Management of oral dental foci of infection

FRENCH SOCIETY OF ORAL SURGERY

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Abbreviations used

G1	Group of scorers from the different specialities concerned
G2	Group of scorers oral cavity specialists
HPA	High professional agreement
IE	Infective endocarditis
NC	No consensus
PIRS	Potential infectious risk situation
ODFI	Oral dental focus of infection
RC	Relative consensus

General methodology

Objective

Management of oral dental foci of infection (ODFI) is a daily task for oral dental specialists. However, no consensus exists to define measures to be taken and approaches vary greatly depending on the experience and training of practitioners. However, management of this issue is incredibly important in terms of public health. This situation has led the French Society of Oral Surgery (FSCO) to formulate recommendations which are intended to provide clarification to practitioners and to harmonise practices.

Methodology

In light of the lack of valuable resources from the literature and faced with data that poorly reflect the range of situations encountered in practice, it has been necessary to adopt the formalised consensus method, codified by the college of the HAS (French National Agency for Health)[*]. In compliance with this methodology, the steering group has specified the objectives sought, the targets of recommendations and partners to associate with the group (scientific societies). Essential questions concerning the selected clinical situations have been sorted into 4 elementary subject areas:

1) What are the clinical situations in which a search for ODFI must be conducted?
2) How to conduct this search?
3) What strategies are to be adopted?
4) What follow-up measures are to be planned?

After an in-depth research on the literature, the steering group selected relevant references, performed an analysis and critical synthesis of the literature in the form of a bibliography-based argument and has proposed recommendations based on the analysis of the literature.

Two scoring groups have been comprised. The experts in the first group (G1) came from the different specialities which were particularly involved in this subject matter. They were designated by the following societies:

- French Dental Association
- National College of Instructor General Practitioners
- French Society of Cardiology
- French Society of Oral Surgery
- French Society of Dermatology
- French Society of Haematology
- French Society of Ophthalmology
- French Society of Periodontics and Oral Implantology
- French Society of Oncological Radiotherapy
- French Society of Rheumatology
- French Society of Stomatology and Maxillofacial Surgery
- Society of Nephrology
- French Society of Infectious Diseases

[*] Methodological basis to formulate professional recommendations by formalised consensus, HAS, January 2006, **http://www.has-sante.fr/portail/upload/docs/application/pdf/base_methodo_CFE.pdf** (consulted on 12/09/2009)

The second group of scorers (G2) consisted solely of specialist experts on the oral cavity: dental surgeons and stomatologists.
All these scorers were chosen for representativeness based on their professional experience, their method of practice (university hospital, hospital, private practice) and their geographic origin. Studies by these two groups have been directed by a chairman, while a rapporteur wrote the final document.
Questionnaires have been sent to members of the scoring group to collect their opinion on proposals formulated by the steering group.
Out of concern for legibility, in the text of the present argument, mention is made of the "scoring group" to designate which of the two expert groups had performed scoring for each chapter considered; it is understood that the G1 group decided on questions involving various specialities concerned and the G2 group on topics specifically relating to the oral cavity.
HAS has been kept informed of the progress of these studies at each of their stages.

Documentary search

A documentary search was performed by systematic search of the bibliographic databanks (Medline, Cochrane, ISI Web of knowledge and Dentistry and Oral Sciences Source) covering the period January 1980 to April 2011. The languages selected have been English and French. The equations for the search have been:

Periodontitis	AND	diabetes
Apical periodontitis		atherosclerosis
Caries		infective endocarditis
Cellulitis		chemotherapy
gingivitis		radiotherapy
dental abscess		immunodepression
dental infection		pregnancy
		lupus erythematosus
		uveitis
		bisphosphonate
		anti TNF-alpha
		targeted biological therapy
		transplantation
		brain abscess
		cyclosporine
		tacrolimus
		glucocorticoid
		dialysis
		renal impairment
		prosthetic joint
		rheumatoid arthritis

periodontitis	AND	evaluation
apical periodontitis		management

caries		radiograph
Cellulitis		orthopantomogramme
gingivitis		retro-alveolar
dental abscess		CT-scan
dental infection		Diagnosis

Recommendations have been sought for clinical practice, consensus conferences, articles on medical decision-making, reviews of the literature, meta-analyses and other studies on evaluation already published nationally and internationally.
For the purpose of selecting articles not identified during the search, the references mentioned in the articles analysed also were sought.
Furthermore, legislative and regulatory texts were consulted that could be related to the topic, as well as the useful Internet sites (governmental agencies, scientific societies), as well as in-depth articles from the literature by members of the steering group and of the scoring group.
Among the references which have been selected and analysed, 143 were used to write the text.
Each article has been analysed by assessing the methodological quality of the studies in order to assign a level of scientific evidence to each study. Recommendations have been classified according to their strength, taking into account the level of evidence of studies on which they are based*.

Level of evidence 1	• High power randomised comparative trials • Meta-analysis of randomised comparative trials • Analysis of decision based on well conducted studies	Established scientific evidence
Level of evidence 2	• Low power randomised comparative trials • Well conducted non-randomised comparative studies • Cohort studies	Scientific presumption
Level of evidence 3	• Case control studies	Low level of scientific evidence
Level of evidence 4	• Comparative studies containing important bias • Retrospective studies • Case series	

Writing of proposed recommendations
Data obtained from the critical analysis and synthesis of these data have been discussed in the session held by the steering group which established the first proposed recommendations. All these proposals, whether founded on a high level of evidence or not, have been submitted to the scoring groups. In the final text, recommendations based on the highest levels of evidence have been clearly differentiated from proposed recommendations based on professional consensus only.

* Guide to analysis of the literature and grading of recommendations, ANAES, January 2000
http://www.has-sante.fr/portail/upload/docs/application/pdf/analiterat.pdf (consulted on 12/09/2009)

Scoring
Two phases of scoring have taken place successively for each scoring group:

The first phase of scoring was accompanied by dispatch of the bibliographical argument and of proposed recommendations written by the steering group.
For each proposal, members of the scoring groups had to provide a response ranging from 1 (totally inappropriate) to 9 (totally appropriate). Scoring was based on the synthesis of data published in the literature (attached to the questionnaire and whose aim was to inform on the state of published knowledge) and/or on experience of the scorer in the field examined.
In analysis of results of the first round of scoring, all responses were taken into account. In the event of missing values during scoring, the scorers concerned were contacted individually in order to ask them to take a position.
The spread of the responses enabled us to define if there was agreement or disagreement between members of a group on a given proposal. In the event of agreement between members of the group, analysis of responses also enabled the strength of the agreement to be specified. Therefore, if the interval of responses was located within limits of only one of the 3 areas [1 to 3] or [4 to 6] or [7 to 9], "strong" agreement existed between members of the scoring group on the appropriate nature of the procedure, on its inappropriate nature or on uncertainty regarding its appropriate nature. If the interval of responses overlap onto an adjacent area, agreement existed qualified as "relative" between members of the scoring group. In the event that the responses were spread out over all 3 areas or the response comprised in the 2 extreme areas [1 to 3] and [7 to 9], disagreement existed between members of the scoring group on the appropriate nature of a proposal.
In the text, results are expressed by using the following abbreviations:

HPA	High professional agreement
RC	Relative consensus
NC	No consensus

At the end of the first phase of scoring, the scoring group met for a discussion on proposed recommendations and on the bibliographic argument supporting them.

The second phase of scoring was conducted after this meeting by dispatch in an individual letter of a document and of a questionnaire modified according to the discussion conducted in the session at time of the meeting.
In analysis of the results of the second round of scoring, a degree of tolerance in definition of agreement and of its strength has been accepted insofar as the two of the extreme responses, one minimal and the other maximum, have been ruled out.
The proposed recommendations were established only if at most only one response existed at the extreme end of the area in which the median of responses was located.
This was carried out in the same manner in each of the two scoring groups.

Formulation of recommendations
At the end of analysis of responses of the scoring groups, the steering group formulated recommendations based on these responses and finalised the documents to be sent to the review group (as well as to the scoring groups for information).

The authors did not mention in the synthesis the cases for which no consensus emerged, apart from situations for which they considered it important that this absence of consensus be known.

Control of recommendations

Recommendations have been presented and discussed in an assembly held on 21 May 2011 at the scientific session of the French Society of Oral Surgery in Nantes.

The text of the recommendations and of the argument then was submitted to a review group, outside of the scoring group, before being definitively finalised. The review group consisted of experts chosen, in particular, for the diversity of their expertise (cardiology, general surgery, maxillofacial surgery and stomatology, vascular and thoracic surgery, dermatology, infectious disease, general medicine, nephrology, oncology, odontology, ophthalmology, otolaryngology, radiotherapy, rheumatology), their type of practice (university hospital, hospital, private practice) and their geographic origin. Experts in the review group were in charge of providing a reasoned opinion on the methodological quality and scientific validity of the text proposed. The comments of the review group were sent to the scoring groups for modification of the text and validation of the final document.

Control of validity of the scoring phase

Since three members of the steering group were erroneously requested to participate in the scoring phase, an in-depth analysis of the impact of their presence on each score was performed at the request of the project leader of HAS. This analysis showed that the presence of absence of members of the steering group had no impact on result of scores.

Financing of these recommendations was ensured solely by the French Society for Oral Surgery, with the logistical support of the French Dental Association.

Introduction

Infectious disease of the oral cavity is an especially vast field which is the reason behind a considerable proportion of consultations. Caries and periodontal disease represent the most frequent situations, more frequent than disease of the oral mucosa, whether fungal, bacterial or viral. Apart from these strictly oral daily concerns, oral dental specialists also receive patients referred by practitioners from different specialities to look for oral dental foci of infection (ODFI).

The search for foci of infection is ordered mainly by the correspondent in four circumstances:

- Because of a specific **general condition,** i.e. in patients for whom occurrence of secondary infection is of concern (diabetes mellitus, AIDS, patient at risk for infective endocarditis) or for the purpose of stabilising a general disease (diabetes mellitus, rheumatoid arthritis);
- To search for **a starting point** of secondary infection (cerebral abscess, endocarditis, sepsis);
- Before initiating medical or physical **therapy** followed by a patient, that may promote or worsen an infectious process (cancer, chemotherapy, radiotherapy, immunosuppressant treatment, treatment with bisphosphonates, etc.);
- To **prepare** the patient for a surgical procedure (placement of a cardiac prosthetic valve, placement of a stent, a prosthetic joint, etc.) or following such a procedure.

ODFI can in fact worsen or destabilise certain disorders (for example diabetes mellitus or rheumatoid arthritis). Conversely, pathological conditions that can decrease the body's defence mechanism may reactivate oral infection. Lastly, even minimal ODFI can have a significant distant impact on different bodily systems: this is the concept which has been presented at the start of the last century under the term foci of infection.

Screening for ODFI for prophylactic or curative purposes has special importance in patients presenting with a major risk of infection (risk of endocarditis, transplantations, patients with immuno-compromised status), or a disease of unknown aetiology (explained fever of unknown origin, septicaemia).

All infectious diseases of the oral cavity are concerned by these problems. However, in light of the amplitude of the field, the steering group deliberately chose to limit the scope of these recommendations to the most common cases, that is:

- First, infectious manifestations solely of bacterial origin (and therefore, excluded in principal fungal or viral diseases)
- And second, solely dental and periodontal foci of infection: therefore, in principle, other infectious diseases of the mucosa (stomatitis, pharyngitis, etc.) and of the salivary glands have been excluded.

Targets of these recommendations

This report has been designed, in particular, to help practitioners who are oral cavity specialists isolated from hospital institutions, to manage practical situations. It is also aimed at cardiologists, dermatologists, endocrinologist, haematologists, specialists in infectious diseases, general practitioners, nephrologists, oncologists, radiotherapists, rheumatologists, orthopaedic surgeons, thoracic surgeons, vascular surgeons, and generally practitioners from all specialities by these problems.

A chapter on definitions and pathophysiology of dental and periodontal foci of infections has been written at the start of this document expressly for practitioners who are not dental specialists. The notions which are developed in it will evidently appear basic for oral cavity specialists. This same is true for the chapter on the conduct of examination of the oral cavity.

Lastly, the title of this document suggests “oral dental” foci of infection. This usual expression has been chosen for reasons of legibility, so as not to divert or to discourage practitioners who are not dental specialists. In reality, in this text only dental and/or periodontal foci of infection will be discussed.

1. Definitions and pathophysiology of dental and periodontal foci of infection

1.1. General aspects

Since this work is aimed at practitioners from many medical specialities, it appeared necessary to the steering group to remind them of the pathophysiological context of dental and periodontal infection.

Dental and periodontal foci of infection are associated with a specific bacterial flora; thus, certain pathogenic microorganisms are involved in caries, endodontic infection and periodontal disease. Endodontic and periodontal lesions are recognised as being the two major causes of primary infections[1]. The literature indicates that many microorganisms characteristic of the oral bacterial flora are responsible for distant infection and general disorders.

