also frequent (2,26).

Patients with local or systemic infection risk factors are those that have an increased general susceptibility to infections. These are oncological patients, patients with congenital or immunological immunodepression (for ex. lupus erythematosus), patients with immunodepression due to medication (corticotherapy, chemotherapy) after transplantation, implant or for any other reason, patients with infectious immunodepression (AIDS), patients with metabolic disorders (diabetes) and patients with renal or hepatic insufficiency (26). There are also splenectomized patients who have a higher risk of infection by the genera *Streptococcus* and *Haemophilus* (32,33).

Patients with post-bacteraemia focal infection risk factors are those who present risk of infectious endocarditis or infection of joint prostheses. With respect to infectious endocarditis, 14-20% have an oral origin (9,34). Antibiotics, apart from minimizing the prevalence and magnitude of bacteraemia (9,35) (they never manage to eliminate it completely), prevent the bacterial adherence to the endocardium (36), which could be the ultimate prophylactic effectiveness mechanism. The pathological conditions associated with risk of infectious endocarditis have been defined by the American Heart Association (AHA) in the United States,

the British Society of Antimicrobial Chemotherapy (BSAC) in the United Kingdom and the Agence Française de Sécurité Sanitaire des Produits de Santé (Afssaps)2,37,38 among others. With respect to infections of joint prostheses, the choice of antibiotic prophylaxis of the dental procedure would be based on its devastating morbidity and high mortality (39), and not on the low prevalence of these infections' association with dental procedures (32). Despite this low prevalence, prophylaxis is indicated in prostheses implanted less than 2 years previously or when there has been prior prosthesis infection (2).
Table 2 indicates patients considered at risk.

1. INFLAMMATORY ARTHROPATHIES: rheumatoid arthritis, systemic lupus erythematosus
2. IMMUNOSUPPRESSION due to Disease, Drugs, Transplants or Radiotherapy
3. DIABETES Mellitus type I
4. INFECTIOUS ENDOCARDITIS protocols: prior endocarditis, valve prostheses, congenital heart disease, surgical bypasses, acquired valve disease, hypertrophic cardiomyopathy, mitral prolapse, sustained murmur and Marfan's syndrome
5. Osteoarticular prosthesis protocols: less than 2 years after implant and having experienced PRIOR INFECTION in the prosthesis.
6. MALNUTRITION
7. HAEMOPHILIA
8. GRAFTS (local factor)
9. Other associated UNCONTROLLED factors (RENAL or HEPATIC INSUFFICIENCY) and SPLENECTOMIZED subjects

Table 2. Patients at risk.

What dental procedures require antibiotic prophylaxis?
Considering these facts, we need to differentiate between invasive oral-dental procedures, those likely to produce significant bleeding (Table 3), and non-invasive ones, those not likely to produce significant bleeding. Generally, invasive procedures may be considered to be high risk in fragile patients.
Surgical wounds were classified by Altemeier in accordance with their potential risk of contamination and infection, in a classification (40), that time has confirmed as of practical utility;
• Type I. Clean wounds (no opening of mucosa such as oral cavity): Confirmed infection rate of 1 to 4%. Antibiotic prophylaxis not required.
• Type II. Clean-contaminated wounds (opening of mucosa such as oral cavity or intervention of inflammatory pathology): Confirmed infection rate of 5 to 15%. These require antibiotic prophylaxis with drugs covering Gram positive and anaerobic micro-organisms.
• Type III. Contaminated wounds (oncological pathology in which there is simultaneous action on the oral cavity and the neck): Confirmed infection rate of 16 to 25%. Antibiotic prophylaxis must be carried out to cover Gram negative organisms whose coverage in clean and clean-contaminated surgeries is disputed.
• Type IV. Dirty and infected wounds. Confirmed infection rate of above 26%. These always need adequate antibiotic treatment.
All the invasive procedures cited in Table 3 are candidates for prophylaxis in patients with risk factors for local or system infection (patients with immunodepressive factors).
Prophylaxis is always indicated prior to invasive procedures performed on patients with post-bacteraemia risk of focal infection (endocarditis, prosthetic infection).
In healthy subjects, prophylaxis is only recommended in the case of included tooth exodontia, periapical surgery, bone surgery, implant surgery, bone grafts and benign tumour surgery.

Selection criteria: bacterial target, normal flora, pharmacokinetic and pharmacodynamic aspects and selection of the right antibiotic

Antibiotics and the bacterial target of the prophylaxis

The bacteria that cause odontogenic infections are generally saprophytes. During evolution of dental caries, the bacteria penetrating dentinal tubules are basically opportunistic anaerobes such as *Streptococcus* spp, *Staphylococcus* spp and *lactobacilli*. When the pulp is necrosed, the bacteria advance along the root canal and the process evolves toward periapical inflammation. Predominating in this phase are *Prevotella* spp, *Porphyromonas* spp, *Fusobacterium* spp and *Peptostreptococci* spp. The microbiology of infectious complications is varied: there are many combinations of all these organisms, with different characteristics, but both anaerobic and aerobic bacteria are habitually present.
Against aerobic or opportunistic Gram positive bacilli involved (*Eubacterium*, *Actinomyces* and *Propionibacterium*) and spirochetes, all the groups of antibiotics normally used (aminopenicillins, amoxicillin + clavulanate, macrolides, lincosamides and metronidazole) are active except for metronidazole. Against the Gram positive cocci involved (*Streptococcus*, *Staphylococcus* and *Peptostreptococcus*) only amoxicillin + clavulanate present adequate coverage (2). Against *Veillonella*, all are active except the macro-

