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Acute gingival and periodontal lesions

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ABSTRACT

This is a review and update on acute conditions affecting the gingival tissues, including abscesses in the periodontium, necrotizing periodontal diseases, and other acute conditions that cause gingival lesions with acute presentation, such as infectious processes not associated with oral bacterial biofilms, muco-cutaneous disorders, and traumatic and allergic lesions. A periodontal abscess is clinically important since it is a relatively frequent dental emergency, it can compromise the periodontal prognosis of the affected tooth, and because bacteria within the abscess can spread and cause infections in other body sites. Different types of abscesses have been identified, mainly by the type of etiology, and there are clear differences between those affecting a previously existing periodontal pocket and those affecting healthy sites. Therapy for this acute condition consists of drainage and tissue debridement, with individual evaluation of the need for systemic antimicrobial therapy. The definitive treatment of the pre-existing condition should be accomplished after the acute phase is controlled. Necrotizing periodontal diseases (NPD) present three typical clinical features: papilla necrosis, gingival bleeding, and pain. Although the prevalence of these diseases is not high, their importance is clear, since they represent the most severe conditions associated with the dental biofilm, with very rapid tissue destruction. In addition to bacteria, the etiology of NPD includes numerous factors that alter the host response and predispose to these diseases, including HIV infection, malnutrition, stress, and tobacco smoking. The treatment consists of superficial debridement, careful mechanical oral hygiene, rinsing with chlorhexidine, and daily re-evaluation. Systemic antimicrobials may be used adjunctively in severe cases or in non-responding conditions, and the best option is metronidazole. Once the acute disease is under control, definitive treatment should be provided, including the adequate therapy for the pre-existing gingivitis or periodontitis. Among other acute conditions affecting the periodontal tissues, but not caused by the microorganisms present in oral biofilms, are infectious diseases, muco-cutaneous diseases and traumatic or allergic lesions. In most cases, the gingival involvement is not severe, though they are common and may prompt a dental emergency visit. These conditions may have the appearance of an erythematous lesion, sometime erosive. Erosive lesions may be the direct result of a trauma or the consequence of the breaking of vesicles and bullae. A proper differential

diagnosis is important for an adequate management of the case.

INTRODUCTION

Acute lesions in the periodontium, such as abscesses and necrotizing periodontal diseases, are among the few clinical situations in periodontics where patients may seek urgent care, mostly due to the associated pain. In addition, and in contrast to most other periodontal conditions, a rapid destruction of periodontal tissues may occur during the course of these lesions, thus stressing the importance of prompt diagnosis and treatment. In spite of this, the available scientific knowledge on these conditions is limited and based on somewhat outdated literature. This lack of contemporary data makes it rather challenging to devise evidence-based therapeutic guidelines. Hence, an update is imperative, though it must be confined to an evaluation of narrative reviews and expert opinions.

Other gingival and periodontal lesions may also show an acute presentation, including different infectious processes not related to oral bacterial biofilms, muco-cutaneous disorders or traumatic and allergic lesions.

This chapter provides an overview and update of existing information on acute conditions affecting the gingival tissues, including abscesses in the periodontium, necrotizing periodontal diseases, and other acute conditions.

ABSCESSSES IN THE PERIODONTIUM

Definition of periodontal abscess

Abscesses in the periodontium are odontogenic infections, which may be caused by pulp necrosis, periodontal infections, pericoronitis, trauma, or surgery (109). Odontogenic or dental abscesses are classified, according to the infection source, into periapical (dentoalveolar) abscess, periodontal abscess, and pericoronal abscess (327).

A periodontal abscess has been defined as a localized purulent infection in the periodontal tissues (210). A more comprehensive definition has also been proposed: a lesion with an expressed periodontal breakdown occurring during a limited period of time, and with easily detectable clinical symptoms, including a localised accumulation of pus located within the gingival wall of the periodontal pocket (130). See Figure 1.

Classification of periodontal abscesses

Different criteria have been used to classify periodontal abscesses:

- By the location of the abscess: gingival and periodontal abscesses (110). A gingival abscess is a localised painful swelling, affecting only the marginal and interdental gingiva, normally associated with subgingivally impacted foreign objects. These conditions may occur in a previously healthy gingiva (7). A periodontal abscess is a localised painful swelling, affecting deeper periodontal structures, including deep pockets, furcations and vertical osseous defects, and they are usually located beyond the mucogingival line. Histologically, both lesions are identical, but the gingival abscess affects only the marginal soft tissues of previously healthy sites, while the periodontal abscess occurs in a periodontal pocket related to a periodontitis lesion (76).

- By the course of the lesion: acute and chronic periodontal abscesses. The acute periodontal abscess usually manifests symptoms like pain, tenderness, sensitivity to palpation, and suppuration upon gentle pressure. The chronic abscess is normally associated with a sinus tract, and it is usually asymptomatic, although the patient can refer mild symptoms (250). A localised acute abscess may become a chronic abscess

when drainage is established through a sinus or through the sulcus. Similarly, a chronic abscess may have an acute exacerbation.

- By the number of abscesses: single and multiple periodontal abscesses (321). A single periodontal abscess is usually associated with local factors, which contribute to the closure of the drainage of a periodontal pocket. Multiple periodontal abscesses have been reported in uncontrolled diabetes mellitus, medically compromised patients, and in patients with untreated periodontitis after systemic antibiotic therapy for non-oral reasons (125, 126, 321). Multiple abscesses have also been described in a patient with multiple external root resorptions (339).

- By the type of etiological factors: a periodontal abscess is usually associated with a previously existing periodontal pocket, though it also can develop without presence of a pocket (130). This classification is detailed in the section on etiology.

- According to the *International Workshop for a Classification of Periodontal Diseases and Conditions* (1999), abscesses in the periodontium include gingival, periodontal, pericoronal and periapical abscesses (210). A gingival abscess is defined as “a localized, painful, rapidly expanding lesion involving the marginal gingiva or interdental papilla sometimes in a previously disease-free area”. A periodontal abscess (that can be acute or chronic) is defined as “a localized accumulation of pus within the gingival wall of a periodontal pocket resulting in the destruction of the collagen fibre attachment and the loss of nearby alveolar bone. A pericoronal abscess is “a localized accumulation of pus within the overlying gingival flap surrounding the crown of an incompletely erupted tooth” (Figure 2).