1.1.1. Dental infection:

1.1.1.1. Dental caries:

Dental caries is an infectious multi-microbial and multi-factorial disease. It is the result of the interaction between the host, caries-inducing bacteria of dental biofilm and eating patterns. Clinically, it is manifest by lesions of caries, that is progressive destruction of the hard tissue of the tooth (the enamel, dentine, cementum). A large number of bacterial species are found in deep caries and in root caries. However, the bacteria mainly found are streptococci, lactobacilli and actinomyces.

1.1.1.2. Endodontic periradicular inflammatory lesions (EOPIL)

This involves infectious diseases that involve the endodontic tissue with participation of the periapex; they can be acute or chronic, symptomatic or asymptomatic, associated with a periapical or lateral-radicular lesion or not.

Primary endodontic infection (pulp necrosis) is a multi-microbial infection. It is characterised by a wide variety of bacterial combinations: 4 to 7 species on average, in particular, anaerobes, including Gram positive and Gram negative bacteria. This flora varies depending on the endocanal location and progressively to which are added Gram negative bacteria and anaerobes (the "anaerobic drift").

Primary periapical infections

It can involve acute or chronic disorders, symptomatic or not, with or without peri-maxillary complications.

The following are found:

- Acute disorders:
  - Acute apical desmodontitis (also called acute apical periodontitis or symptomatic apical periodontitis)
  - Acute apical abscess: symptomatic infected tooth without a peri-maxillary complication (suppurated, acute desmodontitis, suppurated periapical periodontitis, sub-periosteal or sub-mucosal abscess)
  - Serious or suppurated cellulitis: a symptomatic infected tooth with a peri-maxillary complication
- Chronic disorders
  - Asymptomatic necrosis (necrobiosis)
  - Asymptomatic necrosis with an apical lesion (apical granuloma, radiculo-dental cyst, chronic apical periodontitis)
  - Suppurated chronic periapical desmodontitis
  - Recurrent apical periodontitis

Whatever the type, periapical lesions are septic. The endocanalar flora of teeth presenting apical lesions are often identical to that of abscesses, granulomas and cysts. It is comprised of 87% anaerobic species.

Symptoms may be related to the nature of the ecosystem of the infected canals; for example, in the event of an asymptomatic tooth, it consists mainly of strict anaerobes (64 to 87%) (*Porphyromonas* and *Prevotella*)

Secondary endodontic and periapical infection

This involves periapical infections involving teeth which have undergone endodontic treatment. Such infections are due either to bacteria initially present in the infected canal and which persist in spite of chemo-mechanical canalar treatment, or to bacteria which were absent from the infected canals and which have penetrated the endocanalar system during an initial therapeutic procedure, or again by circulatory route. The flora is not very numerous and is dominated by Gram positive facultative anaerobes (*Actinomyces, Enterococcus and Streptococcus*).

1.1.2. Periodontal infection

Periodontal disorders or periodontopathies can be defined as multi-factorial infectious diseases. These foci of infection are often underestimated. According to Roth[2], periodontal foci of infections are more dangerous than apical foci of infection since the lesional area is larger.

Periodontal disorders can be manifest by visible inflammation or not, by spontaneous or induced gingival bleeding of variable degree, formation of pockets in relation to loss of attachment and of alveolar bone, mobility of teeth and can lead to tooth loss.

The passage from healthy gums to gingivitis and then periodontitis follows the so-called "anaerobic drift" process.[3]

Chronic gingivitis

This is an inflammation of microbial origin of the superficial periodontium without damage to the deep periodontium. It is related to a lack of dental hygiene and accumulation of dental plaque and tartar.

Periodontitis

This is bacterial inflammation of the deep periodontium. It is accompanied by loss of epithelio-connective attachment, of alveolysis with result of exposure of the root which can continue up to loss of the tooth. The flora is comprised mainly of Gram negative anaerobes and spirochetes.

Several types of periodontitis can be differentiated, which differ by their clinical, radiological signs, their context and their microbiology:

- Chronic periodontitis
- Aggressive periodontitis
- Periodontitis associated with general or infectious diseases
- Refractory periodontitis
- Ulcero-necrotic periodontitis.

1.1.3. Other foci

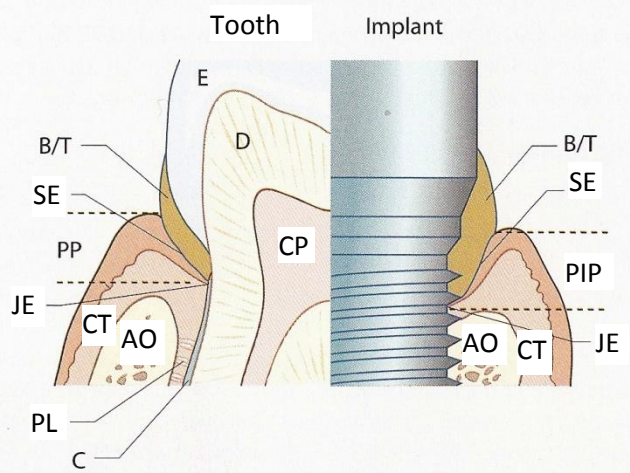
Disimpacted teeth and pericoronitis:

A tooth that is disimpacted is a tooth which is undergoing eruption whose crown is in communication with the oral medium following opening of the pericoronal sac.

Pericoronitis is an inflammatory disease of the pericoronal sac. It can be acute, congestive, suppurated or chronic.

"Peri-implantitis"

Dental implants unlike orthopaedic implants have a transmucosal part that is exposed to the outside medium of the oral cavity. A biofilm develops on transmucosal parts. On this biofilm, infection can develop that may destroy the peri-implant tissue and ultimately result in loss of the implant. This is also called peri-implant mucositis[4] (reversible inflammation located in the superficial soft tissue) or e "peri-implantitis" (destructive inflammatory process) depending on damage to the tissue surrounding the osteo-integrated implant[5]. These lesions can form a peri-implant pocket.



Comparison of development of periodontal disease and of peri-implant periodontitis.
E = enamel
D = dentine
CP = central pulp
C = cementum
PL = periodontal ligament
AO = alveolar bone
CT = connective tissue
JE = junctional epithelium
SE = sulcular epithelium
PP = periodontal pocket
PIP = peri-implant pocket
B/T = biofilm/tartar

Extract from Microbiology in odontostomatology (Fig 3.41)
Chardin H, Barsotti O, Bonnaure-Mallet M. Ed Maloine Paris 2006.

1.2. Microbiological aspects

Microbiology of oral dental infection (from AFSSAPS(French Health Products Safety Agency))[6]

The flora of the oral cavity comprises a complex ecosystem with many bacteria and consisting of over 500 species, divided into about 20 bacterial types. This flora varies over time, but also depend on site of sampling and sometimes according to persons [7].

Starting from birth, the flora of the oral cavity, which is non-existent *in utero*, is comprised from the surrounding environment, and primarily, in contact with the mother during mothering. Bacteria are

present temporarily, but some of them colonise the child's mouth for a persistent period by adhering thanks for specific receptors. At this stage, immunological immaturity authorises this first bacterial colonisation.

Then, the first tooth significantly increases the potential number of niches and sites of bacterial binding, and the gingival grooves enable other bacterial colonisations under anaerobic conditions.

During the first years of life, the oral flora is continuously modified until eruption of the permanent teeth. The saliva and gingival fluid ensure the supply of nutrients necessary for bacteria growth. They also transport enzymes and antibodies which will inhibit adhesion and growth of microorganisms.

Bacteria do not only adhere to the surface; they can form co-aggregates. It is in this way that initial colonisation by streptococci (*S. salivarius, S. mitis*) followed by co-aggregation with actinomycetes (*Actinomyces odontolyticus*) to comprise an acquired exogenous film on the surface of teeth on which other bacteria can then bind (*Fusobacterium nucleatum*), creating new niches for survival for other strict anaerobes which are found in this aerated medium. A cascade of successive colonisations will result in formation of an increasingly complex oral biofilm. The latter evolves throughout life.

In 1995, M.J. Elder *et al.*[8] proposed a review of the different behaviour of microorganisms and of their propensity to organise into a biofilm to cope with less favourable environmental conditions.

Although it was recognised that a periodontal biofilm exists that is largely variable depending on the condition of the periodontal tissue and different from the biofilm covering the tooth in its intra-oral part, it is more recently that the existence of an endodontial, pulpal biofilm has been recognised on teeth which have lost their viability[9]. The same conditions exist around various human prosthetics: replacement products replace a natural structure and form the bed for development of a biofilm. Furthermore, this production takes place under conditions of relatively strict anaerobiosis, even total anaerobiosis, and at a distance from the body's defence mechanism, i.e. under optimum conditions for occurrence and extension of the biofilm.

Debelian *et al*. [10] have demonstrated that all endodontic canals without a symptomatic apical reaction contain microorganisms (*Fusobacterium nucleatum*, *Prevotella intermedia, Propionibacterium acnes, Propionibacterium propionicus, Peptostreptococcus anaerobius, Eubacterium sp., Porphyromonas endodonticis, Staphylococcus aureus, etc.*), with a marked dominance of anaerobes. Furthermore, it is during an orthograde endodontic procedure on this type of tooth where it goes beyond or ends 2 mm below the apical foramen, bacteraemia is observed in 33 to 50% of cases.

Leonardo *et al*. [11] have demonstrated that teeth that present pulp necrosis and a chronic periapical lesion, as well as teeth with persistent infection or resistant to therapies, contain microorganisms in the totality of their canalar system, from the principal canal up to the dentine tubuli, going through lateral, secondary and accessory canals, the branchings of the apical delta, the apical foramen, as well as areas of absorption of apical cementum and periapical tissue. The regions of resorption of cementum adjacent to the apical foramen are invaded by many microorganism, either alone (cocci, bacilli or filaments) or in combination (bacilli and filaments).

In the event of periodontitis, the flora of the periodontal pocket contains a higher percentage of Gram negative bacilli. Among these bacilli, *Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis* and *Prevotella intermedia* are considered as the three main bacteria responsible for these

disorders. These pathogens are absent from the oral flora in infants before 3 years of age. Colonisation is done by contact of the subject with other persons. These pathogens are found more frequently in the flora of children who are from families affected by periodontitis. This contamination seems to occur relatively late and occurs rarely in childhood, except for *Aggregatibacter actinomycetemcomitans* which starts to colonise a child at age around 4 to 7 years. Taxonomic advances have made it possible to show that this is a heterogeneous group. Although *Prevotella pallens* and *Prevotella nigrescens* are found in young children, the same is not true for *Prevotella intermedia which strictly speaking* now is considered as a periodontal pathogen. During initial colonisation, a very wide clonal heterogeneity of pioneering strains exists. It is known that mother to child transmission is common, but in some disease situations the origin of the pathogen remains unknown. Although adhesion is the major step in colonisation, it is not known which factors enable persistent of some clones. *Tannerella forsythensis*, more recently isolated, is considered as another periodontal pathogenic agent.

Dental and peri-dental clinical disease results from complex interactions between the host and an ecological microenvironment.

Since the extent of bacterial organisation into the biofilm has been demonstrated, it is necessary to supplement this notion of spatial organisation by the notion of qualitative organisation. Relations between bacteria in fact are not the result of chance. Socransky[12-13], in 1998, showed that bacterial species involved in periodontal diseases can be combined by groups. The notion of bacterial complexes in periodontal pathogenic flora takes shape: it no longer is possible to refer to periodontal pathogenics associated with a single bacteria, apart from *Aggregatibacter actinomycetemcomitans*.

Thus, the following are found:

- *Aggregatibacter actinomycetemcomitans* serotype b which forms a complex by itself, which has not been compared to other bacteria;
- yellow complex: formed by *Streptococcus gordonii, Streptococcus intermedius, Streptococcus mitis* and *Streptococcus sanguis*
- green complex: *Capnocytophaga* spp., *Aggregatibacter actinomycetemcomitans* serotype a, *Eikenella corrodens* and *Campylobacter concisus;*
- violet complex: *Veillonella parvula* and *Actinomyces odontolyticus;*
- orange complex: *Campylobacter gracilis, Campylobacter rectus, Campylobacter showae, Eubacterium nodatum, Prevotella intermedia, Prevotella nigrescens, Peptostreptococcus micros,* and the subspecies of *Fusobacterium nucleatum;*
- red complex: *Porphyromonas gingivalis, Tannerella forsythensis* and *Treponema denticola.*

1.3. Pathophysiology of development and of dissemination of infection

Two types of pathophysiology can be differentiated: first, disorders generated by caries and second, periodontal diseases.

1.3.1. Pathophysiology of caries

Superficial caries

Superficial caries limited to the dentine at first generates sensitivity to temperature and chemical stimuli (mainly acid and sugar, in particular, in the stickiest forms: candies, chocolate, honey). This sensitivity, which is increasingly intense and durable in relation to the depth of the caries damaged, is still however limited by the duration of application of the triggering cause. It is found in examination by spraying of teeth with cold or hot water.

Pulpitis

Pulpitis differs by intensity of pain: it is the traditional “tooth ache”; pain is induced, but this time by minimal temperature changes: the warmth of a pillow or simple intake of room air. It persists after application of the triggering cause and only abates slowly. It most often is preceded by pain induced during meals and neglected. Pulpitis is immediately relieved by excision of the essential vasculo-nervous bundle present in the pulp chamber and the endocanalar system.