PROCEDURE	RISK
USE OF STAPLES FOR ABSOLUTE ISOLATION WITH RUBBER DIKE	Low risk
PERIODONTAL PROPHYLAXIS AND IMPLANTS PERIODONTAL PROBING	Low risk Low risk
INTRALIGAMENTOUS ANAESTHESIA TRUNK ANAESTHESIA TECHNIQUES	High risk Low risk
EXTRACTIONS	High risk
DENTAL RE-IMPLANTS (Intentional and Traumatic)	High risk
BIOPSIES	High risk
DRAINAGE INCISIONS	High risk
BONE IMPLANTS	High risk
APPLICATION AND REMOVAL OF SURGICAL SUTURES	Low risk
RADICULAR SCRAPING AND SMOOTHING PERIODONTAL SURGERY	High risk High risk
IMPLANT INSERTION SURGERY MUCOSA-GINGIVAL SURGERY REMOVAL OF IMPLANT POSTS	High risk High risk Low risk
ENDODONTIA ENDODONTIA SURGERY AND APICECTOMY	Low risk High risk
PROCEDURES FOR AND PLACEMENT OF ORTHODONTIA BANDS PLACEMENT OF REMOVABLE ORTHODONTIA APPARATUS	Low risk Low risk
TAKING IMPRESSIONS PLACEMENT OF RETRACTION THREAD SCULPTING PROCEDURES WITH BLEEDING PRE-PROSTHETIC SURGERY	Low risk Low risk High risk High risk
ORTHOGNATIC SURGERY	High risk
REDUCTION OF MAXILLARY FRACTURES	High risk
SURGERY ON SALIVARY GLANDS	High risk
MAXILLO-FACIAL ONCOLOGICAL SURGERY	High risk

Table 3. Invasive procedures and risk.

lides (erythromycin, clarithromycin and azithromycin). Against the Gram negative bacilli involved (*Prevotella*, *Porphyromonas*, *Fusobacterium*, *Selenomonas*, *Eikenella*, *Capnocytophaga*, *Actinobacillus*, *Campylobacter rectus* and *Tanerella forsythensis*), amoxicillin + clavulanate and clindamycin present adequate coverage (except for *Eikenella corrodens* in the case of lincosamide). The high prevalence of β-lactamase production in normal or pathologic oral anaerobic flora means that without β-lactamase inhibitor (clavulanate) amoxicillin is not an adequate antibiotic from the physiopathological point of view. Table 4 summarizes the activity of the main antibiotics against the most frequent odontogenic pathogens (41).

Antibiotics and normal flora

The right antibiotic regime will be the one that acts most selectively on the bacteria that may produce complications, respecting as much as possible, the usual saprophyte flora. It is important to consider the ecological aspect when choosing the antibiotic regime to use. Choose the antibiotic and the dose (this factor with less importance if the prophylactic course is short or of a single dose) that least alters the normal saprophyte flora. Taking *Escherichia coli* as an intestinal flora index, macrolides and cetolides are respectful since this micro-organism is resistant to these compounds. Quinolones, however, have selected a high degree of resistance (42), but these compounds are not indicated in dentistry. While amoxicillin has selected high rates of resistance to *E. coli* due to production of β-lactamase, the sensitivity of amoxicillin combined with clavulanate is very high. Where normal flora has been studied most extensively, is in the nasopharynx, taking *Streptococcus pneumoniae* as the index bacteria, a micro-organism of the same genus as other species that are prevalent isolates in odontogenic infections *(viridans* group) (43).

	Aa Actinobacillus Actinomycetemcomitans	*Peptostreptococcus* spp	*Prevotella* spp	*Porphyromonas* spp	*Fusobacterium* spp	Oral *Streptococci*
Penicillin G	±	+	±	±	+	+
Amoxicillin	+	+	±	±	+	+
Amoxicillin/ Clavulanate	+	+	+	+	+	+
Doxicycline	+	±	±	±	+	±
Clindamycin	O	+	+	+	+	+
Metronidazole	O	+	+	+	+	O
Macrolides	±	±	±	±	±	±

Table 4. Activity of various antimicrobials on periodontal pathogens.
+ More than 80% of strains sensitive; O Less than 30% of strains sensitive; ± 30-80% of strains sensitive.