Clinical significance of a periodontal abscess

- *A common periodontal emergency:*

Periodontal abscesses represented approximately 14% of all dental emergencies in a study in the USA (7). In general practices in the United Kingdom, 6–7% of the patients treated in one month suffered from a periodontal abscess, being the third most prevalent infection demanding emergency treatment, after dentoalveolar abscesses

(14– 25‰) and pericoronitis (10–11‰) (177). In an army dental clinic, 3.7% of the patients had periodontitis, and among these 27.5% had a periodontal abscess, with clear differences between patients undergoing active periodontal treatment (13.5%) and untreated patients (59.7%) (117). Among patients in supportive periodontal therapy (SPT), a periodontal abscess was detected in 37% of the patients and 3.7 of the teeth, followed for 5–29 years before (mean 12.5 years) (209); in the Nebraska prospective longitudinal study, 53% of the patients, followed for 7 years, showed a periodontal abscess, and 85% of these abscesses were associated to teeth only treated with coronal scaling. Sixteen out of 27 abscess sites had initial probing pocket depths (PPD) deeper than 6 mm, and in eight sites PPD was 5–6 mm (156). Abscesses occur more often in molar sites, representing more than 50% of all sites affected by abscess formation (128, 209, 300), probably due to the presence of furcation, and complex anatomy and root morphology. However, one case series suggested that the lower anterior incisors were the most frequently affected teeth (149).

- *Periodontal abscesses* may lead to tooth loss, especially if they affect teeth with previous moderate to severe attachment loss, as it occurs during SPT in patients with severe chronic periodontitis. In fact, it has been considered the main cause for tooth extraction during SPT (55, 209, 294, 300). Similarly, teeth with repeated abscess formation were considered to have a hopeless prognosis (36), and 45% of teeth with a periodontal abscess during SPT were extracted (209). The main reason for tooth extraction in teeth with a questionable prognosis, followed for 8.8 years, was a periodontal abscess (55). Taken into account these reports, it has been suggested that when facing a periodontal abscess in SPT patients, early diagnosis and adequate therapy are crucial to preserve the prognosis of the affected tooth (294).

- *Periodontal abscesses may be associated with systemic dissemination of a localized infection.* Numerous case reports have described the occurrence of systemic infections from a suspected source in a periodontal abscess, either through dissemination occurring during therapy or related to an untreated abscess. During the treatment of an abscess, the concomitant bacteraemia may lead to colonization of pathogenic microorganisms in other body sites and the developing of different infections, such as:

pulmonary actinomycosis (315), a brain abscess containing *P. melaninogenica* and other *Prevotella* spp. (103), or a total knee arthroplasty infection (330). It has been suggested that the risk of bacteraemia during abscess drainage may be reduced if a needle aspiration of the content of the abscess is performed before the procedure (99, 265).

There are also case reports of bacteraemia originating from untreated abscesses, such as in cellulitis in breast cancer patients (198), a cervical necrotizing fasciitis (57), a necrotising cavernositis containing *Peptostreptococcus* spp. and *Fusobacterium* spp. (245), or a sickle cell crisis in a patient with sickle cell anaemia (255).

Etiology, pathogenesis and histopathology of a periodontal abscess

Periodontal abscesses may develop in periodontitis-affected sites (with a pre-existing periodontal pocket) or in healthy sites (without a previous pocket):

- In periodontitis, a periodontal abscess may represent a period of disease exacerbation, favoured by the existence of tortuous pockets, the presence of furcation involvement (Figure 3) or a vertical defect, in which the marginal closure of the pocket may lead to an extension of the infection into the surrounding periodontal tissues (76, 158, 224). Also changes in the composition of the subgingival microbiota, with an increase in bacterial virulence, or a decrease in the host defences, could also result in an inefficient capacity to drain the increased suppuration. Among periodontal abscesses in periodontitis patients, different subgroups can be distinguished:

- Acute exacerbation of an untreated periodontitis (74). See Figure 4.
- After non-surgical periodontal therapy: after scaling or professional prophylaxis, dislodged calculus fragments can be pushed into the tissues (74), or inadequate scaling may allow calculus to remain in deep pocket areas, while the coronal part will occlude the normal drainage (156).
- After surgical periodontal therapy: associated with the presence of foreign bodies such as membranes for regeneration or sutures (106).
- Acute exacerbation in refractory periodontitis (97).
- Acute exacerbation in supportive periodontal therapy, as described above (55, 209, 294).

- Systemic antimicrobial intake without subgingival debridement, in patients with advanced periodontitis may also cause abscess formation (125, 126, 321), probably related to an overgrowth of opportunistic bacteria (125).
- Non-periodontitis periodontal abscesses. Periodontal abscesses can occur in previously healthy sites, due to the impaction of foreign bodies or to alteration of the root surfaces:
- Different foreign bodies have been described associated with the development of a periodontal abscess: an orthodontic elastic (250), a piece of dental floss (5), a dislodged cemental tear (124), a piece of a toothpick (100), pieces of nails in subjects with nail-biting habits (304), etc. The term “oral hygiene abscesses” has been proposed for abscesses caused by the impaction of foreign bodies that are oral hygiene aids (110).
 - The root surface may be altered due to different factors: perforation by an endodontic instrument (4); cervical cemental tears (124, 146); external root resorption (339); invaginated tooth (60); cracked tooth (116).

In the development of a periodontal abscess, the first step may be the bacterial invasion of the soft tissues surrounding the periodontal pocket, which will develop an inflammatory process through the chemotactic factors released by bacteria that attract inflammatory cells and lead to the destruction of the connective tissues and the encapsulation of the bacterial infection and the production of pus. Once the abscess is formed, the rate of destruction within the abscess will depend on the growth of bacteria inside the foci, its virulence and the local pH (an acidic environment will favour the activity of lysosomal enzymes) (76).

The histopathology of periodontal abscess lesions was described by the evaluation of biopsies retrieved from 12 abscesses (76), describing the following areas from the outside to the inside of the lesion:

- A normal oral epithelium and lamina propria.
- An acute inflammatory infiltrate.

- An intense focus of inflammation, with presence of neutrophils and lymphocytes in an area of destroyed and necrotic connective tissue.
- A destroyed and ulcerated pocket epithelium.

In seven biopsies observed through electronic microscopy, gram-negative bacteria were identified invading the pocket epithelium and the affected connective tissue forming a mass of granular, acidophilic and amorphous debris.

Microbiological findings

Purulent oral infections are usually poly-microbial and caused by commensal bacteria (317). In microbiological reports on periodontal abscesses, gram-negative bacteria predominated over gram-positives, and rods over cocci (224), with a predominant composition of large proportions of strict anaerobes (128, 224, 321).

The most prevalent bacterial species identified in periodontal abscess using cultural or molecular-based diagnostic techniques are *Porphyromonas gingivalis* ranging from 50-100% (82, 123, 128, 149, 224, 321, 327)(Figure 5). Other strict anaerobes frequently detected included: *P. intermedia*, *P. melaninogenica*, *F. nucleatum*, *Tannerella forsythia*, *Treponema* spp. *Parvimonas micra*, *Actinomyces* spp. and *Bifidobacterium* spp. Among the facultative anaerobic gram-negative bacteria, *Campylobacter* spp., *Capnocytophaga* spp. and *Aggregatibacter actinomycetemcomitans* have been reported (123), as well as gram-negative enteric rods (149).