Pulp necrosis and desmodontitis

Sometimes after a fleeting stage of acute pulpitis, the pulp lesion progresses to necrosis. At first, asymptomatic, necrosis then becomes responsible for development of an anaerobic microbacterial infection, so-called “desmodontitis”: pain is induced by pressure or tapping on the tooth. The inflammatory widening of the desmodontal ligament results in mild egress of the tooth toward the occlusive plane and thus premature contact on the tooth concerned. This contact that is very painful is inevitable, for example, during automatic swallowing of saliva which causes dental occlusion. Spraying with cold water is asymptomatic or even relieves pain, but warmth on the contrary, exaggerates it.

Apical disease

The infection can worsen further, either right away or after a chronic phase during which an apical granuloma is formed, for which warming results in a dental abscess. The pain then becomes permanent, sharp, while the clinical presentation consists of signs of maxillary and peri-maxillary infection: swelling and fever.

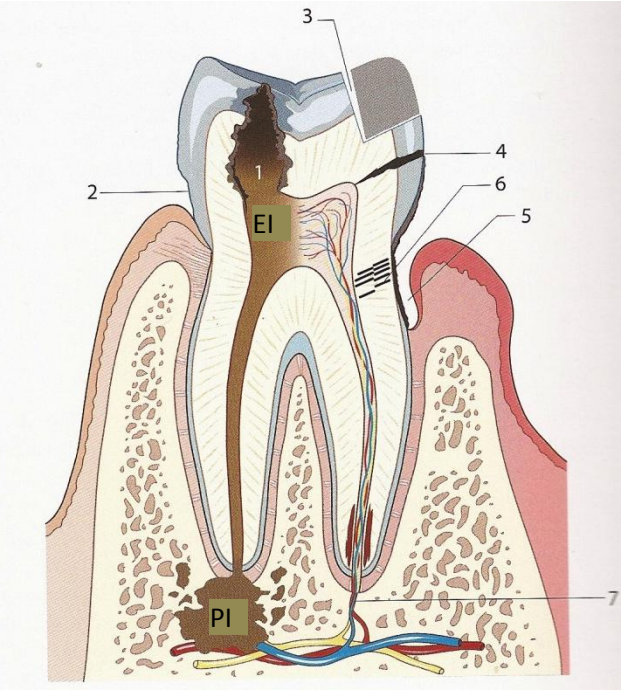
1.3.2. Pathophysiology of periodontal disease

Bacterial invasion is the first factor essential to development of periodontal disease.

Tartar is formed by mineralised dental plaque. Inflammation is related to local irritation due to tartar which forms the ideal support for the oral pathogenic flora. Inflammation and bacteria cause proteolysis, resulting in fragilisation and more or less localised destruction of the gum.

Periodontitis progresses by cyclical phases of activity and of quiescence. The existence of periodontal pockets is not considered as an indicator of the activity of the disease, but tends to represent the total

amount of periodontal destruction generated by periods of previous exacerbation. The cyclical feature observed may be in close relation with the efficacy of the host's immune response.



Endodontic and periapical infection.
Pathways of penetration of bacteria into the endodontium:
1 = carious lesion
2= erosion
3 = non-waterproof restoration
4= fracture
5 = periodontal pocket
6 = dentine tubuli
7 = blood circulation
EI = endondontal infection
PI = periapical infection

Extract of Microbiology in odontostomatology (Fig 3.22)
Chardin H, Barsotti O, Bonnaure-Mallet M. Ed Maloine Paris 2006.

1.3.3. Dissemination of infection

1.3.3.1. Foci of infection

Historically, the notion of oral infection developed with Miller in 1891. Billings in 1912, attempted to demonstrated a link between cases of chronic arthritis and oral infection.

The theory of Thoden van Velzen[13] suggested three possible mechanisms responsible for distant foci of infection:

1) metastatic infection: the secondary focus is caused by distant colonisation of a background favourable to development of microorganisms present in the primary focus, generally in a frail subject.
2) metastatic focus "due to microbial toxins"; these are exo- and endotoxins released by microorganisms which may produce platelets reactions and can cause tissue invasion.
3) "metastatic inflammation" due to "immunological trauma": soluble antigens released may produce formation of immune complexes that are deposited on tissue.

1.3.3.2. Bacteraemia

Bacteraemia is translated by existence of bacteria in the circulation. Passage of bacteria into the blood or lymphatic circulation can result from mechanical action.

Theoretically, dental treatment represents situations with a risk of infection. The number of bacteria which enter into the blood circulation during dental treatment is estimated at 1 to 10 bacteria per ml of blood (or CFU/ml), with a fall in this level of 10 to 15% after 10 minutes. Thus, microorganisms

disseminated in the body are quickly destroyed by the immune system. Nevertheless, under unfavourable conditions, this bacteraemia can result in foci of infection.

The incidence of bacteraemia after dental treatment is highly variable depending on authors and procedures performed. For Okabe *et al.*[14], in a study on 183 patients, bacteraemia was found in 72% of cases of tooth extraction; this risk of bacteraemia during tooth extraction may rise with age of the patient, periapical and gingival inflammation, duration of treatment (longer than 100 minutes), bleeding (more than 50 ml) and number of teeth extracted (100% bacteraemia was found starting with 15 tooth extractions performed in the same treatment session). Other studies show similar figures with risk of bacteraemia after dental extraction of between 51 and 100%[15]. Transient bacteraemia after dental treatment is detectable 5 minutes after the start of treatment and persists 10 to 30 minutes[16]. Bacteria found in these episodes of bacteraemia in particular are anaerobes[10,14].

A study by Maestre *et al.*[17] in 2008 showed that radicular surfacing caused bacteraemia in 77 % of cases. Here again, the bacteria found most often were anaerobes (*Prevotella spp., Micromonas micros and Fusobacterium nucleatum*).

In 1986, Bender et Montgomery[18] showed that non-surgical endodontic treatments by themselves do not cause bacteraemia, but that associated procedures may be the origin of bacteraemia. The latter may be largely avoided by simple measures for eradication of microorganisms in the mouth by means of preoperative oral antiseptics. These authors analysed bacteraemia subsequent to different types of dental procedures, immediately after treatment and 10 minutes later. Results allow to believe that the immediate incidence of bacteraemia after dental treatment depends on the degree of trauma, the local concentration of bacteria and the extent of gingival inflammation.

It seems that more bacteraemia is spontaneously caused by actions of daily living than that of bacteraemia induced by dental treatment[19]. In fact, it is clearly established that bacteraemia of dental origin occurs spontaneously and daily outside of any particular dental treatment [20]. Mastication of chewing-gum, for example, may produce bacteraemia in 17 to 51% of cases [15,21]. According to Bhanji *et al.*[22], manual tooth brushing causes bacteraemia in 46% of cases and brushing with an electric toothbrush in 78% of cases. According to these authors, regular tooth brushing during a month exposes the subject to a cumulative risk of 5,376 minutes of bacteraemia , while an uncomplicated tooth extraction only results in 6 minutes of bacteraemia on average. Similarly, Roberts *et al.*[23] found bacteraemia in 38.5% of cases after tooth brushing, with the latter lasting only a few seconds. In comparison, in another study, the same team demonstrated that average time of bacteraemia after a tooth extraction was about 11 minutes[24].

In summary, there are many more cases of bacteraemia caused by actions of daily living (tooth brushing, mastication) than by dental treatment[25] (Level of evidence 2)[*].

Bacteraemias induced by oral dental procedure

Procedure	% bacteraemia
Exodontal	
Simple	40-50

[*] See classification levels of evidence, p6

multiple	70-100
Periodontology	
Non-surgical	
Surface tartar removal	10-90
Surgical	
Access flap	40-90
Gingivectomy	80
Endodontic	
Non-surgical	
Intracanalar	0-30
Extracanalar	0-50
Surgical	
Periapical curettage	30
Elevation of a flap	80
Anaesthesia	
periapical	20
intra-ligamentary	90
Placement of orthodontic rings	10
Placement of a dental dam	30
Placement of matrices	30

According to Seymour[24].

Moreover, the results of bacteraemia must be taken in relative context. Shariff *et al.*[26] in 2004, in a study that was both prospective and retrospective, evaluated the relations between bacteria of the oral cavity and infection in patients undergoing haemodialysis. None of the blood cultures performed in 87 patients revealed a microorganism in the oral cavity.

1.4. Classifications of foci of infection

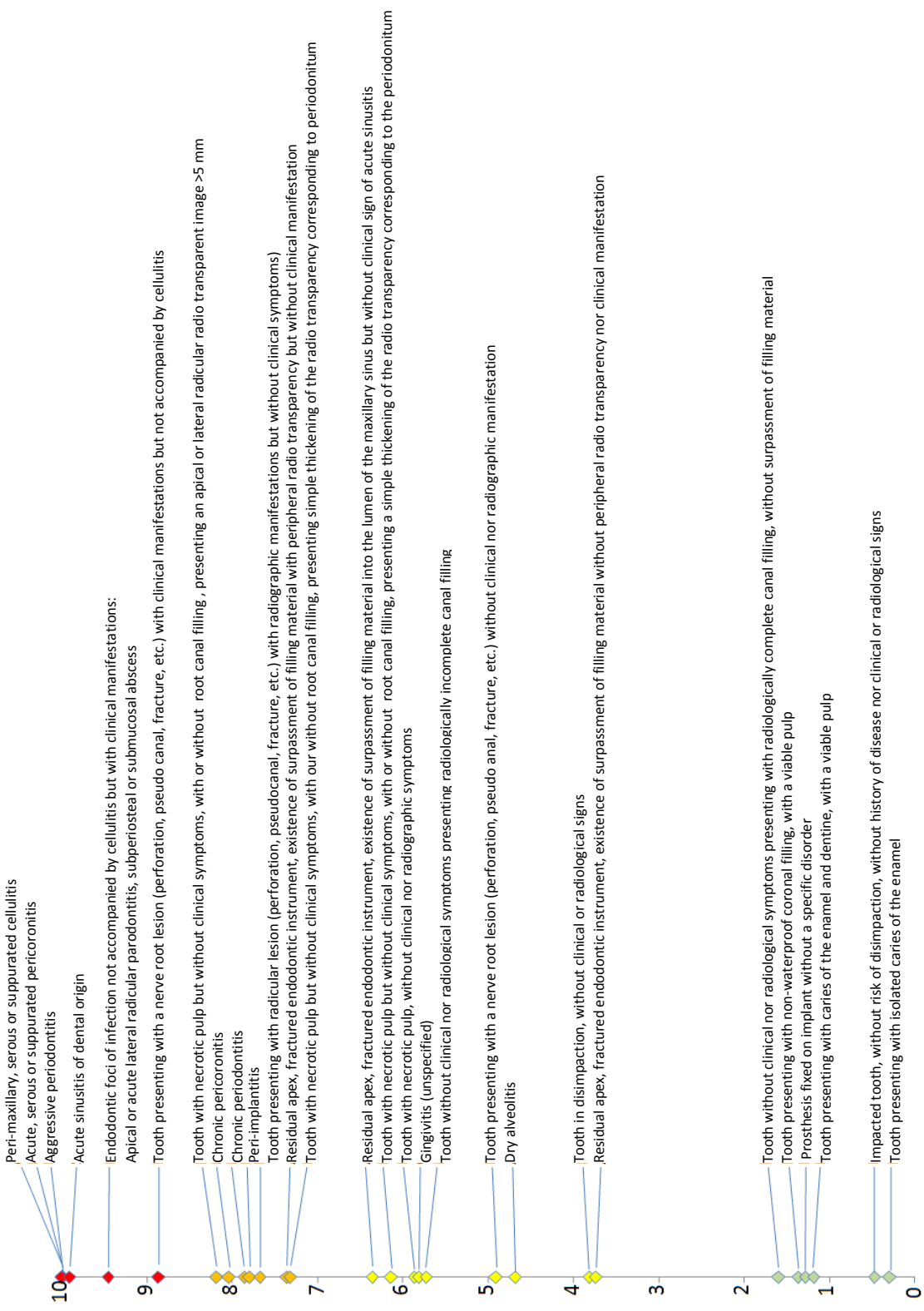
Among cases which correspond to risk of infection, the following can be differentiated:

- ODFI (active or latent): actual existence of bacterial foci, whether it involves confirmed infection or if there is not clinical impact at time of observation;
- Potential infectious risk situations (PIRS): that may become foci of infection in the future as the result of conditions satisfied locally. This possible outcome can only be evaluated from a statistical standpoint.

In the literature, no study based on scientific evidence proposes classification of cases by risk of infection. To compensate for this lack and to help readers form an idea on the virulence of the situations most commonly encountered, a questionnaire has been submitted to the scoring group comprised of dental surgeons and stomatologists (G2).