With respect to streptococci, the consumption of antibiotics has been reported as the sole cause of resistance in the species *S. pyogenes* and *S. pneumoniae*, both from a time point of view (44,45) and from a geographical standpoint (45,47), with resistance to macrolides in these two species being connected at the local level (48). While the responsibility of aminopenicillins in the selection of resistances in *S. pneumoniae* is low, the drugs that select most resistances to penicillin and macrolides in *S. pneumoniae* are the oral cephalosporins administered twice daily, but they are not drugs of choice in dentistry and particularly, macrolides administered once or twice a day in *S. pneumoniae* and *S. pyogenes*. These facts are visible in the species of the *viridans* group of the genus *Streptococcus*, where the high resistance to macrolides (erythromycin, clarithromycin) (49) is frequently associated with high resistance to tetracyclines50 and to clindamycin and azalides (azithromycin) (52). Considering that consumption of antibiotics in dentistry assumes 10% of the total consumption of antibiotics in the community, as mentioned above, it is possible to suspect a not unappreciable degree of responsibility in the selection of resistances due to antimicrobial treatments in dentistry. A high prevalence of oral iatrogenic bacteraemia has been described in our country caused by *Streptococci* resistant to erythromycin (40.8%) and clindamycin (21%), the majority of the isolates being sensitive to aminopenicillins (52).

Pharmacokinetic and pharmacodynamic aspects

For some antibiotics, the antibiotic concentrations in the gingival fluid are similar to or above the serum concentrations, as seen in the case of amoxicillin + clavulanate (53,54), spiramycin, metronidazole (55), and quinolones (drugs not indicated in the dental field at present). Pharmacodynamic coverage is understood as the value of the "relationship between the serous pharmacokinetic parameters and in vitro susceptibility" predicting for efficacy: a) percentage of the dosing interval at which the antibiotic levels surpass the MIC (minimum antibiotic concentration that produces inhibition of bacterial growth in vitro) that has to be above 40-50% for β-lactamics, macrolides and lincosamides, and b) relationship of the area under the curve of the serous levels/MIC that must be above 25 for azalides (azithromycin). Papers have been published that apply these concepts in dentistry, analyzing different antibiotics against the five most prevalent isolates (but not against all the bacteria involved) in odontogenic infections (*Streptococcus,* group *viridans, Peptostreptococcus* sp*., Prevotella intermedia, Porphyromonas gingivalis* and *Fusobacterium nucleatum*) (43). Only amoxicillin + clavulanate at a dose of 875/125 mg every 8h or the new formula of 2,000/125 mg every 12h as well as clindamycin 3,200 mg every 6-8 h comply with the pharmacodynamic requirements (43,56,57), However, clindamycin offers worse coverage against oral *streptococci* and adequately for *Peptostreptococcus*, presenting a not unappreciable level of resistances. Metronidazole has no activity against aerobic bacteria and macrolides, including spiramycin, have a high percentage of resistance to oral *streptococci* and offer very limited activity against *Peptostreptococcus* spp and *Fusobcterium nucleatum*.
Table 5 shows the recommended doses for prophylaxis with different antibiotics.

Selection of the right antibiotic

The antibiotic of choice (if prophylaxis is considered necessary because of the type of procedure and patient type) must fulfil the following characteristics:
1- Adequate bacterial spectrum, covering all the species involved in local multi-microbial infections or distal focal mono-microbial infections, including aerobic micro-organisms, micro-aerophils, without forgetting the anaerobes that, because of the difficulty in isolating them, are sometimes not considered prevalent in oral-origin bacteraemias.
2- Wide clinical spectrum, covering the greatest number of dental procedures.
3- Restricted ecological spectrum in order to limit the effects on the usual saprophyte flora as much as possible.
4- Adequate pharmacokinetics and pharmacodynamics, to allow use in single pre-operative dose in the case of prophylaxis, or wide dosing intervals in preventive, short-term treatment, with half-lives or prolonged-release formulas that maintain adequate concentrations locally (gingival fluid) or systemically (serum) during the entire time the dental procedure lasts (prophylaxis).
5- Adequate safety profile, including in paediatric and elderly populations.
Antibiotics administered orally that are effective against

Antibiotic	Adult dose	Paediatric dose†
Amoxicillin	2 g VO	50 mg/Kg VO
Ampicillin	2 g IM or IV	50 mg/Kg IM or IV
Amoxicillin + Clavulanate	2 g +125 mg VO 2 g + 200 mg IV	50 + 6,25 mg/Kg VO 50 + 5 mg/Kg IV
Cefazolin*	1 g IM or IV	25 mg/kg IM or IV
Cephalexin or cefadroxil*	2 g VO	50 mg/Kg VO
Clindamycin	Clindamycin 600 mg VO Clindamycin 600 mg IV	Clindamycin 20 mg/Kg VO Clindamycin 15 mg/Kg IV
Clarithromycin and azithromycin	500 mg VO	15 mg/kg VO
Gentamycin	1,5 mg/Kg IV (do not exceed 120 mg)	1,5 mg/kg IV
Metronidazole	1 g IV	15 mg/kg IV
Vancomycin	1 g IV	20 mg/Kg IV