In summary, previous studies have shown that the microbiota of periodontal abscess is not different from the microbiota of chronic periodontitis lesions. It is poly-microbial and dominated by non-motile, gram-negative, strict anaerobic, rod-shaped species. Among these bacteria, *P. gingivalis* is probably the most virulent and relevant microorganism. Although it is not clearly mentioned, these studies described the microbiology of abscesses in patients with periodontitis. Conversely, there is limited information on the microbiota of other type of abscesses, except those associated with systemic antibiotic intake in periodontitis patients for non-oral reasons (125, 126, 321): in these abscesses, the occurrence of periodontal pathogens is similar to other abscesses in periodontitis, although opportunistic bacteria were also detected,

especially *Staphylococcus aureus*, leading the authors to suggest that this type of abscess could be considered as a super-infection.

Diagnosis of a periodontal abscess

The diagnosis of a periodontal abscess should be based on the overall evaluation and interpretation of the patient's symptomatology, together with the clinical and radiological signs found during the oral examination (67).

A series of symptoms have been described associated with an abscess, ranging from light discomfort to severe pain, tenderness of the gingiva, swelling, tooth mobility, tooth elevation and sensitivity of the tooth to palpation (7, 128, 145).

The most prominent sign during the oral examination is the presence of an ovoid elevation in the gingiva along the lateral part of the root, although abscesses located deep in the periodontium may be more difficult to identify and may be found as a diffuse swelling or simply as a red area. Another common finding is suppuration either through a fistula or, most commonly, through the pocket opening (Figure 6), that may be spontaneous, or occur after applying pressure on the lesion. The abscess is usually found at a site with a deep periodontal pocket, and signs of periodontitis including bleeding on probing, suppuration or increased tooth mobility are also frequent (123, 128, 300)

The radiographic examination may reveal a normal appearance, or some degree of bone loss (since most abscesses will occur in a previously existing periodontal pocket). Periodontal abscess may be associated with elevated body temperature, malaise and regional lymphadenopathy (128, 145, 300), and 30% of the patients may have the number of blood leukocytes elevated (128).

The anamnesis may also provide relevant information, especially in abscesses associated with previous treatment, either dental or periodontal treatments or non-oral therapies, such as systemic antimicrobials. Also in abscesses related to impaction of foreign bodies, the interview with the patient may be of great help.

Differential diagnosis is critical, since periodontal abscesses may be similar to other oral conditions:

- Other abscesses in the mouth: periapical or dento-alveolar or endodontic abscesses, lateral periapical cyst, vertical root fractures, endo-periodontal abscess, postoperative infection (7). A combination of different factors, such as pulp vitality, presence of dental caries, presence of periodontal pockets, the location of the abscess, and a careful radiographic examination should be carefully assessed to reach an accurate diagnosis.
- Other serious oral diseases may also have a similar appearance: osteomyelitis in periodontitis patients (241), squamous cell carcinomas (162, 163, 322), a metastatic carcinoma from pancreatic origin (289), a metastatic head and neck cancer (85), an eosinophilic granuloma (111) or a pyogenic granuloma (237). Therefore, in cases not responding to conventional therapy, a biopsy and histopathologic diagnosis should be recommended.
- Self-inflicted gingival injuries: including trauma of the gingiva with a pencil (267) or with a safety pin (37), or nail biting habit (304). A careful anamnesis is the key factor in the diagnosis of these lesions.

Treatment of a periodontal abscess

The treatment of a periodontal abscess should include two distinct phases: the control of the acute condition to arrest tissue destruction and control the symptoms, and the management of the pre-existing and/or residual lesion, especially in periodontitis patients.

Control of the acute condition

Four therapeutic alternatives have been proposed: tooth extraction, drainage and debridement, systemic or local antimicrobials and surgery.

If the tooth is severely damaged, and its prognosis is hopeless after the destruction caused by the abscess, the preferred treatment should be **tooth extraction** (300).

The most logical treatment of a periodontal abscess, as in other abscesses in medicine, should include **drainage** (through the pocket or through an external incision), compression and debridement of the soft tissue wall, and the application of topical antiseptics after the drainage. If the abscess is associated with a foreign body impaction, the object has to be eliminated through careful debridement (5), although it may not be present anymore.

Systemic antimicrobials may be used as sole treatment, as initial treatment or as an adjunctive treatment to drainage. As sole or as initial treatment may be only recommended if there is a need of pre-medication, or when the infection is not well localized or when adequate drainage cannot be ascertained (176). As an adjunctive treatment, it should always be considered if a clear systemic involvement is present (7, 176). The duration and the type of the antibiotic therapy is also a matter of discussion, including the recommendation of shorter courses of therapy (176, 202). The available scientific evidence on the efficacy of these therapies, however, is very limited, with only two prospective case series and two randomized clinical trials. Smith & Davies (1986) evaluated the incision and drainage of the abscess, together with adjunctive systemic metronidazole (200 mg, tid, 5 days), followed by a delayed periodontal therapy, in 22 abscesses for up to 3 years (300). Hafström et al. (1994) proposed drainage through the periodontal pocket, irrigation with sterile saline, supragingival scaling and tetracycline for 2 weeks (1 g/day), and tested this therapy in 20 abscesses, with 13 followed for 180 days, highlighting the importance of drainage and the potential of regeneration (123). Herrera et al. (2000) compared azithromycin (500 mg, once per day, 3 days) versus amoxicillin plus clavulanate (500+125 mg, tid, 8 days), with delayed scaling (after 12 days), in 29 patients with abscess followed for 1 month, concluding that both protocols were similarly effective (129). Eguchi et al. (2008) compared irrigation with sterile physiological saline and 2% minocycline hydrochloride ointment, versus irrigation with sterile physiological saline without the local antibiotic in 91 patients for 7 days (82).

Surgical procedures have also been proposed, mainly for abscesses associated with deep vertical defects (158), or in cases occurring after periodontal debridement in

which calculus is left subgingivally after the treatment (74). A case series evaluating a combination of an access flap with deep scaling and irrigation with doxycycline is also available, reporting “good results”, but scientific data was not provided (316).

After drainage and debridement the patient should be recalled in 24-48 hours to evaluate the resolution of the abscess (Figures 7a and 7b) and the duration of the antimicrobial intake. Once the acute phase has resolved, the patient should be scheduled for a follow-up therapeutic phase.

In summary, numerous treatment protocols have been proposed, but sufficient scientific evidence is not available to recommend a definitive approach. It is, however, clear that drainage and debridement should be established when the systemic condition and the access to the abscess is adequate. When the immediate drainage is not possible or a systemic affect is evident, a therapy with systemic antimicrobials should be considered. The drug with the most adequate profile is metronidazole (normally prescribed, for acute conditions, at 250 mg, tid). Azithromycin (500 mg, once per day) and amoxicillin plus clavulanate (500+125 mg, tid) have also shown good clinical results. The duration of the therapy should be restricted to the duration of the acute lesion, which is normally 2-3 days.