It involved estimating the degree of virulence of various clinical situations. This rating scale reproduces the average of opinions of the scoring group on assumed virulence of different situations by taking as the basis the case of a natural tooth in a dental arch and by estimating the additional risk compared to that of a healthy tooth, at time of an examination (without prejudging the possible course of this virulence overtime): from 0 (no additional risk) to 10 (maximum risk of infection). The grading obtained is presented in the following table. Values represent solely opinions of the experts. This table has no scientific value and therefore is provided only for purposes of an example.

Presumed virulence of different clinical situations:
Graph modelling of opinions of the experts of the G2 group



(additional risk of infection compared to a health tooth in a dental arch from 0 to 10)

Presumed virulence under different clinical situations:
Detailed table of the opinions of the experts of the G2 group
(additional risk of infection compared to a health tooth in a dental arch from 0 to 10)

	Case	Estimated virulence	Standard deviation
Very high virulence	Peri-maxillary, serous or suppurated cellulitis	10.00	0.00
	Acute serous or suppurated pericoronitis	10.00	0.00
	Aggressive periodontitis	10.00	0.00
	Acute sinusitis of dental origin	9.91	0.20
	Endodontic foci of infection not accompanied by cellulitis, but with clinical manifestations: apical or acute latero-radicular periodontitis, sub-periosteal or sub-musocal abscess	9.46	0.56
	Tooth presenting with a root lesion (perforation, pseudo canal, fracture, etc.) with clinical manifestations, but not accompanied by cellulitis.	8.86	1.10
Elevated virulence	Tooth with necrotic pulp, but without clinical symptoms, with or without filling of the canal, presenting an apical or latero-radicular radio-transparent image > 5 mm	8.18	1.17
	Chronic pericoronitis	8.05	1.06
	Chronic periodontitis	7.86	0.84
	Peri-implantitis	7.80	1.48
	Tooth presenting with a root lesion (perforation, pseudo canal, fracture, etc.) with radiographic manifestations, but without clinical symptoms	7.68	1.23
	Residual apex, fractured endodontic instrument, existence of surpassment of filling material with peripheral radio-transparency, but without clinical symptoms	7.36	1.21
	Tooth with necrotic pulp, but without clinical symptoms, with or without filling of the canal, with an apical or latero-radicular radio-transparent image > 5 mm	7.32	1.35
Medium virulence	Residual apex, fractured endodontic instrument, existence of surpassment of filling material into the lumen of the maxillary sinus, but without clinical sign of acute sinusitis	6.36	1.91
	Tooth with necrotic pulp, but without clinical symptoms, with or without filling of the canal, presenting a simple thickening of the radio-transparency corresponding to the periodontium	6.14	1.55
	Tooth with necrotic pulp, without clinical nor radiological symptoms	5.86	1.67
	Gingivitis (unspecified)	5.82	1.66
	Tooth without clinical nor radiographic symptoms presenting with radiologically incomplete canal filling	5.73	1.74
	Tooth presenting with a root lesion (perforation, pseudo canal, fracture, etc.) without clinical nor radiographic manifestation	4.91	1.38
	Dry alveolitis	4.68	2.03
	Impacted tooth without clinical nor radiological sign	3.82	1.08
	Residual apex, fractured endodontic instrument, existence of surpassment of filling material without peripheral radio-transparency nor clinical manifestation	3.73	1.01
Low virulence	Tooth without clinical nor radiological symptoms presenting with radiologically complete root canal filling without surpassment of filling material	1.59	1.07
	Tooth presenting with non-waterproof coronal filling with viable pulp	1.36	0.95
	Prosthesis fixed on an implant without any specific disorder	1.27	0.88
	Tooth presenting caries of the enamel and dentine with a viable pulp	1.18	0.90
	Impacted tooth without risk of disimpaction with no history of disease nor clinical nor radiological sign	0.46	0.46
	Tooth presenting with isolated caries of the enamel	0.28	0.46

Another questionnaire was sent to the same G2 scoring group, which involved definition and management of foci of infection, according to formalised method of consensus (See methodology).

Results obtained made it possible to collect a high professional consensus for the following cases:

- A viable tooth with caries whose treatment does not carry a risk of a break in the pulp does not represent a focus of infection that may give rise to dissemination (HPA)*.
- By comparison with endodontic treatment with a viable tooth,
  - Endodontic treatment of a necrotic tooth
  - Repeat endodontic treatment

  Representing an enhanced risk of resulting in bacteraemia (HPA).
- A necrotic tooth represented by ODFI or PIRS (potential infectious risk situation) (HPA).
- Disimpacted teeth represent active or latent foci of infection (HPA).

On the contrary, no consensus was obtained for the following cases:

- No consensus to confirm that by comparison with a viable tooth, a dental implant represents an enhanced risk of infection (it should be noted that in grading of infectious risk situations established by the scoring group, virulence of a unit prosthesis on an implant however was estimated at slightly greater than that of the natural tooth) (NC).
- No consensus to confirm that a healthy tooth located in a field (beam) of therapeutic radiation (with a higher probability of caries damage as the result, in particular, due to the absence of saliva) represents an enhanced risk of infection (NC).

* See p7 table of abbreviations used

2. Clinical cases in which screening for ODFI must be conducted

It is the duty of the dental specialist to look for ODFI systematically. The preferred position of the general practitioner also makes him or her a health care player who can detect dental and periodontal infectious diseases in a systematic clinical examination.

Since oral cavity infections can interact with the patient's general condition, it is especially necessary to look for the existence of ODFI in a certain number of clinical cases.

2.1. Patients presenting with sepsis and/or a chronic inflammatory syndrome distant from the oral cavity

2.1.1. Sepsis and foci of infection

Sepsis is defined as the combination of a generalised inflammatory reaction and of organ failure secondary to infection. Severe sepsis can lead to septic shock defined as induced hypotension, persistent in spite of appropriate vascular filling therapy[27]. The causal pathogenic agent is most often a bacterium (more rarely it may involve a virus, a fungus or a parasite). Currently, the focus of infection found is most frequently urinary, abdominal, cutaneous or in particular a lung infection.

Electing to look for ODFI will occur depending on type of bacterium found.

In the literature, many studies emphasise the severity and consequences of infections distant from oral-dental origin. A retrospective study[28], concerning observation of 35 patients with need for hospitalisation, reported a 29% rate of general complications (septicaemia, endocarditis, brain abscess, etc.). The authors reported three deaths among the patients who had a general complication; the three had a concomitant serious general disorder.

The overall incidence of brain abscess is about 1 per 100,000. It can have different causes: post-traumatic, diffusion by contiguity, and metastatic haematogenic origin. A brain abscess of haematogenic origin is manifest in particular in the frontal, parietal or frontal-parietal lobe areas[29]. Brewer[30] classified 60 cases of brain abscess, among which a dental origin was demonstrated in 6.6%. In a retrospective study, out of 163 patients hospitalised for a brain abscess, Roche *et al*.[31] found a dental origin in less than 2.5% of cases; the most common origin was a sinus starting point (34%).

The microbial flora found in a brain abscess of dental origin is polymorphous. In 70% of cases streptococci are found, as well as *Bacteroides* and *Fusobacterium*. Meningitis sometimes accompanies a brain abscess and can be the first clinical sign detected. In 0.3 to 2.4% of cases, streptococci in the oral cavity are the microorganisms implicated[32].

A pyogenic liver abscess most often is of GI origin with infection occurring via the biliary tract or the portal system. Only a few cases of dental origin have been reported in the literature. Most often this involves infection caused by *Fusobacterium nucleatum*[33-34].

Studies have also established a relation between pneumonia and periodontitis[35]. The risk of developing pneumonia appears 1.67 times higher if patients have not received active dental care; conversely, treatment of periodontitis would make it possible to reduce this risk[36].

2.1.2. Chronic inflammatory syndrome

Fever (fever, chronic fever, undulating fever) most often reveals a bacterial or viral process. The clinical examination is very important and must take into account possible oral-dental disease. However, a study of the literature revealed only a few reports of cases where this combination could be established.

2.1.3. Immune disorders triggered by or promoted by infection

It is suggested that an immune disorder can be triggered by an infection. Here again, only a few cases reported are found which implicated oral-dental infection[37].

Patients with rheumatoid arthritis suffer earlier, more often, and with more severe forms of periodontitis than the rest of the population[38]. Other studies[39-40] have suggested that treatment of periodontal disease reduces the activity of rheumatoid arthritis (Level of evidence 2).

2.2. Patients presenting with an increased risk of oral-dental infection as the result of cervicofacial radiotherapy

Cervicofacial radiotherapy exposes the patient to the risk of osteonecrosis.

External radiotherapy is administered in over 70% of cancers of the upper aerodigestive pathways. Oral-dental complications of cervicofacial radiotherapy result from adverse effects which affect the oral mucosa, maxilla and mandible, salivary glands or teeth[41].

Dental caries[42-43] spontaneously occurs in the four to six months following the end of external radiotherapy. It progresses in unusual sites and does not spare any tooth. It affects mainly the neck of the tooth in the form of annular proliferative caries which progresses up to coronal-radicular fracture, but also, after erosion, the free borders and the occlusive points. Such post-radiation caries differs from ordinary caries by its greater aggressiveness and rapid progression. Such caries is related to hyposalivation and oral cavity acidity. Untreated, it can result in osteoradionecrosis. This major complication is also likely to occur following tooth extraction or a break in the mucosa (in particular ulceration by a removable denture), or even with no apparent cause.

Traditionally, osteoradionecrosis occurs a few weeks to a few years after radiation (81% within three years)[44]. In a series of 413 patients who underwent cervicofacial radiotherapy, 8.9% developed osteoradionecrosis.[44]

Al-Nawaz and Grötz[45] studied the change in the oral cavity flora in 22 patients after radiation greater than 30 Gy. Five periodontal pathogens were studied (*Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, Prevotella intermedia, Tannerella forsythensis, Treponema denticola*) with the aid of DNA probes, as well as existence of lactobacilli and *Streptococcus mutans*. No change was observed for periodontal pathogens in contrast to an increase in number of pathogens involved in development of caries.

Hyposalivation, whatever its origin, enhances the risk of infection as the result of qualitative and quantitative changes in saliva. Studies[42,46-47] demonstrated a tolerance dose to the parotid gland of

about 25 to 30 Gy on average (Level of evidence 2). However, even if the dose delivered is low, a post-treatment period of major decrease in flow of saliva exists. The rate of recovery is inversely proportional to the dose of radiation received and the period of recovery extends from one to two years.

Insofar as sparing of one or both submandibular glands does not compromise tumour control, the mean dose delivered to the glandular tissue should not exceed 39 Gy[48]. The clinical benefit of sparing of the submandibular glands, however, currently has not been demonstrated.

Radiation and dental implants

The rare articles published on this topic are almost all retrospective studies with a small sample size[49]. Implant failures are relatively rare but are unforeseeable. They occur mainly with doses of radiation greater than 45 Gy. Most often it involves the absence or loss of osteointegration and in rare cases osteoradionecrosis.

Ben Slama *et al.*[50] reported a case of osteoradionecrosis that developed 3 months after the end of radiotherapy around implants that had been osteointegrated for 10 years.

Ozen *et al*.[51], in an in vitro study, reported a 21% increase in dose of radiation in the vicinity of titanium implants (up to 2 mm). This observation suggests an additional risk factor around the implant.

Proposed recommendation:

Before any cervicofacial radiotherapy, an oral-dental evaluation must be undertaken as quickly as possible (HPA).

2.3. Patients who may develop an infection from an oral-dental starting point due to systemic factors

2.3.1. Cases relating to an abnormal condition

2.3.1.1. HIV infection

Cases of gingivitis and ulceronecrotic periodontitis are reported in 16 to 17% of patients with HIV infection (human immunodeficiency virus) in Africa [52] and 23% in India. In Europe, this rate fluctuated between 10 and 19% before the advent of three-drug anti-retroviral therapies[53-54].

Among oral lesions strongly correlated with HIV are gingivitis and ulceronecrotic periodontitis. Rams *et al.*[55] evaluated the serological status of patients with ulceronecrotic gingivitis (UNG). Results indicated that 69% of patients were seropositive and that this lesion was often the first manifestation of the disease. Furthermore, a correlation exists between decrease in the CD4 count and the probability of developing UNG: patients presenting with a CD4 count <200/mm3 have 20.8 times more risk of developing UNG than patients with a CD4 >200/mm3.

Proposed recommendation:

If HIV seropositive status is diagnosed in a patient, it is desirable to perform an oral-dental evaluation to look for an ODFI (HPA).

2.3.1.2. Renal impairment

A poor oral-dental condition is often observed in patients undergoing haemodialysis, which is explained in particular by the frequency of poor oral-dental hygiene. However, the literature contains different findings. Bayraktar *et al.*[56] in a case-controlled study showed that patients who undergo dialysis presented with more dental plaque, tartar and gum bleeding. However, the depth of the surveys was not statistically significant (Level of evidence 3). A case-control study by Garcez *et al.*[57] concerning patients who did not undergo dialysis did not demonstrate a significant difference between patients with renal impairment and a control group (Level of evidence 3).