Table 5. Initial pre-intervention doses recommended in prophylaxis.
† The total dose in children should not surpass the adult dose; follow-up doses one-half the initial dose. * Cephalosporins should not be used in patients with type I penicillin hypersensitivity reaction (rash, angioedema or anaphylaxis). VO: orally ; IM: intramuscular; IV: intravenous

odontogenic infections include penicillin, clindamycin, erythromycin, cefadroxil, metronidazole and the tetracyclines. These antibiotics are effective against oral *streptococci* and anaerobes. Penicillin V is the penicillin of choice for odontogenic infections. It is a bactericide, and although its spectrum of action is relatively narrow, it is appropriate for odontogenic infection treatments. For the prophylaxis of endocarditis associated with dental treatments, amoxicillin is the antibiotic of choice (37). Amoxicillin plus clavulanate is currently the drug of choice for this group as it has the great advantage of keeping its activity against the β-lactamases produced commonly by micro-organisms associated with odontogenic infections.

One option, where patients are allergic to penicillins, is clindamycin. It is a bacteriostatic, but its bactericide activity is obtained clinically with the generally recommended dose. The latest macrolides, clarithromycin and azithromycin, may also be used if the patient is allergic to penicillin. Cefadroxil cephalosporin can be used when a wider antibacterial spectrum of action is needed. Metronidazole tends to be used only against anaerobes and is generally reserved for situations in which only anaerobic bacteria are suspected. Tetracyclines are of very limited use in dentistry. Since tetracyclines can cause changes in the colour of the teeth, they should not be prescribed for children under 8, pregnant women, or breast-feeding mothers.

Value of antiseptics and oro-dental hygiene

The use of topical antiseptics in the oral cavity reduces the bacterial inoculate, but it has not been shown to be effective in the prophylaxis of bacterial colonization. However, the pre-operative use of antiseptics in the oral cavity can reduce complications derived from trauma in the mucosa, especially in patients with valve disease, implants of alloplastic material, bone grafts, immunodepressed subjects, the elderly and in patients with bad oral hygiene.

4. ANALYSIS OF DENTAL PATHOLOGY

Tooth decay is a multi-factorial disease involving, among other factors, a wide variety of microbiote; the most frequent bacteria are *streptococci* of the *mutans* group, followed by the genus *Lactobacillus*. These bacteria are involved in the formation of bacterial plaque, but with a different composition depending on the location (58,59).

Bacterial penetration of the tooth occurs without an edge being necessary on the outside surface, and is produced fundamentally through flakes or cracks, pits and the interprism areas of the enamel, even in normal teeth without caries. In cases of incipient enamel caries without cavity, bacterial invasion in the deeper layers of the enamel can be observed, reaching the dentin amelar limit and even the deep dentin layers (60,61), where basically Lactobacillus is detected during the initial stages of dentine caries, prior to later colonization by *Streptococcus* and *Actinomyces* spp.

Streptococci of the *mutans* group (*S. mutans, S. sobrinus, S. cricetus, S. ratius, S. ferus, S. downwi* and *S. macacae) (*62) are the most important in the aetiopathogeny of tooth decay. Consequently, prescribing antibacterial treatment in patients at high risk is advisable for prophylactic purposes even when they do not have an evident lesion (63). Chlorhexidine, topical fluoride and vancomycin type antibiotics are used (to block protein synthesis), as well as iodine- and fluorine-based halogenated solutions (63).

The number of bacteria that invade the pulp or the periapical tissues is directly proportional to the degree of extension of the routes for penetration. Bacterial invasion of the pulp is always a condition for inflammatory pulp response and the seriousness of the process that develops will depend on a series of factors such as: the nature of the invasion, the microbiote, the number of micro-organisms, the endotoxins, the exoenzymes, the metabolites, the exotoxins, the acting time and the host's defensive capability (64).

The bacteria that contaminate pulp tissue can also invade

the periapical tissues, but the degree of bacterial invasion depends not only on the ability to multiply, but also on the motility of the bacteria (64).

Most of the bacteria that originate periapical pathology are sensitive, in order of effectiveness, to treatment with amoxicillin/clavulanate, ampicillin/sulbactam, clindamycin, metronidazole, macrolides, and penicillins (ampicillins, amoxicillins).

One of the big problems of endodontal failure is due to the persistence of bacterial invasion at the canal or periapical level: *Actinomyces israelii65* and *Enterococcus faecalis.66 Actinomyces israelli (*67) has been observed to be resistant to metronidazole and *Enterococcus faecalis* to clindamycin (68).

5. ANALYSIS OF ORAL AND MAXILLO-FACIAL SURGICAL PATHOLOGY

The data in the literature are contradictory, although the series seem to indicate that the reduction in post-operative complications is due as much to improved surgical technique as to rational use of antibiotic prophylaxis. In general terms antibiotic therapy pre- and post-operatively is recommended in those cases that have a high risk of infection or obvious clinical signs of infection.