Management of a pre-existing and/or residual lesion

Since most periodontal abscesses occur in a previously existing periodontal pocket, periodontal therapy should be evaluated after resolution of the acute phase. In cases where the patient has not been treated previously, the appropriate periodontal treatment should be provided. If the patient is within the active phase of therapy, once the acute lesion is treated the periodontal therapy should be completed. In patients during SPT, a careful evaluation of the recurrence of the abscesses should be made as well as an adequate evaluation of the tissue damage and how this affects tooth prognosis.

Summary

Abscesses in the periodontium are important since they are a relatively frequent dental emergency, they can compromise the periodontal prognosis of the affected tooth and because the bacteria within the abscess can spread and cause infections in other body sites.

Although histologically all abscess lesions are similar, different type of abscesses have been identified, mainly by their different etiology, since there are clear differences between those affecting a previously existing periodontal pocket and those affecting healthy sites.

For the management of this condition, a rapid and accurate diagnosis, mainly based on clinical features, and provision of early therapy is mandatory. Therapy for the acute condition should be based on drainage and debridement, with individual evaluation of the need of systemic antimicrobial therapy. When the supporting tissues have been destroyed to that extent of compromising the tooth prognosis, tooth extraction may be the only valid alternative. The definitive treatment of the pre-existing condition should be accomplished after the acute phase is controlled, since most abscesses are found in untreated periodontitis patients.

NECROTIZING PERIODONTAL DISEASES (NPD)

Definition

NPD is a group of infectious diseases that includes: necrotizing ulcerative gingivitis (NUG), necrotizing ulcerative periodontitis (NUP) and necrotizing stomatitis (NS). However, it has also been suggested that these conditions may be different stages of the same disease, since they have similar etiology, clinical characteristics, and treatment, although they vary in disease severity (138, 140). These diseases share common clinical features consisting of an acute inflammatory process and the presence of periodontal destruction (Figure 8).

NUG has been diagnosed for centuries though termed various names, such as: Vincent's disease, trench-mouth disease, necrotizing gingivo-estomatitis, fusospirochaetal stomatitis, ulcerative membranous gingivitis, acute ulcerative gingivitis, necrotizing ulcerative gingivitis or acute necrotizing ulcerative gingivitis (138, 152, 269). NUP was defined both in the 1989 World Workshop (54) and in the 1993 European Workshop (26). At the International Workshop for a Classification of Periodontal Diseases and Conditions in 1999 (22), the new category of "Necrotizing Periodontal Diseases" was introduced, which includes NUG and NUP. More recently, the terms necrotizing gingivitis (NG) and necrotizing periodontitis (NP) have been used instead of the terms NUG and NUP (137). The simpler terms NG and NP adequately describe these diseases and these term will be used in the rest of the text.

Classification of necrotizing periodontal diseases

According to the location of the tissue affected by the acute disease process, NPD can be classified as (138, 140):

- Necrotizing gingivitis: when only the gingival tissues are affected.
- Necrotizing periodontitis: when the necrosis progresses into the periodontal ligament and the alveolar bone, leading to attachment loss.
- Necrotizing stomatitis: the necrosis progresses to deeper tissues beyond the mucogingival line, including the lip or cheek mucosa, the tongue, etc.

Clinical significance of necrotizing periodontal diseases

NPD are considered among the most severe inflammatory conditions associated with oral biofilm bacteria (138). It is, therefore important to control predisposing factors, and once the disease developed, to act quickly in order to limit its progression and exacerbation.

The prevalence of NPD in systemically healthy populations has not been adequately established, since most studies have focused on specific group of patients with clear predisposing factors, such as military personal (141, 248), students (108, 188, 307), patients positive for human immunodeficiency virus (HIV) (136), or subjects with severe malnutrition (88, 234). In addition, data from these conditions originate from

hospitals or dental clinic settings, which may overestimate the true epidemiological information. A high prevalence of NG (14%) was observed in civil and military populations during the 2nd World War (12, 138), and a moderately high rate (2.2%) in North America in the 1950s (122). After the war, the prevalence clearly decreased in developed countries and nowadays it has a low prevalence.

NPD have been described in young people, both in developed and in developing countries (12). In North America and Europe these diseases have been studied mostly in groups aged late teens to mid-twenties. In 326 North-American students in the 1960s (108) the prevalence ranged from 2.5-6.7%. The current estimates in developed countries are 0.5% or less (33, 141), with 0.001% reported in young Danish army recruits (138)

In developing countries, the reported prevalence is higher, especially in children (12). In Chile, among 9.203 students, 6.7% presented, at least a papilla with necrosis. In India, 54-68% of the cases were observed in children younger than 10 years (249). In South Africa, 3.3% of subjects aged 3-48 years presented NG, with 73% aged 5-12 years and mostly from a low socioeconomic class (20). In Nigeria, the prevalence of NG ranged between 1.7-15% in 2-6 years old children, and was 27.2% in children with severe malnutrition (12, 88, 292). In Kenya, 0.15% of patients attended the Nairobi Hospital during one year were diagnosed with NG, and 58.5% of them were younger than 11 years (155). In spite of these figures, subjects of any age may be affected.

NP is less frequent and it has been most frequently reported in HIV-positive patients, with a prevalence 0-11% among these patients (40, 136, 261, 338). This prevalence is lower when studies were performed outside hospitals or dental clinics. In HIV-positive patients under anti-retroviral therapy (204, 272, 318) the prevalence of NP may not differ from that in the general population.

Necrotizing periodontal diseases can progress rapidly and cause severe tissue destruction. It is therefore, important that these conditions are managed promptly, since there is evidence proving that NPD can be controlled by means of an adequate

periodontal treatment, combined with effective oral hygiene measures and control of predisposing factors (152). NG patients, however, are frequently susceptible to future disease recurrence, mostly due to the difficulties in controlling predisposing factors as well as the difficulty in achieving proper supragingival biofilm control, in part due to the sequelae of these diseases, mainly the presence of gingival craters (196).

NG can heal without clinical sequelae (38), but often the necrotizing lesion extends laterally from the papilla to the gingival margin, affecting both the buccal and lingual sites and progresses to other sites in the mouth, evolving from a localized into a generalized disease (Figure 9). It may also progress apically evolving into NP (Figure 10). In fact NP can be the result of one or various episodes of NG, or it can be the result of a NPD affecting a site previously affected with periodontitis (227). NPD can also become chronic, with a slow reduction in its symptomatology and progression, with ensuing destruction, although at a slower rate (138, 248). Some authors believe that these conditions remain acute and may be “recurrent” (152).