Shariff *et al.*[26] studied infection of the venous line in patients undergoing dialysis. They concluded that bacteria of oral origin are rarely or never the cause of this type of infection.

In a cross-sectional study on 11,211 patients, Fischer *et al.*[58] estimated that periodontitis may be a risk factor for chronic renal impairment in the same capacity as hypertension, smoking and hypercholesterolemia.

2.3.1.3. Diabetes mellitus

The relation between diabetes mellitus and periodontal disease has been established by many epidemiological studies which are sometimes contradictory. But they are in agreement, in the vast majority, in demonstrating both that diabetes is a risk factor that can promote development of periodontitis, and also that periodontal infection seems to affect control of blood glucose.

Grossi *et al.*[59] followed 113 subjects with type II diabetes and periodontal disease; they divided them into 5 groups depending on the periodontal treatment received during initial preparation. Groups treated with 100 mg doxycycline by systemic route during two weeks had a glycosylated haemoglobin (HbA1c) reduced by 10% compared to baseline; however, this percentage rose slightly between 3 and 6 months and, according to the authors, this situation may correspond to a return of a pathogenic flora which had not been totally eradicated.

Christgau *et al.*[60], did not observe a significant improvement in metabolic control of diabetes (insulin dependent or non-insulin dependent) after treatment of periodontal disease. However, their group of patients had good metabolic control of diabetes from the outset.

According to Taylor [61], periodontal treatment enables better control of blood glucose. A meta-analysis confirmed these results[62].

Periodontal infection appears increasingly frequently as a potential factor in altering homeostatic balance that may cause pathological manifestations at a distance from the starting focus of disease.

In summary:

Eradication of ODFI improves control of blood glucose in diabetic patients (Level of evidence 1).

Treatment of periodontal disease improves control of blood glucose within three months (Level of evidence 2).

Proposed recommendation:

Whenever a patient is diagnosed with diabetes, it is recommended that an oral-dental evaluation be performed (HPA).

2.3.1.4. Atherosclerosis

Janket *et al*.[63] in a meta-analysis showed that periodontal disease was associated with a 19% increase in risk of development of cardiovascular disease (Level of evidence 1).

Over the last 15 years, many epidemiological studies have demonstrated that a relation exists between periodontal infection and coronary artery disease, but with wide variations in the strength of this link. A meta-analysis in 2008[64] showed that periodontal disease is a risk factor independent of other known risk factors for coronary artery disease, and whose relative risk is estimated between 1.24 and 1.35 (Level of evidence 1).

According to another meta-analysis[65], the prevalence and incidence of coronary artery disease is significantly increased in patients with periodontal disease. Another study[66] showed that periodontal disease was also a risk factor for stroke, in particular non-haemorrhagic stroke.

Mechanisms of this associated have not yet been clearly established. Among the direct links, general inflammation can be suggested, revealed by an increase in different biomarkers including CRP[67]. Among other proposed hypotheses would be the possibility that some periodontal microorganism may initiate or exacerbate a disease process on the wall of the arteries as the result of their pro-aggregant activity (theory of the infected thrombus). Concerning indirect links, periodontal disease and atherosclerosis may share the same risk factors, such as tobacco, obesity, hyperlipidaemia, diabetes.

2.3.1.5. Bronchopulmonary infection

Pneumonia is an infection of lung tissue caused by a wide variety of infectious agents. It can be life-threatening, in particular in the elderly or in a patient with immunocompromised status. Anaerobic bacteria can be the cause of pneumonia, and dental plaque logically appears as an origin for these bacteria, in particular in patients with periodontal disease[68-70].

2.3.1.6. Dermatological disorders

A search of the literature did not reveal any series of oral-dental infection relating to a dermatological disease. However, isolated clinical cases have been reported. Lesclous and Maman[71] for example observed disappearance of rosacea following treatment of oral-dental infection.

In the absence of confirmed data, it is legitimate to eliminate possible causes of oral irritation. Therefore, it is appropriate to look for and to treat an ODFI in the event of oral lichen planus to prevent worsening by Koëbner's phenomenon. Similarly, in the event of facial erysipelas, ODFI or a focal sinus infection can be sought[72].

2.3.1.7. Other cases without a level of evidence

In a certain number of disease cases and oral-dental cause can be suggested, although the scientific literature cannot provide formal evidence. This is the case in particular for uveitis or pelade.

Currently, a consensus has emerged in dermatology to consider that cases which have been reported probably were only chance coincidences and that it is not necessary to look for a dental or periodontal origin in cases of pelade.

Similarly, in ophthalmology, it appears that advances in immunology over the last 30 years have clarified the causes of uveitis. Currently, it is generally recognised that it is not necessary to look for a dental or periodontal origin in a case of uveitis.

Furthermore, in terms of sports medicine, there is no longer any evidence to confirm that ODFI could cause tendonitis.

2.3.2. Cases related to use of medicinal products

2.3.2.1. Immunosuppressant therapies

In the event of transplantations and autoimmune diseases, the following recommendations are found:

Little *et al.*[73] suggest, prior to liver transplantation, oral-dental evaluation with elimination of active foci of infection. For patients with good oral-dental condition, they suggest that treatment be as conservative as possible, with tightening of measures of prevention. On the contrary, they advise treating patients with poor dental hygiene and presenting with severe periodontal disease or many caries with or without periapical foci of infection, by tooth extraction followed by prosthetic rehabilitation.

Little *et al.*[74] also suggest that prior to chemotherapy or hematopoietic stem cell transplantation (HSCT), dental and/or periodontal care be performed as quickly as possible before transplantation and at least one week before start of chemotherapy.

Apart from grafting and organ transplantation, several autoimmune diseases may be treated by immunosuppressant or immunomodulated treatments. Among the most common:

- Rheumatoid arthritis
- Disseminated lupus erythematosus
- Immunological thrombocytopenic purpura
- Autoimmune haemolytic anaemia
- Autoimmune erythroblastopaenia
- Polymyositis and dermatomyositis
- Sjögren's syndrome
- Cryoglobulinaemia
- Vasculitis
- Anti-factor VIII auto-antibody
- Thrombotic micro-angiopathies
- Extramembranous glomerulonephritis

- Pemphigus vulgarus
- Myasthenia gravis
- Neuropathy with anti-MAG antibody
- Multiple sclerosis

These autoimmune diseases can be treated with different immunomodulator treatments:

2.3.2.1.1. Treatment with corticosteroids

Inhibition of the immune system and of the inflammatory process are two central components of the action of glucocorticoids. The result is an increase in risk of infection during steroid therapy. Furthermore, their anti-inflammatory action partly masks signs of infection, which can delay diagnosis and therefore management.

In a retrospective study analysing 71 clinical studies, Stuck *et al.* evaluated the increase in relative risk of infection as 1.6 in patients undergoing long term steroid therapy. The risk of infection was not increased for patients receiving a dose of less than 10 mg prednisone-equivalent per day. Although this risk is not strongly increased by moderate dose of glucocorticoids, opportunistic infection and infectious complications nevertheless seem to be more frequent outside of short term courses of therapy.

Proposed recommendation:

Systemic corticosteroid therapy does not justify specific management solely as the result of its existence:

- If administered at dosage of less than 10 mg/d prednisone-equivalent (HPA)

or

- If given for a duration of less than 8 days at a dosage less than or equal to 1 mg/Kg/d prednisone-equivalent (HPA).

2.3.2.1.2. Targeted biological therapies for immunosuppressant purposes

The targeted therapies for immunosuppressant purposes obtained by biological genetic engineering currently are widely used in many specialties (rheumatology, oncology, haematology, immunology, dermatology, gastroenterology, etc.). It involves for example the following:

- Abatacept (Orencia®)
- Adalimumab (Humira®)
- Alemtuzumab (Mabcampath®)
- Etanercept (Enbrel®)
- Infliximab (Remicade®)
- Ofatumumab (Arzerra®)
- Rituximab (Mabthera®)
- Tocilizumab (RoActemra®)

Their links with oral-dental infection lie in their ability to inhibit one or more pathways of the adapted immune response. Although their mechanisms of action are different, a common denominator exists, resulting in weakening the immune defence mechanisms and promoting infection. Infliximab, adalimumab and etanercept inhibit TNF alpha, abatacept inhibits pathways of co-stimulation, rituximab and ofatumumab cause lymphopenia B, alemtuzumab causes severe lymphopenia B and T, and tocilizumab inhibits interleukin 6.

The use of these new immunosuppressant agents represents an important risk factor for oral-dental infection. Measures to be taken in treated patients are detailed in paragraph 4.1.2 (p 45).

2.3.2.1.3. Other immunosuppressant therapies

Cyclosporine, tacrolimus, sirolimus and everolimus due to their immunosuppressant activity are part of treatments intended to reduce risk of rejection after transplantation of a solid organ or of graft versus host disease after haemopoietic stem cell transplantation. Patients who undergo organ transplantation or hematopoietic stem cell transplantation are often treated with combinations of immunosuppressant agents usually including steroids. Therefore, it is necessary to consider them as at an especially high risk of infection.

NB: Cancer chemotherapies, potentially immunosuppressant, are mentioned in the following chapter for further legibility.

Proposed recommendation:

An oral-dental evaluation must be performed as soon as possible before transplantation or initiation of immunosuppressant therapy insofar as the urgency to initiate treatment authorises it (HPA).

2.3.2.2. Cancer chemotherapy

During cancer chemotherapy, oral-dental infections have high morbidity and can sometimes even result in death of the patient[76]. Patients present with an increased risk of infection, either by occurrence of new oral-dental infection, or by exacerbation of chronic lesions[77-78]. Chemotherapy in particular can induce mucitis, which can itself be a portal of entry for bacteria and cause bacteraemia.

It should be noted that inflammatory responses can be modified during the bone marrow suppressant phase: usual signs, such as erythema and swelling, can be altered; therefore, their absence is not sufficient to rule out infection[79].

Bergmann *et al.*[80] studied changes in the flora of the oral cavity and of saliva in patients followed for leukaemia. They observed a decrease of 64% in flow of saliva in 28 days following start of chemotherapy. Concomitantly, they observed a doubling of number of bacteria, with no qualitative change in the flora.

The study by Dreizen *et al.*[81] concerning 1500 subjects with leukaemia reported that one third of these patients had an oral infection during chemotherapy. In another study,[82-83] the same authors identified a 9.7% rate of oral infection in the context of different types of cancer.

Patients undergoing chemotherapy are especially sensitive to periodontal infection during periods of neutropaenia[83].

2.3.2.3. Bisphosphonates

Proposed recommendation:

At time of initiation of treatment with a bisphosphonate (whatever the indication), it is recommended that an oral-dental evaluation be performed (RC).

Refer to recommendations of AFSSAPS*.
See also paragraph 4.4 (p 49).

2.4. Patients who may develop a focus of infection from an oral-dental starting point

ODFI, even minimal, can have a distant important impact on different body systems.

2.4.1. Risk of infective endocarditis

The best known example of an infectious complication related to secondary localisation of bacteria in the aftermath of an oral-dental procedure is that of infective endocarditis (IE).

Infective endocarditis results from colonisation by circulating bacteria (bacteraemia) of a fibrinous platelet vegetation that has developed on the endocardium most often is abraded or on a prosthetic heart valve. This disorder remains relatively rare, but its incidence does not seem to have decreased over the last 10 years in spite of efforts at prevention. This apparent stability conceals profound epidemiological changes with an increasingly elderly population that is affected, the increase in incidence of endocarditis on a prosthesis and of staphylococcal endocarditis.

In a prospective epidemiological study by Hoen *et al.*[84], conducted during a year (1999) in all hospitals of six areas representing 26% of French population (390 patients chosen with IE according to *Duke University* criteria), the incidence of IE in Metropolitan France was estimated at 31 new cases per million population and per year. The incidence seems higher in men with 44 new cases per million population and per year versus 17 in women. The course of microbiological profile is marked by an increase in incidence of IE caused by group D streptococci and staphylococci. The authors observed a marked decrease in the incidence of IE caused by oral streptococci, which decreased from 27% in 1991 to 17% in 1999, concomitantly with an increase in the incidence of IE caused by Staphylococcus aureus.

The majority of series reported only a very low number of cases of endocarditis complicating an invasive oral-dental procedure (2.7 to 7% of epidemiological series). However, even in the event of a

* Recommendations on oral-dental management of patients treated witih bisphosphonates (19/12/2007), **http://www.afssaps.fr/Infos-de-securite/Lettres-aux-professionnels-de-sante/Recommandations-sur-la-prise-en-charge-bucco-dentaire-des-patients-traites-par-bisphosphonates** (consulted on 12/09/2009)

time correspondence retrospectively suggested between conduct of an oral-dental procedure and occurrence of endocarditis, it is not possible to determine with certainty if bacteria at the origin of the endocarditis was caused by the procedure, if it had been caused by oral-dental disease which was the reason for conduct of the procedure or if it had been induced by an action of daily life (tooth brushing, mastication).