Surgical interventions can be classified in two large groups, depending on the presence or absence of germs in the surgical zone. A series of standard operations in the speciality are listed below:

1. Surgery with the presence of germs: undescended teeth; exostosis, torus; odontogenic tumours, cysts (uninfected epulis, pre-prosthetic and pre-orthodontic surgery; maxillary fractures (closed); glandular affection; osteotomies; grafts, flaps, and others.
2. Surgeries in the presence of germs: pericoronaritis of the third molar, inflammatory cysts, radicular remains, granulomas, etc.; sialolithiasis, open fractures, traumas, wounds with contusions; super-infection added to the tumour lesion, radionecrosis and others.

Oral surgery

The infection rate is low, and therefore, in healthy patients most oral surgery procedures do not require antibiotic therapy. Prophylactic antibiotic treatment will be used in cases of active infection, patients with co-morbidity or who are immunocompromised.

Exodontia de wisdom teeth: Some series seem to demonstrate that the use of antibiotic therapy post-operatively does not improve prognosis in relation to the possibility of post-operative infection (69,70). However, some authors recommend the use of prophylaxis based on the significant drop in post-surgical complications such as pain, trismus, delayed scarring of the wound and tumefaction (71-74). In a recent randomized, double blind clinical trial of parallel groups the efficacy of pre- and post-operative antibiotherapy was compared with placebo. In the study patients were randomized to three groups: Placebo group, pre-operative prophylaxis group (amoxicillin/clavulanate 2000/125 mg in a single dose prior to surgery) and post-operative prophylaxis or preventive treatment group (amoxicillin/clavulanate 2000/125 mg every 12 hours for 5 days). The prevalence of post-operative infection was significantly higher ($p = 0.006$) in the group of patients treated with placebo (16%) than in the group of patients who received amoxicillin/clavulanate 2000/125 mg, either as pre-operative (5.3%) or post-operative prophylaxis (2.7%). In surgeries that need osteotomy, preventive treatment was better than pre-operative prophylaxis and placebo (24%, 9% and 4% respectively) (3).

Implantology. A recent review of the literature on efficacy of antibiotics in preventing complications and failures following dental implants concluded that there is no evidence either to recommend or to discourage the use of antibiotics for prevention of dental implant complications and failures, due to the absence of randomized, controlled clinical trials (75).

Gynther et al. compared the efficacy of penicillin V administered before and after the surgery against placebo in 279 patients, without differences being found in relation to post-operative infection rate or survival of the implant among the two groups (76). Dent et al., in a multi-centric study of 2,641 dental implants, found a significantly smaller rate of failures in those that had received pre-operative antibiotics in comparison with those who had not. Lastly, in a recent study, no greater efficacy was observed with the use of post-operative antibiotherapy during 7 days as against a single dose during surgery (77). In patients with prior radiotherapy, prolonged antibiotherapy regimes are used to avoided the presence of osteomyelitis or loss of the osteointegrated implant devices. Likewise, based on clinical experience, the use of antibiotics would be recommended in patients with immunodeficiency, metabolic diseases (like diabetes) and risk factors for endocarditis.

Traumatology

Prophylactic antibiotherapy in compound fractures is widely accepted.

Mandibular and dentoalveolar fractures: the antibiotic treatment plans are the classic ones for other cervical-facial pathology (penicillin and derivatives and third-generation cephalosporins). Prophylactic antibiotic treatment in uncomplicated fractures does not seem to provide any benefit although many professionals do treat these fractures in order to cover possible infections and so reduce their incidence. Antibiotic treatment in the first 72 hours is not necessary. Antibiotic treatment of infectious complications (abscesses, pseudoarthrosis, osteomyelitis…) is where there is more consensus, although in this case it stops being prophylactic antibiotherapy and becomes therapeutic.

Orbital fractures: there is no consensus in the literature (some authors defend antibiotic treatment while others do not).

Mid and upper third fractures: third-generation cephalosporins are used in those cases where there is liquorrhea.

Orthognatic surgery and pre-prosthetic surgery

Clean-contaminated surgeries, in which some series have demonstrated effectiveness of post-operative antibiotic