In cases of severe systemic involvement, such as in AIDS or severe malnutrition NG and NP can progress further with rapid involvement of the oral mucosae. The severity of these lesions are normally related to the severity of the systemic condition and the compromised immune host-response, leading to extensive bone destruction and presence of large osteitis lesions and oral-antral fistulae (335). NE has common features with *Cancrun Oris* or *NOMA*. Some investigators suggested that *NOMA* is a progression of NE affecting the skin, whereas others believe that NE and *NOMA* are two distinct clinical entities. *NOMA* is a destructive gangrenous disease affecting the facial tissues. It is associated with high mortality and morbidity rates (32, 89, 91), and it is almost exclusively observed in developing countries, especially in children suffering from systemic diseases, including severe malnutrition. *NOMA* is normally preceded by measles, malaria, severe diarrhea and NG; which highlights the importance of prevention, early detection and treatment during the first stages of the disease (269).

Etiology, pathogenesis and histopathology of necrotizing periodontal diseases

NPD are caused by infectious agents, although the predisposing factors, such as the compromised host immune response are the main factors facilitating the bacterial pathogenicity. This bacterial etiology was already demonstrated by Plaut in 1894 and by Vicent in 1896 (269), since the microscopic exams of the plaque sample retrieved from affected subjects clearly showed the presence of spirochetes and fusiform bacteria, even within the tissues. Moreover, clinical resolution was observed after mechanical debridement and antimicrobial treatments (302). However, the knowledge on the pathogenesis of these diseases is limited, since it is not clear whether these bacteria observed in the lesions are the cause or the consequence, as secondary bacterial colonization may ensue after periodontal destruction, since the necrotic tissues are the perfect environment for bacterial colonization and tissue invasion (138, 269).

The spirochetes and fusiform bacteria described in the necrotic lesions have the capacity to invade the epithelium (131) and connective tissue (181), as well as to release endotoxins that may cause periodontal tissue destruction through the activation or modification of the host response.

In NG lesions observed through light microscopy have shown a distinct pathology (181), with presence of an ulcer within the stratified squamous epithelium and the superficial layer of the gingival connective tissue surrounded with a non-specific acute inflammatory reaction. Four regions have been described within these lesions:

- The bacterial area with a superficial fibrous mesh composed of degenerated epithelial cells, leukocytes, cellular rests, and a wide variety of bacterial cells, including rods, fusiforms and spirochetes.
- The neutrophil-rich zone, composed of a great number of leukocytes, especially neutrophils, and numerous spirochetes of different sizes and other bacterial morphotypes located between the host cells.
- The necrotic zone, with presence of disintegrated cells, together with medium and large size spirochetes and fusiform bacteria.

- The spirochetal infiltration zone, where the tissue components are adequately preserved, but infiltrated by large and medium size spirochetes. Other bacterial morphotypes are not found.

Microbiology of necrotizing periodontal diseases

The microbiology of NPD has been described in different studies with a similar composition of the associated microbiota, including *Treponema* spp., *Selenomonas* spp., *Fusobacterium* spp. and *P. intermedia*. Other microorganisms have also been described although defined as “variable” flora and not present in all cases (187). Since this typical microbiological description can also be detected in healthy, gingivitis or periodontitis sites, the use of the microbiological testing does not provide relevant diagnostic information (67, 152).

In HIV-positive patients with NPD the microbiological findings are also non-specific (204, 266, 338), except in regards to the counts of yeast (namely, *Candida albicans*) and the presence herpes viruses (62, 272, 338, 340), or the detection of superinfecting bacterial species, such as enterics including *Enterococcus avium*, *E. faecalis*, *Clostridium clostridiiforme*, *C. difficile*, *Mycoplasma* spp. and *Klebsiella pneumoniae* (258, 340). Most recently, with the use of molecular technologies (polymerase chain reaction), some bacterial species have been frequently associated with NPD lesions, including *Eubacterium saphenum*, *E. sabburum*, *Filifactor alocis*, *Dialister* spp. and *P. endodontalis*, while the typical periodontitis-associated pathogens *P. gingivalis* and *T. forsythia* were less frequently found (243).

Some researchers have pointed out the possible etiological role of viruses in NPD, including human cytomegalovirus (HCMV) (78, 273). In children with NG in Nigeria, in addition to the presence of HCMV in the lesions, other viruses were detected including Epstein Barr virus type 1 and herpes simplex virus (64).

Predisposing factors for necrotizing periodontal diseases

The most common predisposing factors are those altering the host immune response, although usually more than one factor is necessary for initiating the disease (138). In a

study in USA, the most important factor was HIV infection. In non-HIV patients, the most important factors were previous history of NPD, poor oral hygiene, inadequate sleep, unusual psychological stress, poor diet, recent systemic diseases, alcohol abuse, tobacco smoking, Caucasian ethnicity and age below 21 (140).

Systemic conditions

Those conditions lowering the host immune response favor NPD. Patients infected with HIV or diseases affecting leukocytes (e.g. leukemia) are among the most important predisposing factors. Other systemic conditions that have shown a positive association include: malnutrition, measles, chickenpox, tuberculosis, herpetic gingivostomatitis, malaria, or even diabetes, which was identified in a study with Chilean adolescents (188).

Among predisposing systemic conditions, HIV infection and malnutrition have been studied more in depth:

- In HIV-positive patients, NPD are more frequent and show a faster progression, although no differences have been detected between the characteristics of the disease in HIV-negative and positive patients. It has been suggested that HIV-positive patients have a higher tendency for recurrence and diminished response to both mechanical and/or pharmacological periodontal treatment (227). In HIV-positive patients, the reduction in the counts of peripheral CD4 lymphocytes has been correlated with NG and NP (113, 303) and therefore, the diagnosis of NPD should prompt the likelihood that the patient may have an HIV infection, and therefore the affected subjects should be screened for HIV (138, 139).
- Malnutrition has also been reported as predisposing factor (269) especially in developing countries (88, 90, 234). The basis for this interaction has been termed “protein-energy malnutrition”, implying a marked reduction in key antioxidant nutrients and an altered acute phase response against infection. Other consequences are an inversed proportion in the ratio of helper/suppressor T-lymphocytes, histaminemia, increased free cortisol in blood and saliva, and defects in mucosal integrity (90).

Psychological stress and insufficient sleep

Acute psychological stress and acute stressing situations have been associated with NG (140, 152, 291). Certain situations may predispose individuals to NPD, such as military personnel in wartime, new recruits for military services, drug-abusers during abstinence syndrome, students during exam periods, and patients with depression or other psychological conditions (108, 122, 248). During these stress periods, not only the immune response is altered, but also the subject's behavior, leading to inadequate oral hygiene, poor diet or increased tobacco consumption. The proposed mechanisms to explain this association are based on a reduction in the gingival microcirculation and salivary flow and an increase in serum and urine levels of 17-hydroxycorticosteroid (17-OHCS), which are associated with an alteration in the function of polymorphonuclear leukocytes (PMN) and lymphocytes, or even an increase in the levels of periodontal pathogens, such as *P. intermedia* (187). In patients with NG, higher urine levels of 17-OHCS have been reported, when compared with healthy or treated patients; in addition, those patients demonstrated statistically significant higher levels of anxiety, depression or emotional alteration (138). Patients with NG also contained PMNs with altered functions, since their bactericidal, phagocytic and chemotactic capacities were depressed (63).