The study by Van der Meer *et al.*[85] concluded that dental procedures only cause a few cases of IE and prophylaxis would have prevented only a small number of such cases. Similarly, in a multicentric study by Strom *et al.*[86], the authors concluded that dental procedures were not a risk factor for IE including in patients with valvular heart disease. Lastly, according to Duval *et al.*[87], "a very large number of doses of prophylaxis would be necessary to prevent only a very small number of IE".

Consequently, the need and efficacy for systematic antibiotic prophylaxis before dental procedures in high risk subjects has been called into question. At the latest updates, recommendations of different scientific societies have evolved in agreement towards a decrease in indications for antibiotic prophylaxis and the emphasis is placed on prevention by oral-dental hygiene and monitoring. The scoring group advises that one should refer to the latest recommendations in force[88].

Currently, it is considered that only patients with a high risk of IE must receive antibiotic prophylaxis[88].

Cases of patients at high risk for infective endocarditis
Carriers of a prosthetic cardiac valve
History of endocarditis
Congenital heart disease: - Cyanogenic not repaired, including shunts and palliative shunts - Completely repaired with prosthetic material (placed by catheterisation or surgically) for 6 months following the procedure - Repaired with residual defects on site or adjacent to the site of the prosthetic patch

NB: See also recommendations of chapter 3.1 on conduct of clinical examination, p ***Erreur ! Signet non défini.****.*

Patients presenting with valvular heart disease who have not undergone surgery have a moderate risk of IE and do not justify antibiotic prophylaxis[88].

Other cases, in particular of patients with an implanted cardiac pacemaker, coronary artery bypass grafting and vascular stents do not increase risk of IE from an oral-dental starting point[88].

2.4.2. Risk related to a prosthetic joint

Infections of prosthetic joints from an oral-dental starting point are rare and may occur in only 0.04 to 0.2% of total of arthroplasties [89-93]

A review of the literature[94] reported a certain number of cases of joint infection strongly associated with foci of infection or with treatment of the oral cavity. However, the level of evidence of the causal relation between ODFI and an infection of a prosthetic joint remains low. The same is true concerning the association between treatment of the oral cavity and joint infection. An elevated risk of bacteraemia does not seem to be correlated with a high risk of infection in arthroplasty. According to this review, staphylococcus is responsible for over 25% of cases of infection of a prosthetic joint after dental care, even though it represents only 0.005% of the oral flora and is only very rarely found in cases of bacteraemia of dental origin.

Proposed recommendation:

However, before surgery for prosthetic joint placement, it is recommended that an oral-dental evaluation be performed as soon as possible (HPA).

2.5. Specific case of pregnancy

Two epidemiological cases have been identified as the leading cause of neonatal morbidity and mortality[95]: they involve preterm birth (<37 weeks, with an overall percentage in Europe of 5 to 9%) and/or low birth weight (<2500 g, i.e. 6.4% of births in Europe).

Several promoting factors have been demonstrated in these events (socioeconomic level, age at time of pregnancy). Genitourinary inflammation and infection are also found. However, 50% of causes of preterm birth remain unknown[96].

Periodontal diseases have been suggested as a possible source of inflammation and of infection relating to this event.

Some studies in fact have shown the existence of periodontal pathogens (*P gingivalis*) in the placenta (Level of evidence 3) [97-99].

Moreover, a study by Rakoto-Alson[100] conducted on 204 pregnant Madagascan patients showed that the index of plaque and index of papillary bleeding were significantly higher in cases of preterm births or of low birth weights. Furthermore, the existence of periodontal disease was significantly associated with risk of preterm birth (77% vs. 8%).

A multicentric case-controlled study[101] conducted on 1108 women who had a preterm birth and 1094 women who gave birth at full term showed a rise in risk of preeclampsia (odds ratio 2.46) in patients with generalised periodontitis. The association between periodontitis and preeclampsia may be related to an increase in C reactive protein and other mediators of inflammation (cytokines, PGE2) [102-104]. Therefore, periodontal disease may be a marker for susceptibility to inflammation. However, treatment of periodontal disease would not make it possible to reduce risk of a preterm birth[105].

A review of the literature reported contrasting results regarding effect of periodontal treatment during pregnancy; it would not make possible a decrease in number of preterm births or of low birth weights of neonates (Level of evidence 2). Nevertheless, treatment of periodontal disease is possible during pregnancy and preferably during the 2nd trimester.

Proposed recommendation:

In pregnant women or women who intend to become pregnant, it is recommended that an oral-dental evaluation be performed(HPA).

3. How to conduct screening for an ODFI?

Whenever it involves screening for ODFI in a medical context, an oral-dental evaluation must be especially complete and careful. Its objective is to demonstrate all ODFI, patent or latent, and to reveal possible factors promoting the infection. It requires a rigorous interview, as well as clinical and radiographic examination, and even laboratory tests.

3.1. Clinical Examination

Interview

The interview will focus on investigating the patient's general and loco-regional history. Its purpose is to define the patient's general condition and thus the inherent risk. It is necessary to look for general and functional signs suggestive of ODFI.

Physical examination

Exo-oral examination

It must look to detect all clinical signs that may be associated with oral-dental infection:

- Cervicofacial swelling
- Cutaneous fistula
- Cervicofacial adenopathy, specifying their characteristics (location, number, size, consistency, adherence, inflammatory characteristic)

Endobuccal examination

Examination of the dentition, performed under proper lighting with a mirror, with a straight probe, with a hooked probe and a periodontal probe will detail the following:

- General dental condition
- Number intrinsic and extrinsic value of remaining teeth
- Existence of caries, existence of loss of coronal substance
- Existence of hairline cracks or fractures
- Existence of disimpacted teeth
- Existence of quality of coronal restoration
- Tooth mobility according to Mülheman's index
    - 0: ankylosis
    - 1: perceptible physiological mobility between two fingers
    - 2: transverse mobility visible with the naked eye less than 1 mm
    - 3: transverse mobility greater than 1 mm
    - 4: axial mobility
- Viability of the pulp (use of electrical or thermal tests)

In their study evaluating diagnostic performance of the different tests, Petersson *et al.*[106] observed that for viable teeth, the probability of obtaining sensitivity to the test was evaluated at 90% for the cold test, 83% for the warm test and 84% for electrical test; for necrotic teeth, the probability of not obtaining sensitivity with the same test was evaluated at 89%, 48% and

88% respectively. The authors concluded that a positive response to cold or to electrical tests was highly associated with probability of vitality of the pulp.

- Changes to colour of the coronal structure
- Existence of pain on palpation or on percussion

Examination of the periodontium

It is important to diagnose the cause of possible halitosis in order to determine its origin. Volatile sulphur compounds produced by Gram negative anaerobes, the majority of which are periodontal pathogens, have toxic effects on periodontal tissue and weaken non-keratinised mucosa, by modifying the structure of fibroblasts, by activating monocytes and altering the healing process[107].

The practitioner must be able to evaluate whether a relationship exists between the extent of inflammation and the quantity of plaque and plaque retention factors (tartar, overlapping restoration, untreated lesions of caries). This report can help the practitioner determine the patient's susceptibility with respect to bacterial invasion.

Examination of the periodontium must evidence the following:

- Inflammation, translated by a change in colour (erythema), size (oedema or hyperplasia) and increase in tendency to bleeding (during tooth brushing, mastication or spontaneous bleeding). Inflammation translates the extent of reaction of the gingival tissue to supragingival bacterial plaque.

- Oedema, which is the result of extravasation of intravascular fluid into the extracellular compartment of the gingival connective tissue. The tissue then takes on a smooth and shiny appearance, most often starting from the papillae which partially emerge from the spaces between teeth.

- Silness and Loë's plaque index (valid index)
    - 0: no plaque
    - 1: thin plaque film and contact with the marginal gum visible only after investigation with a probe
    - 2: moderate accumulation of plaque in contact with marginal gum; no plaque in the spaces between the teeth; visible deposits with naked eye
    - 3: large accumulation of plaque in contact with the marginal gum; existence of plaque in the spaces between the teeth

- Probing can demonstrate two important parameters: depth of a pocket and loss of attachment. It provides information on severity of lesions produced by periodontal disease but also is used as a guide and a therapeutic marker during the re-evaluation and maintenance phases. It is considered that a site is healthy when the depth of a pocket does not exceed 2.5 to 3 mm.

- Bleeding during probing: Probing of a healthy sulcus with a soft-tip probe does not cause bleeding. Bleeding during probing provides the best diagnostic criterion of gingival

inflammation; although it does not prove the activity of a lesion, on the other hand its absence seems to be significant for stability over time of the lesion observed[108].

- Loë and Silness gingival index (validated index)
    - 0: no sign of inflammation
    - 1: change in colour
    - 2: inflammation visible with the naked eye and a tendency to bleeding during passage of a probe
    - 3: important inflammation and tendency to spontaneous bleeding

- Suppuration: Oozing or discharge of pus which can occur either in response to probing or when the practitioner exerts pressure on the free gum with a finger. It is a late sign of periodontal infection. It is necessary to establish a differential diagnosis with a lesion of endodontic origin (pulp viability, clinical signs of gingival inflammation, radiological signs).

- The existence of lesions between the dental roots. This examination is performed with a Nabers probe to demonstrate areas of root separation: horizontal bony loss is measured, which makes it possible to divide lesions according to Hamp *et al*.'s classification[109].
    - Class I: horizontal bony lysis less than 3 mm.
    - Class II: horizontal bony lysis greater than 3 mm non-transfixing
    - Class III: transfixing bony lysis

Proposed recommendations:

An evaluation to look for ODFI must imperatively include a clinical examination (interview, periodontal probing, tests to determine viability, percussion, palpation of lymph nodes, etc. (HPA).

In a clinical examination in patients at high risk for infective endocarditis, periodontal probing must be performed under antibiotic prophylaxis (HPA).

3.2. Radiological examination

Its purpose is to look for or to verify existence of manifest or assumed disease in a clinical examination. It will specify the extent and type of lesion (dental caries, apical lesion, apex or residual roots, impacted tooth, foreign bodies).

The orthopantomogramme (OTP or panoramic radiograph) often is a first-line examination. In fact, it makes it possible to obtain, simply and quickly, an overall image of all dental-alveolar structures. The dental panoramic radiograph completes the clinical examination. It appears essential in the initial evaluation and provides information in particular on existence of impacted teeth, dystopia, dysplasia, residual roots or cysts, caries, granuloma, periodontal disease and endodontic treatments.

Endobuccal x-ray views (retroalveolar or retrocoronal) complete the orthopantomogramme, with superiority in evidencing the integrity of the periodontium (lamina dura, ligamentary thickness, alveolysis), of the root, the quality of canal filling, and existence of apical lesions.

In a prospective study, Bishay *et al.*[110] in 1999 compared in 65 patients who were to undergo haematopoietic stem cell transplantation, the contribution of a dental panoramic radiograph with that of a long-cone retroalveolar evaluation. The latter made it possible to detect in a significant manner caries, periodontal lesions and defect in coronal restoration. They did not find a difference for detection of periapical foci of infection. On the contrary, the panoramic radiograph was proven to be significantly better in detecting impacted teeth. These authors concluded that the two examinations are complementary and that they must be used jointly in a radiological examination of high risk patients.

According to recommendations of HAS[111], concerning prescription of radiological examinations:

- Before radiotherapy or chemotherapy, the treatment and restoration of the oral-dental status requires a panoramic radiograph which completes the clinical examination and provides information on existence of impacted teeth, residual roots or cysts and value of endodontic treatment. Retroalveolar radiographs can refine the panoramic examination (Level of evidence 3).
- Generally, in a search to detect a focus of infection in the context of a systemic disorder or before surgery, a complete dental imaging study will be performed (Level of evidence 2).

In the event of doubt on existence of a periapical foci of infection, a CT-examination may be prescribed. In an experimental study in animals, Jorge *et al.*[112] in fact showed that a CT-scan was able to demonstrate periapical lesions before they were visible in a conventional radiological examination.

Proposed recommendations:

An initial evaluation to look for ODFI must imperatively include a panoramic radiograph (HPA).

In the event of doubt of the reading of the panoramic X-ray, the radiographic examination must be completed by other tests: retroalveolar views, cone-beam volumetric tomography, a CT-scan (HPA).

3.3. Laboratory test evaluation

A complete blood count is part of the general evaluation of infection, as well as measurement of certain plasma proteins (CRP, procalcitonin). But although it can call attention to an unspecified inflammatory syndrome, the laboratory evaluation cannot confirm the dental or periodontal origin.

4. Which therapeutic strategies should be adopted?

All studies found by a documental search showed a high disparity regarding proposed measures to be taken with regard to ODFI. In light of this heterogeneity of data of the literature, the scoring group was asked to issue an opinion on management of foci of infection in high risk patients.

Proposed recommendations:

General population

For the overall population, independently of any notion of disease:

- It is recommended that ODFI be ruled out(HPA).
- It is recommended that PIRS be ruled out (RC).

Information

Discovery of ODFI must be mentioned in the information given to the patient (HPA).

This information must specify the possible consequences of this infection (HPA).

Discovery of a PIRS must be mentioned in the information given to the patient (HPA).

This information must consist of the following:

- Contain an evaluation of risk of development of an infection (RC).
- Clarify the possible consequences of such infection (HPA).