prophylaxis (penicillin, cephalosporins that do not improve prognosis and involve higher cost), although other authors appear to demonstrate there is no evidence of better prognosis related to infection due to post-operative antibiotherapy, especially if administered orally.
Greater incidence of infections in bi-maxillary surgery without antibiotic treatment has been described.
Some studies have used oral levofloxacin or cefazolin IV in mandibular osteotomies, but in this latter case, it is better to use amoxicillin-clavulanate for strains resistant to cefazolin.
In prior publications, the treatment time had been established at 5 days for prophylactic antibiotic coverage, but the incidence of post-operative infection is the same in regimens of 1 or 5 days, although there is a certain improvement in post-operative morbidity by prolonging treatment during 5 days.
Salivary Glands
No effectiveness with the use of antibiotic prophylaxis has been demonstrated in surgeries such as parotidectomy or submaxillectomy.
Oncological, reconstructive and cervical surgery.
It has been demonstrated that peri-operative use of antibiotics significantly lowers the rate of post-operative infections.
As in the above cases, in cervical pathology and, fundamentally, in oncological surgery, prophylactic antibiotherapy regimens can be used combining clindamycin and cefazolin, cephalosporins, aminoglucosides, quinolones or penicillin derivatives with betalactamase inhibitors.
The risk of infection arises with the possibility of clean areas being put in contact with the oral mucosa, since the principal source of contamination in these patients is saliva, which transports a large number of bacteria. Other contributing factors are a bad general condition, immunosuppression states, radiotherapy or chemotherapy preoperatively, reconstruction flaps or those procedures that expose tissues to tissue ischemia or necrosis. The sources of micro-organisms in these pathologies are saliva, skin, teeth and the tumour itself, and therefore the antibiotic of choice must cover not just the common micro-organisms of saliva, such as Gram positive cocci and anaerobes, but also Gram negative organisms that are commonly isolated in tumours. A large number of references in the literature do not consider that Gram negative micro organisms have to be covered in oncological surgery of the head and neck, but recent publications do seem to associate better prognosis with coverage of Gram negative organisms.
An antibiotherapy guideline may be gentamycin + clindamycin, that do well in covering Gram positive, Gram negative and anaerobic organisms (not so cefazolin that does not cover anaerobes). Amoxicillin-clavulanate and ampicillin-sulbactam also have the same spectrum as against clindamycin that does not cover anaerobes sufficiently.
The duration of treatment is not standardized and in many cases is at the discretion of the surgeon. Post-operative antibiotherapy tends to be maintained until removal of drains, although it is prolonged in cases of surgical wound infection, dehiscence or fistula.

Incidence of bacteraemias in relation to dental treatments and oral hygiene	
Bacteraemia due to dental treatments	*Bacteraemia due to oral hygiene*
Dental extraction 51-85%	Tooth brushing 0-26%
Periodontal surgery 36-88%	Flossing 20-58%
Radicular scraping and smoothing 8-80%	Use of dental picks 20-40%
Periodontal prophylaxis 0-40%	Irrigation 7-50%
Endodontia 0-15%	Chewing 17-51%

Table 6. Incidence of bacteraemias comparing dental treatment actions and oral hygiene operations.
Bender IB 1984, Everett ED 1977, Guntheroth WG 1984.

6. ANALYSIS OF PERIODONTAL PATHOLOGY:

Although most rules for antibiotic prophylaxis in periodontia are based on concepts that can be generalized to prophylaxis for surgical oral procedures, periodontal infections present particular situations that should be treated separately.

What procedures in periodontia require prophylactic treatment with antibiotherapy?

This question could be posed in another way: what procedures in periodontia produce bacteraemias?
All dental procedures that induce bleeding will develop bacteraemia that will rarely persist more than 15 minutes (78).
The following procedures or techniques could be considered to fulfil these criteria in Periodontia:
It has been observed that periodontal probing in humans causes transitory bacteraemia, confirmed via blood cultures (79,80). Studies in animals have also demonstrated that radicular scraping and smoothing techniques can cause it (81). In humans, it has been observed that radicular scraping and smoothing techniques cause transitory bacteraemia, whether these are with curette instruments or ultrasonic instruments are used (82,83). Application of chlorhexidine 0.12% by subgingival irrigation, immediately or during use of ultrasonic apparatus or curettes reduces but does not eliminate the transitory bacteraemia (82,83). The use of other antiseptics such as povidone iodide after periodontal use of instruments has not been shown to be effective in reducing or eliminating the transitory bacteraemia (84).
Periodontal surgery causes transitory bacteraemia that is significantly reduced with the use of antibiotic prophylaxis (85). Although the use of antibiotherapy in periodontal surgery procedures is discussed a great deal, post-operative infections occur despite the fact that the prevalence of these infections is low (86). Transitory bacteraemia also occurs with suture removal (87).
The controversy could occur when the evidence of bacteraemias produced by non-invasive manoeuvres such as tooth brushing or gum chewing is analyzed (88,89). Table 6 shows the rate of bacteraemias, comparing dental treatment actions and oral hygiene operations (90-92).

The question that arises then is, if bacteraemia-producing stimuli occur spontaneously several times a day with no type of antibiotic coverage, do other invasive procedures related to surgical manipulations have to be done under antibiotic coverage?
Although it is said that the extent of the inflammation and its seriousness might be related to the magnitude of the bacteraemia and it is logical to think this, it has not been connected in experiments with the clinical-anatomical-pathological degree of the inflammation.
Histological studies have demonstrated that even under normal clinical conditions, a certain tissue alteration is always present that would be compatible with a favourable environment for bacteraemias (93). Nor has any difference been established between gingivitis and periodontitis in the production of bacteraemias (94).
Besides, epidemiology studies report that most of the population at any age has a certain level of clinical inflammation and healthy gums are found in very low percentages of the population (95).