Inadequate oral hygiene, pre-existing gingivitis and previous history of NPD

Plaque accumulation has been considered a predisposing factor (140, 152), although it may also be the consequence of the presence of ulcer and crater lesions that may limit tooth brushing due to pain. NPD usually occurs over a previously existing periodontal disease, usually chronic gingivitis (248) (Figure 11). In one study, 28% of the patients with NPD reported a history of painful gingival inflammation and 21% showed lesions compatible with previous NPD (140).

Alcohol and tobacco consumption

Smoking is a risk factor for NPD (152, 153, 264) and in fact, most HIV-negative patients diagnosed of NPD were smokers (108, 248, 307). The mechanisms explaining this association are probably related to the effect of smoking on inflammation and tissue

response, since smoking interferes with both PMN and lymphocyte function and nicotine induces vasoconstriction in gingival blood vessels.

Alcohol consumption has also been associated with the physiological and psychological factors favoring NPD (139).

Young age and ethnicity

In developed countries, young people are more prone to suffer NPD, mostly between 21-24 years, usually combined with other predisposing factors, such as smoking and stress (139, 140, 307). In developing countries, NPD affects even younger people, being malnutrition and occurrence of infections the most frequent predisposing factors, (89, 90, 269). Studies in North America have reported that up to 95% of cases of NPD occurred in Caucasian patients (33, 140, 307), although more studies are needed to confirm this finding.

Diagnosis of necrotizing periodontal diseases

The diagnosis of NPD is mainly based on the clinical findings (67, 269). Although the reported histology and the typical microbiota associated with these lesions have a distinctive character, neither biopsy nor microbiological sampling are usually essential diagnostic tools in these diseases (67). The different stages of NPD share clinical features, but also distinct findings depending on the extent and severity of the lesions (1, 67, 138, 152, 269):

Necrotizing gingivitis

The diagnosis is based on the presence of necrosis and ulcers in the free gingiva. These lesions usually start at the interdental papilla with the typical “punched-out” appearance. In addition, a marginal erythema, named “lineal erythema”, may be present, separating the healthy and the diseased gingiva. These necrotic lesions can progress to the marginal gingiva. The most typical location is the anterior teeth, especially in the mandible (Figure 12). In NG gingival bleeding is a frequent finding, usually spontaneous or after minimal contact (Figure 13). Pain normally occurs soon and with different degrees of severity, depending on the severity and extension of the

lesions. The bouts of pain increase with eating and with the oral hygiene practices and it is normally the reason for patient's consultation.

Other less common findings include the presence of:

- pseudo-membranous formation over the necrotic area. It consists on a meshwork of whitish-yellow color, composed of necrotic tissue, fibrin, erythrocytes, leukocytes and bacterial cells. When this "membrane" is removed, the underlying connective tissue becomes exposed and bleeds;
- halitosis, although it is not an exclusive sign of NG;
- adenopathies, which are usually found in the most severe cases. If present, submandibular lymph nodes are more affected than those in the cervical area (150, 151).
- Fever and a general feeling of discomfort.

Necrotizing periodontitis

The same clinical picture described in NG occurs in NP, but in addition in NP the following characteristics may be present:

- The necrosis affects the periodontal ligament and alveolar bone, leading to loss of attachment. Since there is concomitant necrosis of the soft tissue, presence of pockets is not a usual finding (Figure 14).
- As the disease progresses (Figure 15), the interdental papilla is divided in a buccal and a lingual/palatal part, with a necrotic area in the middle, known as interproximal crater. If the craters are deep, the interdental crestal bone becomes exposed and denudated. In addition, crater formation favors disease progression by allowing the accumulation of more bacteria. Interproximal necrotic areas spread laterally and merge with the neighboring areas, creating an extensive zone of destruction.
- In severe cases, especially in immune-compromised patients, bone sequestrum (necrotic bone fragments within the tissues but separated from the healthy bone) may occur, mainly interdentally, but also in buccal or lingual/palatal alveolar bone.

Necrotizing stomatitis

When bone denudation extends through the alveolar mucosa, larger bone sequestra may occur, with large areas of osteitis and oral-antral fistulae. The severity of these lesions is associated with severely compromised systemic patients, including AIDS patients and severe malnutrition (335).

Management of necrotizing periodontal diseases

Due to the previously listed specific features of NPD (tissue destruction, acute course, pain), diagnosis and treatment have to be performed as soon as possible, and conventional periodontal therapies may need adjunctive therapeutic measures (2, 152).

The treatment should be organized in successive stages, including the treatment of the acute phase and a subsequent treatment phase that should include the treatment of the pre-existing condition, the corrective treatment of the disease sequelae, and the supportive or maintenance phase.

Treatment of the Acute Phase (138)

Two main objectives should be achieved with the therapy: to arrest the disease process and tissue destruction, and to control the patient's general feeling of discomfort and pain, which is interfering with nutrition and oral hygiene practices. The first task should be a careful **superficial debridement**, to remove the soft and mineralized deposits. Power-driven debridement devices (e.g. ultrasonics) are usually recommended exerting minimum pressure over the ulcerated soft tissues. The debridement should be performed daily, getting deeper as the tolerance of the patient improves, and lasting for as long as the acute phase lasts (normally, 2-4 days). Mechanical oral hygiene measures should be limited, in order to avoid pain, since brushing directly in the wounds may impair healing. During this period the patient is advised to use chemical plaque control agents, such as **chlorhexidine-based mouth rinses** (at 0.12-0.2%, twice daily). Other products have also been suggested, such as 3% hydrogen peroxide diluted 1:1 in warm water, and other oxygen-releasing agents, which not only contribute to the mechanical cleaning of the lesions, but also provide

the antibacterial effect of oxygen against anaerobes (333). Other oxygen therapies have also been evaluated, such as a local oxygen therapy, that may help in a reduction or even eradication of microorganisms, resulting in a faster clinical healing with less periodontal destruction (101).

In cases that show unsatisfactory response to debridement or systemic effects (fever, malaise), the use of **systemic antimicrobials** may be considered. Metronidazole, at 250 mg, every 8 hours, may represent the first alternative, due to its action over strict anaerobes (187). Other systemic drugs have also been proposed, with acceptable results, including penicillin, tetracyclines, clindamycin, amoxicillin or amoxicillin plus clavulanate. Conversely, locally delivered antimicrobials are not recommended, due to the large amount of bacteria present within the tissues, where the local drug will not be able to achieve adequate concentrations.