Elimination of foci of infection

Compared to a healthy patient in whom it is the elimination of foci of infection is recommended, the elimination of ODFI is particularly recommended (HPA):

- Before **non-aplastic anaemia-inducing** cancer chemotherapy, insofar as the urgency to initiate treatment authorises it

- In a patient at moderate risk of infective endocarditis

- Before treatment with bisphosphonates (whatever the indication)

- In patients with chronic respiratory disease (chronic obstructive pulmonary disease, asthma, etc.)

- In patients with controlled diabetes

- In a woman who intends to become pregnant

It is **<u>imperative</u>** to eliminate ODFI:

- Before transplantation or initiation of immunosuppressant therapy, insofar as the urgency to initiate the treatment authorises it (HPA)

- Before **aplastic anaemia-inducing** chemotherapy, insofar as the urgency to initiate treatment authorises it (HPA)

- Before cervicofacial radiotherapy (OFDI located in the radiation beam) (HPA)

- In subjects at high risk of infective endocarditis (HPA)

- Before implantation of a prosthetic joint (RC)

- In diabetic patients whose diabetes is not under control (glycosylated haemoglobin > 7%) (RC)

General approach in patients presenting with specific risk of infection (other than dental):

Evaluation of risk:

It is recommended that prior contact with a doctor responsible for follow-up of the patient be established to evaluate the medical risk (HPA).

Infectious emergency:

In the event of occurrence an oral-dental infection, the general medical context (radiotherapy, chemotherapy, cardiac surgery, etc.) must not delay the surgical and/or medical management of the infectious emergency condition. In particular, an abscess must be drained (HPA).

Therapeutic decision:

In the event of ODFI such as PIRS, the choice of oral-dental therapy must integrate multiple notions, in particular (HPA):

- The patient's vital prognosis related to the general disorder
- The risk related to abstention from therapy, in particular depending on assumed virulence of the foci of infection
- Morbidity inherent in each therapeutic solution
- expected benefit of the proposed treatment for patients' comfort of living
- Patients' foreseeable compliance with procedures of hygiene and repeat visits

In all cases, the different treatments must be explained to the patient and his informed consent must be collected (HPA).

Healing

Healing of the mucosa after tooth extraction requires a minimum duration of one week. It must be re-evaluated by a repeat clinical examination (HPA).

4.1. Immunosuppression:

Overall, the scientific literature is not of unanimous opinion on this topic. There are two opposing approaches: to adopt the same practices as for prophylaxis of infective endocarditis in patients at high risk of infection as the result of immunosuppression, or to offer more subtle approaches depending on context. In the majority, these studies are based solely on professional agreement[6].

4.1.1. Chemotherapy

As the result of the requirements to fight the disease, available time before a first course of therapy is often very reduced and thus makes it impossible to administer all the necessary oral-dental treatments[113]. This lack of time requires treating lesions which appear the most virulent as a priority.

An investigation to evaluate professional practices has been conducted on 132 members of the American Academy of Maxillofacial Prosthetics[114]. 68% responded to the questionnaire. All practitioners were agreed on the need for an evaluation before chemotherapy and on the difference between acute and chronic disorders. Endodontic periapical lesions must be treated most often with repeat treatment while teeth which present severe periodontitis must be removed. However, the decision on the conservation of a tooth was adapted based on its strategic value.

Toljanic *et al.*[115] evaluated, in a prospective study, the assessment and dental treatment before aplastic anaemia-inducing chemotherapy. 48 patients were enrolled in the study. Chronic oral-dental infections were classified as mild, moderate or severe, depending on probability of occurrence of an acute infectious event during chemotherapy. 79% of patients presented with at least one chronic lesion and 44% presented with a severe disorder that might be complicated during courses of therapy. The mean duration of hospital stay was 37 days (between 17 and 125 days). During this period, two patients had an abscess which was treated with antibiotic therapy without discontinuation of chemotherapy. The authors concluded in the possibility of administering chemotherapy in patients with a chronic disorder with no additional risk. This approach would make possible more conservative treatment for patients who are to undergo chemotherapy.

Asymptomatic endodontic lesions rarely worsen during chemotherapy[116], unlike periodontal lesions[117-120]

In the context of severe neutropenia (neutrophil count < 1000/mm^3), the American Academy of Paediatric Dentistry recommends antibiotic prophylaxis prior to an invasive procedure[121].

Lastly, several studies are in agreement on the fact that oral dental treatment before chemotherapy may reduce febrile episodes and infections during courses of therapy[118,122-124]

<u>Proposed recommendations:</u>

<u>Before chemotherapy</u>

Insofar as the emergency to initiate treatment so authorises, the oral-dental evaluation must be undertaken as quickly as possible before the start of cancer chemotherapy (HPA).

Surgical management intended to restore the oral cavity must be undertaken as soon as possible so that healing of the mucosa is acquired before start of chemotherapy (HPA).

<u>During chemotherapy</u>

Invasive therapeutic procedures (tooth extraction, etc.) must be performed:

- With knowledge of laboratory test data (complete blood count, coagulation test) (HPA)
- Only if urgent (RC)
- Under antibiotic prophylaxis continued up until complete healing of the mucosa of the wound if the neutrophil count is less than 500/mm^3 of blood (HPA) (no consensus exists on antibiotic prophylaxis for a neutrophil count greater than 500/mm^3) (CP).

Apart from emergency cases, surgery can be performed during a phase when the neutrophil count is normal (HPA).

4.1.2. Targeted biological therapies:

Recommendations* have been published by the French Rheumatism and Inflammation Club (CRI: specialised section of the French Society of Rheumatology).

Recommendations of the CRI concerning oral dental care

1 – Anti TNF alpha

It is recommended that oral-dental hygiene and regular care be performed. In the event of a poor oral-dental condition, appropriate care must be performed before starting treatment with anti-TNF alpha.

Conservative care
There are no items justifying discontinuation of anti-TNF alpha.

Health care with risk of infection (tooth extraction, drainage of an abscess, etc.)
The recommendation is to discontinue anti-TNF alpha and to offer antibiotic prophylaxis.

Placement of implants
There is no formal indication to discontinue anti-TNF alpha by remaining vigilant to the potential risk of infection.

Practical cases
In the event of surgery or of scheduled oral-dental care, prophylaxis is justified, in particular discontinuation of anti-TNF alpha, within a sufficient time period to limit risk of infection. Contact the doctor who prescribed anti-TNF alpha.

Duration of discontinuation of anti-TNF alpha before surgery:
- *Etanercept : at least 2 weeks*
- *Infliximab : at least 4 weeks*
- *Adalimumab : at least 4 weeks*

2 – Rituximab

It is recommended that oral-dental hygiene and regular care be performed. In the event of a poor oral-dental condition, appropriate care must be performed before starting treatment with Rituximab.

Health care with risk of infection (tooth extraction, drainage of an abscess, etc.)
Non-administration of a 2nd intravenous infusion of Rituximab if treatment must be performed between 2 infusions of CT. However, most often, the medicinal product does not need to be discontinued because the cycle of two infusions will have been performed with effects on immunity lasting at least 6 months. The recommendation is to offer antibiotic prophylaxis.

Implants
No special precaution to be observed while remaining vigilant to potential occurrence of infection.

* Rheumatism and Inflammations Club. Practical forms. **http://www.cri-net.com** (consulted on 16/07/2011)

3 – Abatacept

Considering data on safety which reported a higher incidence of serious adverse events of an infectious nature in the Abatacept groups than in the placebo group (3% vs. 1.9%), oral-dental hygiene and regular care are recommended. In the event of poor oral-dental care condition, appropriate care must be performed before starting treatment with Abatacept. For conservative care, antibiotic prophylaxis can be proposed. For care with a risk of infection (tooth extraction, drainage of an abscess, etc.), the recommendation is to postpone the infusion of Abatacept and to offer antibiotic prophylaxis.

4 – Tocilizumab

Oral-dental hygiene and regular care are recommended. In the event of poor oral-dental condition, appropriate care must be performed before starting treatment with Tocilizumab.

Conservative care
There are no items justifying discontinuation of Tocilizumab.

Care with risk of infection (tooth extraction, drainage of abscess, etc.)
The recommendation is to discontinue Tocilizumab before dental care, at least 4 weeks before, and to propose antibiotic prophylaxis.

Implants
There are no formal indications to discontinue Tocilizumab while remaining vigilant for potential risks of infection.

Practical case
Because of a possible delay in healing due to Tocilizumab and its ability to mask post-operative signs of infection (absence of fever and a normal CRP), it is recommended that scheduled surgery be delayed while complying with a period of at least 4 weeks after the last infusion of Tocilizumab.

Proposed recommendations:

It is imperative to eliminate ODFI before initiation of a targeted biological therapy for immunosuppressant purposes (HPA).

If invasive treatment (tooth extraction, implant placement, etc.) is planned during treatment, special attention must be paid to potential occurrence of post-operative infection: vigilance, information of the patient. The treatment decision will be taken on a case by case basis by weighing the benefit/risk ratio with the prescribing doctor who possibly will propose the conditioning of the patient (which may include suspension of treatment) (HPA).

For further details, refer to recommendations of the IRC.

4.1.3. Transplantations

Meyer *et al.*[125] studied dental infection and rejection of cardiac transplantation in 74 patients. They compared two groups of patients before heart transplantation, one with radical treatment (extraction of all non-viable teeth), and the other without treatment. No significant difference was observed between the two groups in terms of mortality, transplant rejection or infection. They concluded that in the event of severe heart failure, patients did not require strict pre-operative oral dental treatment.

Proposed recommendation:

Surgery designed to restore the healthy condition of the oral cavity must be undertaken as soon as possible so that healing of the mucosa is acquired before transplantation or initiation of immunosuppressant therapy (HPA).

4.2. Cardiovascular disorders

In a case control study on 21 patients, Lockhart *et al*.[126] performed tooth extraction at the same time as cardiac valvular surgery, under coverage with antibiotic prophylaxis. No surgical complication was reported. This study places the hazard related to iatrogenic buccodental bacteraemia in a relative aspect.

Proposed recommendations:

An oral-dental evaluation must be undertaken as soon as possible before cardiac valvular surgery (HPA).

Surgery intended to restore the healthy condition of the oral cavity must be undertaken as soon as possible so that the healing of the mucosa is acquired before cardiac valvular surgery (HPA).

4.3. Cervicofacial radiotherapy

It is unanimously recognised that therapeutic cervicofacial radiation must always be preceded by an examination and prior rehabilitation of the dentition. This evaluation must be performed starting with scheduling of radiotherapy for "primary" and "secondary" prevention of post-radiation infection[127]. Concerning the approach to be taken, "systematic and permanent removal of teeth", which was the rule up until the 1970s[128], must now be banned.

Indications for conservation of teeth located in the pathway of the beam of radiation [129]

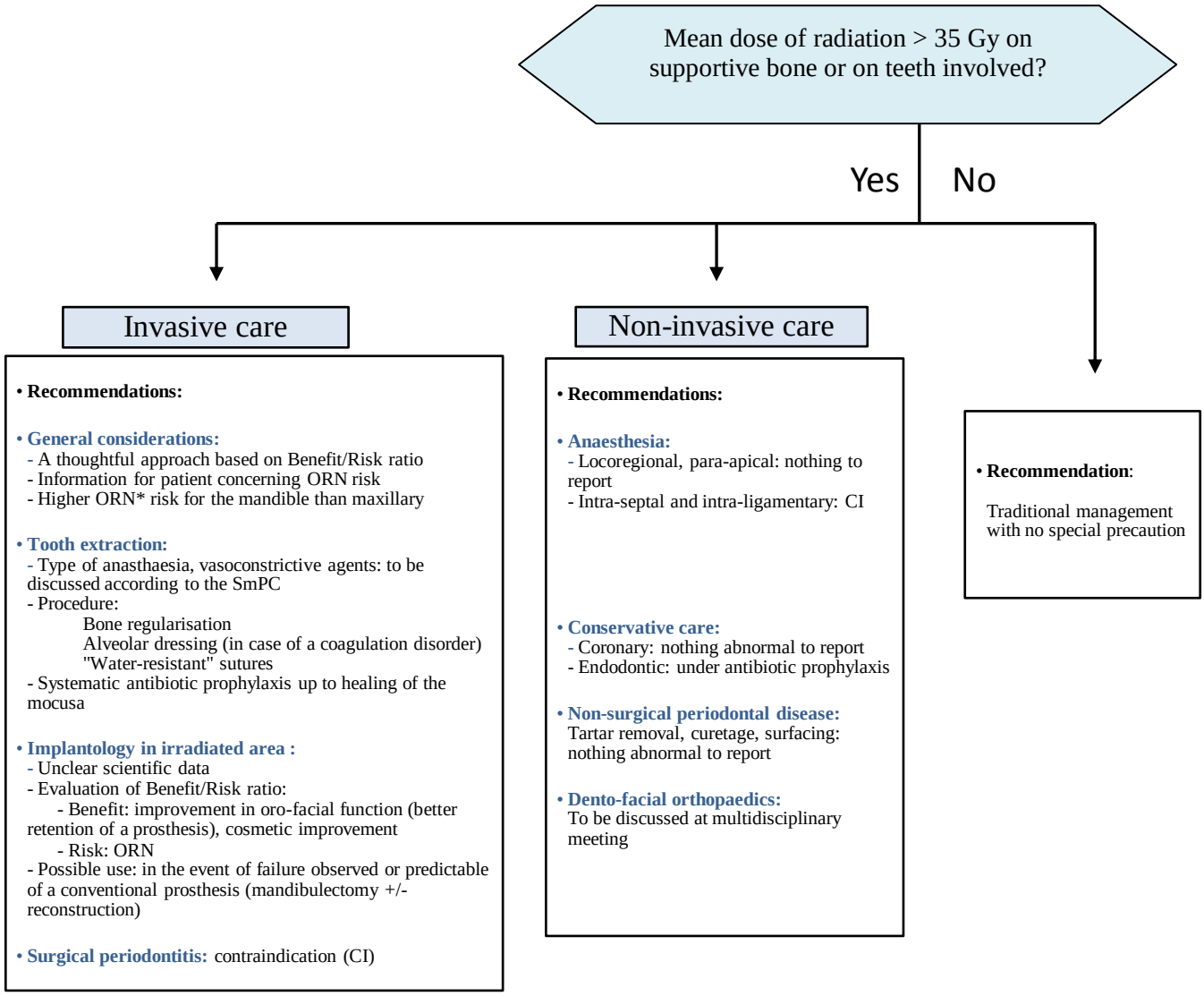
Good practices before radiotherapy are still related to a compromise which takes into account known parameters, such as dose of radiation and oral-dental condition, and parameters that are more difficult to control, such as patient compliance. The goals sought are prevention of complications and preservation of patient's quality of life (masticatory, phonetic and cosmetic rehabilitation). Only teeth considered healthy or properly treated previously can be saved. Teeth must be extracted before stating radiation: teeth in poor condition; teeth with apical or periodontal foci of infection with poor prognosis; teeth with subsequently prove to be unusable from a prosthetic standpoint (improperly