7. ANALYSIS OF THE PATHOLOGY IN CHILDREN

Antibiotic prophylaxis in children follows the same principles as for adults, taking into account only the pharmacokinetic and toxicity peculiarities. In this respect, and by way of example, the use of antibiotics such as quinolones is not recommended for children. Likewise, tetracyclines should not be administered to children less than 8 years of age.
As a starting point, we believe it necessary to define a series of distinctive peculiarities regarding antibiotic treatment in children: a) in the early stages of life, children do not have any medical history leading to suspicion of the presence of possible adverse reactions or drug allergies; b) the larger proportion of water in children's tissues, plus the greater sponginess of the bone tissues, allow faster dissemination of infection on the one hand, and on the other, makes it necessary to ensure a proper adjustment of the dose of the medication prescribed; c) anaesthetic procedures in milk teeth in the process of rhizolysis can include intraligamentary injections, which however, increase the possibility of bacteraemia; and d) the deficient oral hygiene of most children and the consumption of saccharose-rich foods contribute to increasing the number of germ colonies in the oral cavity, and with this, the risk of bacteraemia after oral treatments.
Several studies have assessed the prevalence and extent of bacteraemias after different dental procedures in children. It was demonstrated that just tooth brushing is associated with bacteraemia in more than one in three children (96).Conservative dental treatments, in which wedges or matrices are put in, or orthodontic procedures such as placement or removal of bands can cause bacteraemia in a significant number of children (97). In simple tooth extraction, bacteraemia appears in 40-50% of the children examined (96). The highest levels of bacteraemia are found after intraligamentary injections in local anaesthesia procedures (96.6% of children) (98). *Streptococci* of the *viridans* group were isolated in more than 50% of cases.
The level of oral hygiene has a considerable influence on levels of bacteraemia. Because of this, optimal oral hygiene could be the most important factor in preventing complications consequent to a bacteraemia; in the opinion of some authors, more than any antibiotic course (99).
Dental trauma pathology is an aetiological factor of infection in the oral area, particularly when there is direct exposure of the pulp tissue and/or alteration of the periodontal space. The possibilities of infection will increase when the presence of open wounds in skin or mucosa is added to the trauma in the hard or support dental tissue.

8. PROPHYLAXIS OF BACTERIAL ENCOCARDITIS

These recommendations are a summary of the agreements and consensus documents of the American Academy of Cardiology (37), that has since been accepted by most scientific and professional societies.
It will be applied in all patients with predisposing heart disease who are going to be submitted to a procedure with risk of bacteraemia in oral and maxillo-facial surgery. In relation to the endocarditis risk, we can classify cardiopathies as (37):
1. High risk: endovascular prosthesis, prior endocarditis, complex cyanogenic congenital cardiopathy or systemic-pulmonary fistulas made surgically.
2. Moderate risk: other congenital cardiopathies, acquired valve disease, mitral prolapse with insufficiency, hypertrophic myocardiopathy.
3. Low risk: CIA ostium secundum, operated CIA or CIV, prior by-pass, mitral prolapse without regurgitation, pacemakers, implantable defibrillator.
High and moderate risk patients who are going to have surgery in the maxillo-facial area require antibiotic prophylaxis, using 1 hour before by the oral route or 30 minutes before intravenously as the antibiotic standards. Table 7 shows the antibiotics recommended for children and adults.
In addition, children with a history of IV drug use, and certain syndromes (e.g. Down Syndrome, Marfan's Syndrome) can have a risk of bacterial endocarditis because of the associated cardiac anomalies.
Although not sustained by scientific evidence, the American Academy of Cardiology recommends that "individuals with a risk of developing bacterial endocarditis need to maintain the best possible oral hygiene". Other authors have stated that "maintaining good oral health, thus reducing daily bacteraemias, is probably more important in preventing endocarditis than preventive administration of antibiotics before specific dental interventions."
Another aspect that has to be cleared up in the future is whether bacteraemias associated with active periodontitis are significantly reduced with control of the periodontal infection and therefore, if treatment is a form of prophylaxis

effective against endocarditis. Periodontal pathogenic bacteria rarely cause endocarditis, although the HACEK group of micro-organisms, including *Actinobacillus actinomycetemcomitans* and *Eikenella corrodens,* has increased in importance in the aetiology, which would sustain the hypothesis of a relative increase in the importance of periodontal diseases in the aetiology of endocarditis.

Prophylaxis	Adults	Children†
Standard	Amoxicillin 2 g VO or IV	Amoxicillin 50 mg/kg VO. (maximum 2 g).
Allergic to betalactames	Clindamycin 600 mg VO	Clindamycin 20 mg/kg VO. (Maximum 600 mg)
	Azithromycin 500 mg VO	Azithromycin 15 mg/kg VO
	Clarithromycin 500 mg VO	Clarithromycin 15 mg/kg VO
Oral intolerance	Ampicillin 2 g mg IM or IV	Ampicillin 50 mg/kg IM or IV
Oral intolerance and penicillin allergy	Cefazolin 1 g IM or IV*	Cefazolin 25 mg/kg IM or IV (maximum 1 g)*
	Clindamycin 600 mg IV	Clindamycin 15 mg/kg IV. OR IV. (Maximum 600 mg).

Table 7. Endocarditis prophylaxis recommendations.
† The total dose in children should not surpass the adult dose; follow-up doses one-half the initial dose.
* Cephalosporins should not be used in patients with type I penicillin hypersensitivity reaction (rash, angioedema or anaphylaxis).
VO: orally ; IM: intramuscular; IV: intravenous.