These patients have to be followed-up very closely, daily if possible, and as the symptoms and signs improve, strict mechanical hygiene measures should be enforced, as well as complete debridement of the lesions can be scheduled.

Treatment of the pre-existing condition

NPD normally occurs over a chronic gingivitis or periodontitis. Once the acute phase has been controlled, the treatment of the pre-existing chronic condition should be implemented, including professional prophylaxis and/or scaling and root planing. Oral hygiene instructions and motivation should be enforced. Existing predisposing local factors, such as overhanging restorations, interdental open spaces and tooth malposition should be carefully evaluated and treated (140). At this stage, and also during the acute phase, attention should be paid to the control of the systemic predisposing factors, including smoking, adequate sleep, reduction of stress or treatment of the systemic conditions.

Corrective treatment of disease sequelae

The correction of the altered gingival topography caused by the disease should be considered (Figure 16), since gingival craters may favor plaque accumulation and

disease recurrence. Gingivectomy and/or gingivoplasty procedures may be helpful to treat superficial craters; for deep craters, periodontal flap surgery, or even regenerative surgery represent more suitable options (138).

Supportive or maintenance phase

During this phase, the main goal becomes the compliance with the oral hygiene practices (Figure 17) and the control of the predisposing factors.

Specific considerations for HIV-positive patients

HIV-positive patients may not be aware of their serologic status. Occurrence of NPD in systemically healthy individuals is suggestive of HIV infection, and therefore the affected individuals should be screened for HIV (132, 138, 140). The specific management of NPD in HIV-positive patients includes debridement of bacterial deposits combined with the irrigation of the site with iodine povidone, based on its hypothetic anesthetic and bleeding control effects (338), although no sound scientific evidence is available to support this protocol (271, 336, 338). Careful consideration should be made regarding the use of systemic antimicrobials, due to the risk of over-infections with *Candida* spp. Metronidazole has been recommended due to its narrow spectrum, with limited effects on Gram-positive bacteria, which prevent *Candida* spp. overgrowth (272, 336, 338), although HIV-positive patients may not need antibiotic prophylaxis for the treatment of NPD (194). In non-responding cases, the use of antifungals may be beneficial, including clotrimazole lozenges, nystatin vaginal tablets, systemic fluconazole or itraconazole, mainly in cases of severe immune-suppression (272, 338). In HIV-positive patients the systemic status should be closely monitored, including the viral load and the hematologic and immune condition, leading to a customized periodontal treatment plan (266, 272, 338).

Summary

NPD includes NG, NP and NS, and these may be considered different stages of the same pathologic process. This group of diseases always presents three typical clinical features: papilla necrosis, bleeding and pain, which make them different from other periodontal diseases. Although their prevalence is not high, their importance is clear,

since they represent the most severe biofilm-related periodontal conditions, leading to rapid tissue destruction. In their etiology, together with the bacteria, numerous factors that alter the host response may predispose to these diseases, including HIV infection, malnutrition, stress or tobacco smoking.

Due to their acute presentation, together with the associated pain and tissue destruction, the treatment should be provided immediately once diagnosed, including superficial debridement, careful mechanical oral hygiene, rinsing with chlorhexidine and daily revisions. Systemic antimicrobials may be used adjunctively in severe cases or in non-responding conditions, and the best option is metronidazole. Once the acute disease is under control, definitive treatment should be provided, including the adequate therapy for the pre-existing gingivitis or periodontitis as well as adequate oral hygiene practices and supportive therapy. Surgical treatment of the sequelae should be individually considered.

OTHER ACUTE CONDITIONS IN THE PERIODONTIUM

This group of acute gingival lesions includes lesions manifesting initially as acute conditions or as acute episodes of a chronic condition. They can appear as isolated lesions or as part of complex clinical pictures and they are frequently the cause for emergency consultations.

The presenting clinical lesion is usually an ulcer or erosion, which may be the primary lesion, or secondary to a vesicle-bullous lesion. The most frequent symptom is localized pain, which initiates with the lesion or may precede it, although it may also occur in conjunction with pain in the pharynx or dysphagia. To properly establish the diagnosis, a clinical history, anamnesis and careful examination are mandatory, since most of the times there is a direct and recent relation with the cause (68). In the following description, the lesions are classified according to their etiology, since their clinical appearance is similar and a careful differential diagnosis is key to their therapy (22, 134, 326).

Gingival diseases of infectious origin

Gingival lesions of specific bacterial origin

Specific bacterial infections localized in the oral mucosa are not frequent. They may be caused by bacteria normally present in the oral cavity, that eventually become pathogenic, and also by bacteria exogenous to the oral cavity, such as by gonococci, tularemia or anthrax. In addition, the lesions present in the oral cavity may be a secondary location of generalized infectious disease, as it may happen in scarlatina, diphtheria, syphilis or tuberculosis.

Both staphylococci and streptococci may cause oral infections with gingival involvement, leading to a lesion with a non-specific appearance (usually erythematous or erosive) (102, 201). Group B streptococcal infections frequently result in pharynx-amigdalitis that affects all oral mucosae and may be associated with fever and malaise. Its therapy includes re-hydration, resting, and the prescription of systemic antimicrobials (154, 157, 160, 183). Stomatitis associated with *Staphylococcus aureus* is characterized by bullous generalized dermatitis, with vesicles and desquamation, affecting lips, oral mucosa and other mucosae. Its appearance is similar to multiform erythema or impetigo, and it is usually treated with systemic antimicrobials (102, 299).

Despite the presence of the oral epithelium as a protective barrier against infection of *Neisseria gonorrhoeae*, gonococcal lesions may appear as a result of a direct inoculation. In the newborn, it may be the result of a contact when passing through the birth canal. In adults, transmission may be bucco-genital and superficial lesions are found, as white-yellowish plaques or pseudo-membranes that, when removed, result in a bleeding ulcer. Salivary flow may be reduced and saliva can be denser. The clinical history is crucial and treatment should consist of the administration of systemic antimicrobials (61, 92, 293, 332).

Among the generalized infectious diseases, syphilis may often affect the gingival tissues. Syphilis is caused by *Treponema pallidum* and may be difficult to diagnose due to the similarities with other systemic conditions (96, 172, 256). Syphilis can be congenital and

acquired. In the acquired syphilis, the incubation period may vary from 12-40 days, and the lesions may follow different stages. In primary syphilis, the lesion is located in the point of transmission, normally as a chancre that may be located on the lips, tongue or tonsils (11). The gingiva may be affected by the secondary syphilis, after 6-8 weeks or even 6 months, with the presence of a plaque (elevated papule with central erosion), that may last for weeks or even a year (18, 168, 193, 197, 257, 268). Tertiary syphilis is not frequent and, within the oral cavity, it may affect the palate and the tongue (171). Differential diagnosis is critical and sometimes difficult. The treatment consists of the administration of specific systemic antimicrobials (96, 197).