positioned or oriented teeth, etc.); teeth which are a source of trauma for the lingual or labio-jugal mucosa opposite; disimpacted teeth with a history of pericoronitis. Extraction of impacted teeth must be discussed, taking into account the healing time which will be necessary (at least three to four weeks) and of the "urgency" that there is to start radiation. For all these reasons, generally asymptomatic teeth will be left in place.

Conservation of teeth in the irradiated sector requires excellent motivation by the patient (hygiene, fluoride prophylaxis, monitoring).

A study by Epstein *et al*.[130] in 1998 showed that loss of periodontal attachment was more important after cervicofacial radiotherapy, even with low doses. The authors concluded that pre-radiotherapy evaluation had to take into account this consideration that may modify the therapeutic approach.

For information, a diagram of recommendations on measures to be taken for oral-dental care after radiotherapy according to interregional references in Oncological Supportive Care 2011[131], insisting on need for continuation of antibiotic prophylaxis up until healing of the mucosa:



*ORN: osteoradionecrosis

Proposed recommendations:

Before radiotherapy:

Surgery intended to restore the oral cavity must be undertaken as soon as possible so that healing of the mucosa is acquired before start of radiotherapy (HPA).

After radiotherapy (and whatever the time interval):

It is not necessary to take special measures if dose of radiation received by the maxilla and/or mandible is less than 30 Gy (RC).

In order to decrease the risk of osteoradionecrosis (ORN), tooth extraction that may be necessary must be performed as follows:

- After providing the patient with information on the dose received and the fields of radiation (HPA)
- In a surgical technical facility appropriate for the situation and providing guarantees on quality and safety (HPA)

In the event of a risk of osteoradionecrosis, antibiotic therapy must be initiated as in the event of an invasive procedure (tooth extraction, curettage, etc.) (HPA). It is necessary to start this prescription at least one hour before the procedure (HPA) (no consensus on a longer time interval) and to continue until healing of the mucosa (HPA).

4.4. Bisphosphonate treatment

According to AFSSAPS 2007* recommendations

In the context of a malignancy, it is preferable to start treatment with bisphosphonate (if the patients' clinical condition so permits) after the dental status has been restored and, if possible, after complete bone healing (120 days).

Before initiation of treatment, residual roots, teeth with poor prognosis and disimpacted teeth must be extracted. Similarly, foci of periodontitis or of peri-implantitis must also be healed.

* Recommendations on oral-dental management of patients treated wth bisphosphonates (19/12/2007), **http://www.afssaps.fr/Infos-de-securite/Lettres-aux-professionnels-de-sante/Recommandations-sur-la-prise-en-charge-bucco-dentaire-des-patients-traites-par-bisphosphonates** (consulted on 12/09/2009)

During treatment, only teeth with stage 3 mobility or with an active foci of infection must be extracted. Such procedures will be done under antibiotic treatment of at least 10 days duration.

Proposed recommendations:

In patients who have been treated with bisphosphonates in the context of a malignancy, it is recommended that tooth extraction be performed in a surgical technical facility appropriate for the case and providing guarantees of quality and safety (HPA).

In patients who are or who have been treated with a bisphosphonate outside of the context of a malignancy, tooth extraction can be performed in a general dentist's office in compliance with rules on management (RC).

4.5. Diabetes mellitus

No consensus was found on the need for determination if diabetic patients have their diabetes under control (glycosylated haemoglobin < 7%) require special precautions regarding management of ODFI of the sole fact of their diabetes (PC).

Proposed recommendations:

Diabetic patients can be managed in a general dentist's office after verification of control of diabetes (HPA).

In patients whose diabetes is not under control (glycosylated haemoglobin > 7%), in the event of an invasive procedure, it is necessary to start antibiotic prophylaxis within the hour prior to the procedure and continue up until healing of the mucosa of the wound (RC).

4.6. Prosthetic joints

In a case-controlled prospective study conducted on 339 patients, Berbari *et al.*[132] demonstrated that dental care, whatever the treatment procedure, does not represent a particular risk for patients who have a prosthetic hip or knee. In this study, 339 patients were admitted to hospital between December 2001 and April 2006 for infection of a total knee or hip replacement. 339 controls had also had a knee or hip replacement but with no known infection. Risk factors regarding infection of the prosthetic joint, including oral-dental procedures, within 2 years before diagnosis of infection were collected. Oral-dental procedures were classified as low risk (orthodontics, fluoride treatment) or high (periodontal treatment, tooth extraction). Mean age of patients was 69.5 years and duration of the prosthesis was 15.5 months. Mean age of controls was 71.4 years and duration of the prosthesis 49.9 months. Parameters significantly associated with infection of the prosthetic joint were: diabetes, history of orthoplasty and immunosuppressant therapy. Prophylactic antibiotic therapy before an oral-dental procedure did not differ between the two groups of patients. The result was that, for procedures with low risk, 41 cases and 65 controls did not receive an antibiotic (OR 0.6; 95% CI 0.4 – 1.1) and 59 cases and 87 controls had received antibiotics (OR 0.8; 95% CI 0.5 – 1.2) while, for procedures with a high

risk, 33 cases and 49 controls did not receive an antibiotic and 95 cases and 148 controls had received them (OR 0.8 and 0.7, respectively)[6]. The authors concluded that antibiotic prophylaxis does not make it possible to decrease risk of infection on a prosthetic joint and consequently should be abandoned.

Current data from the literature show that the relationship between joint infections and dental procedures has a low correlation; furthermore, antibiotic prophylaxis is not likely to reduce the risk of infection of a prosthetic joint. Consequently, it is not necessary to propose antibiotic prophylaxis simply because of the existence of a prosthetic joint.

However, precautions can be taken before joint replacement surgery.

Proposed recommendation:

Surgery intended to restore the oral cavity to a healthy condition must be undertaken as soon as possible so that healing of the mucosa is acquired before placement of a prosthetic joint (HPA).

5. What follow-up measures are to be planned?

In patients with an enhanced risk of infection from a dental or periodontal starting point, long term monitoring appears essential. Data from the literature on modalities of such follow-up vary, including within different categories of patients.

As an example, for patients who are free from any known disorder, usually an annual control is recommended by the dental surgeon, together with daily measures of oral dental hygiene.

The consensus conference of 2002 on prevention of infective endocarditis insists in its recommendation on the need for twice yearly monitoring: "systematic monitoring of the oral-dental condition must be done at least twice a year in patients who have a cardiac disorder"[133].
Guillaud *et al*.[134], in two consecutive years and for a population of risk of endocarditis, showed that percentage of patients with oral dental follow-up appears low (48.1%), and that this percentage seems encore lower in the subgroup of high risk patients for IE (43.2%). Oral-dental follow-up seems to decrease with patient's age. A low level of oral-dental follow-up in patients with a risk of IE was also noted in the study by De Geest *et al.*[135] in Belgium, where only one third of patients who had teeth underwent an annual follow-up associated with daily brushing and/or practically no follow-up was noted in patients who were toothless. For Gutschik and Lippert[136], in Denmark, only 50% of patients with a cardiac prosthetic valve attended regular oral-dental visits. Barreira *et al.*[137] insisted, for their part, on prevention with need to manage children at risk of IE.
Recommended twice yearly follow-up for patients of risk of IE therefore unfortunately does not seem to be applied.

Improvement in oral-dental hygiene is essential in order to limit spontaneous bacteraemia occurring following the actions of mastication and tooth brushing. This involves regular check of the patient's oral-dental condition by a oral cavity specialist, at least twice a year, in patients presenting with cardiac disease with a high risk of endocarditis[138].

After radiotherapy, the oral-dental consultation is generally performed at the same frequency as medical monitoring, generally every 3 months during a year and then every 6 months during 2 to 3 years, and then annually. In practice, a panoramic x-ray can be performed every 6 months during the first year and then annually subsequently in order to look for signs of infectious lesion and bone dystrophy (the first signs of osteoradionecrosis).
In a retrospective study comparing the protocol for oral-dental management before and after radiotherapy in two groups of follow-up at 12 years interval (1993 and 2005), Sernnhenn-Kirchner *et al*.[139] showed a significant improvement in follow-up of such patients. The group followed in 2005 received one systematic consultation for oral-dental evaluation before radiation therapy, as well as the placement of fluoride gutters. Patients presented fewer caries before radiotherapy, fewer candidiasis and less tooth loss than in 1993. Treatment before radiotherapy was also more conservative in 2005 than in 1993.
A study by Katsura *et al*.[140] in 2008 showed that the risk of osteoradionecrosis rose when the patient presented with periodontal pockets greater than 5 mm, a plaque score > 40% and alveolysis greater than 60%. The authors therefore recommend regular monitoring with periodontal supportive therapy.
The working group of the SFORL (2005) did not find a consensus on frequency of dental control but proposed a twice-yearly dental examination, based on professional agreement[141].

After chemotherapy, it is not necessary to adopt an approach which differs from the one proposed for a healthy patient with respect to looking for ODFI.

In the context of AFSSAPS* recommendations, an oral-dental repeat visit must be performed every 4 months for patients who are receiving bisphosphonates in the context of a malignancy, and at least once a year in those who are taking these medicinal products in the context of osteoporosis or Paget's disease. Marx *et al*.[142] recommend the same follow-up.

In the event of organ transplantation, there is a major risk of infection during the 3 to 6 months following the transplantation. During this period, only emergency care can be undertaken. After 6 months, care can be done at the usual practitioner's. Antibiotic prophylaxis will be discussed with the specialist in charge of the patient depending on immunosuppression[143].

* Recommendations on oral-dental management of patients treated with bisphosphonates (19/12/2007), **http://www.afssaps.fr/Infos-de-securite/Lettres-aux-professionnels-de-sante/Recommandations-sur-la-prise-en-charge-bucco-dentaire-des-patients-traites-par-bisphosphonates** (consulted on 12/09/2009)

Proposed recommendations:

Frequency of follow-up

After restoration of the patient's oral cavity some time after healing, and after the patient agrees to comply with methods of dental hygiene, oral-dental follow-up must be initiated at a frequency greater than that recommended for the general population (annual) in the following cases (HPA):

- In transplant patients
- In patients at high risk for infective endocarditis
- After therapeutic radiation with doses greater than 30 Gy
- In patients treated with or who have been treated with bisphosphonates in the context of a malignancy
- In diabetic patients whose diabetes is not controlled (glycosylated haemoglobin > 7%)
- In patients with AIDS

In these cases, it is necessary to initiate a frequency of oral-dental follow-up of 4 to 6 months (RC).

NB: It has been noted to suggest a higher frequency than clinically necessary considering the low foreseeable compliance.

On the other hand:

- In a subject with a prosthetic joint,
- In subjects at moderate risk for infective endocarditis,
- In patients who are or who have been treated with bisphosphonates outside of the context of a malignancy

the frequency of follow-up can be identical to that recommended for the general population (annual) (RC).

No consensus has emerged for frequency of follow-up in patients with chronic respiratory disorders (chronic obstructive pulmonary disease, asthma, etc.) (PC).

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