9. CONCLUSIONS

1. The aim of antibiotic prophylaxis in surgery is to prevent the possible appearance of infection of the surgical wound, creating a state of resistance to micro-organisms through antibiotic concentrations in blood that avoid the proliferation and dissemination of bacteria from the point of entry represented by the surgical wound.
2. 10% of antibiotic prescriptions are used for odontogenic infections and a significant part of these are used in prophylaxis.
3. Clinical trials with antibiotics in dental pathologies respond little to the required methodological criteria, and furthermore are not sufficiently numerous.
4. As a general rule, prophylaxis is always indicated when there is an important risk of infection, either because of the characteristics of the operation or due to the patient's local or general conditions.
5. The risk of contamination of the surgical field increases with the time of exposure and the complexity of the trauma produced and is minimized with adequate surgical technique and with the good condition of the patient. However, antibiotic prophylaxis has been shown to be a more critical factor and a subject for discussion.
6. In a study done in our country, it was demonstrated that the complications subsequent to extraction of the third molar are an infection and not exclusively inflammatory, since statistically significant differences were found in the frequency of infectious complications among groups who received preventive treatment (5 days) or pre-operative prophylaxis (single dose) and placebo (2.7%, 5.3% and 16% respectively). Rates of infectious complication were higher in the case of osteotomy or longer surgical duration.
7. Local multi-microbial infections are cutaneous-mucosa or bone infections that occur consequent to invasive dental procedures.
8. Mono-microbial systemic infections are infections that take root in patients with a focus susceptible to infection (endocardial changes, bone or joint prostheses), in patients with greater susceptibility.
9. The physician's criterion for choosing antibiotic prophylaxis or not must be based on the benefit and the cost of the risk. In the last instance, the prophylaxis decision is the choice of the physician, who will use the equation: *risk = degree of damage x probability of experiencing it.* This approach is subjective.
10. To that aim, patients could be classified as: a) healthy patients, b) patients with local or systemic infection risk factors, and c) patients with post-bacteraemia focal infection risk factors. In healthy subjects, prophylaxis is based exclusively on the risk of the procedure.
11. The antibiotic of choice (if prophylaxis is considered necessary because of the type of procedure and patient type) must fulfil the following characteristics:
• Adequate bacterial spectrum, covering all the species involved in local multi-microbial infections or distal focal mono-microbial infections, including aerobic micro-organisms, micro-aerophils, without forgetting the anaerobes that, because of the difficulty in isolating them, are sometimes not considered prevalent in oral-origin bacteraemias.
• Wide clinical spectrum, to cover the greatest number of dental procedures.
• Restricted ecological spectrum in order to limit the effects

on the usual saprophyte flora as much as possible.
- Adequate pharmacokinetics and pharmacodynamics, to allow use in single pre-operative dose in the case of prophylaxis, or wide dosing intervals in preventive, short-term treatment, with half-lives or prolonged-release formulae that maintain adequate concentrations locally (gingival fluid) or systemically (serum) during the entire time the dental procedure lasts (prophylaxis).
- Adequate safety profile, including in paediatric and elderly populations.

Procedure	Prophylaxis in patient at risk (YES/NO)	Prophylaxis in healthy patient (YES/NO)	Antibiotic and regime (pre-intervention dose)
Use of staples for absolute isolation with rubber dikes	YES	NO	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Periodontal prophylaxis and implants	YES	NO	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Periodontal probing	YES	NO	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Periodontal maintenance	YES	NO	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Intraligamentous anaesthesia	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Trunk anaesthesia techniques	YES	NO	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin
			Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Extractions	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Dental re-implants (intentional and traumatic)	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Biopsies	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Drainage incisions	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Bone implants	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Application and removal of surgical sutures	YES	NO	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin

Table 8. Antibiotic prophylaxis in different procedures.

			Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Radicular scraping and smoothing	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Periodontal surgery	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Implant insertion surgery	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Mucosa-gingival surgery	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Removal of implant posts	YES	NO	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Endodontia	YES	NO	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin
			Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Endodontia surgery and apicectomy	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Procedures for and placement of wedges, moulds, orthodontia bands abd pre-formed crowns	YES	NO	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Placement of removable orthodontia apparatus	NO	NO	
Taking impressions	YES	NO	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Placement of retraction thread	YES	NO	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Sculpting procedures with bleeding	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.

Table 8. (cont.)

Pre-prosthetic surgery	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Orthognatic surgery	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Dental and alveolo-dental trauma	YES	NO	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Reduction of maxillary fractures	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Surgery on salivary glands	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.
Maxillo-facial oncological surgery	YES	YES	Amoxicillin + Clavulanic Acid Adults: 2gr+125gr V.O. / 2gr+200gr I.V. Children: 50mgr +6.25 mgr/Kg V.O./ 50mgr+5mgr/Kg I.V. Clindamycin Adults: 600mgr V.O. / 600mgr I.V. Children: 20 mgr/kg V.O. / 15mgr/kg I.V.

Table 8. (cont.)

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