Viral infections

Different viruses may cause lesions in the oral cavity, with or without concomitant skin involvement (215). The most frequently associated viruses causing gingival and periodontal lesions are from the Herpesviridae family (herpes simplex virus type 1 (HSV-1), causal agent of oral and labial herpes lesions; herpes simplex virus type 2 (HSV-2), associated with genital herpes; and varicela zoster virus (HSV-3), responsible for varicela and herpes zoster) (64-66, 119, 137, 211, 240, 298). Herpes virus adapt easily to the host, and after the primary infection they remain inside the infected cells in a latent or silent state; they show tropism for epithelial and neural cells, and the preferred site for latency is the nervous ganglia (66, 83, 84, 324, 337).

Varicela is the result of an infection by *Herpesvirus varicellae* (HSV-3), being the result of the first contact with the virus. It results in a generalized condition, especially in children, with vesicle eruptions in skin after an incubation period of 1-3 weeks. Before or during the skin lesions, vesicles can be evident in the oral cavity, including the gingiva, and they break easily, forming ulcers surrounded by an erythematous halo. The result of the re-activation of the mentioned virus (HSV-3), residing in regional sensitive ganglia, is **herpes zoster**, especially in the elderly or associated with immune-depression. It may affect the trigeminal ganglion with clinical manifestation preceded by pain or itching feeling. Clinical lesions are vesicles surrounded by erythematous halo, with unilateral distribution; vesicles easily break, forming erosive areas (214, 262, 312). **Primary herpetic infection** caused by HSV-1 is normally suffered without notice, but it is

sometimes very evident in the form of generalized gingivo-stomatitis, with dysphagia, fever, malaise and submandibular adenopathy. It is more frequently observed in children 2-5 years, with oral lesions in the form of ulcers or erosions, after the vesicles are broken (Figure 1). Treatment may include antiviral agents and adequate nutritional support, mostly when pain compromises eating (66, 84, 216, 287, 324).

Recurrent herpetic infection by HSV-1 may be either intraoral or labial. Initial symptoms include local discomfort in the form of itching or stinging feeling. The lesions develop as an erythema, and then a variable number of grouped vesicles break forming an erosion in the oral mucosae gingiva or the lip (Figure 2). Lesions normally last 7-10 days and heal without scarring. Differential diagnosis with other conditions showing ulcers, such as recurrent aphthous stomatitis, is important; although the latter lesions will not affect keratinized tissues (178, 252, 254, 284, 341). Since the condition is self-limiting, no treatment is usually required, although if present in immune-compromised patients, antiviral agents should be prescribed (216, 287, 311, 337).

Other viruses, such as Epstein Barr virus (herpes simplex virus type 4, HSV-4), Cytomegalovirus (CMV, or herpes simplex virus type 5, HSV-5) or Coxsackie virus, are frequently transmitted via saliva and may result in specific oral manifestations: infectious mononucleosis (HSV-4) or hand, foot and mouth disease (Coxsackie virus). Sometime, they may also cause unspecific conditions, including acute stomatitis with oral ulcers and malaise and adenopathy. These conditions can be important in immune-compromised patients (25, 127, 189, 218, 231).

In addition to the previous acute conditions, viruses are related to **chronic conditions** that may require emergency attention due to complications during their development, trauma or unexpected findings, including viral wart or condyloma acuminata.

Fungal infections

Many fungal species are part of the resident flora of the mouth, but they may cause pathology when local or systemic factors trigger their overgrowth (114, 207, 222). Among these opportunistic fungal infections, candidiasis is the most frequent, normally

affecting immune-compromised subjects, especially HIV-positive patients or during infancy and elderly (49, 118, 133, 229, 278, 328). Although its localized forms are usually not severe, it may spread and lead to more severe infections, such as esophagic or systemic candidiasis. Among *Candida* spp., *C. albicans* is the most relevant for oral infections (263).

Multiple factors are associated with the pathogenesis of oral candidiasis, and these may be divided into host-related and environmental (49, 134, 275, 278, 314). Among the host-related factors are the presence of concomitant systemic diseases (such as diabetes) or debilitating conditions leading to a reduced host response. The most frequent local associated factors include removable prosthesis, systemic antimicrobials, corticosteroids, and tobacco smoking (9, 49, 104, 114, 118, 134, 207, 275, 278, 314).

Acute candidiasis can present as pseudomembranous or as erythematous candidiasis, with itching or stinging feeling, being the diagnosis mostly clinical (28, 135). Treatment will include antifungal agents, such as nystatin, amphotericin B or miconazole in solutions or gels. In severe cases or immune-compromised patients the treatment of choice is with systemic fluconazole. It is also mandatory to evaluate and control the predisposing/adjunctive local and/or systemic factors associated (9, 43, 104, 319).

Gingival manifestations of systemic conditions

Muco-cutaneous disorders

These represent a group of chronic autoimmune diseases, characterized by the presence of vesicle-bullous lesions, with liquid content (either serum or hemorrhagic). Although the evolution of these diseases is chronic, acute bouts may occur and affect an intra-oral location, as well as lesions in the skin or in other mucosae (50, 310, 331).

Vesicle-bullous diseases usually present in the gingival tissues as desquamative gingivitis. This manifestation reflects the presence of epithelial desquamation and erythematous, vesicle-bullous or erosive lesions in the gingiva. Although it is normally part of a chronic process, painful acute phases can also occur, with intense and diffuse

redness in the attached and free gingiva. The epithelium is fragile and easily detached, leaving a reddish surface, which bleeds after minimum stimulus (313). When the lesions are limited to the gingival tissues, they are more frequently located in dentate areas at buccal sites (Figure 4). Women in the 4th-5th decades of life are more prone to present these lesions (172, 184, 185, 199, 310, 325). Therapy is usually based on application of topical or systemic corticoids (51, 52, 95, 115, 191, 226).

Lichen planus is a chronic inflammatory disease affecting skin and mucosae, being the most frequent non-infectious disease of the oral cavity. The oral manifestation is very frequent, mostly in adult women (30-50 years) of Caucasian ethnicity (186, 213, 280). These oral lesions usually precede the skin lesions or are just the only lesion (Figure 5). Clinical manifestations range from its typical reticular form affecting the buccal and cheek mucosae, to erosive forms usually located in the tongue and gingiva that cause pain and tenderness, as well as bleeding. When present in the gingiva they usually present as a desquamative gingivitis affecting the attached gingiva (Figure 5). The diagnosis is both clinical (bilateral and symmetric lesions, whitish reticular lesions or red lesions, not disappearing after scraping) and histological (53, 186, 213, 281). If some of the diagnosis criteria are not fulfilled, the lesions will be defined as lichenoid reactions, normally associated with restorative materials, pharmaceutical drugs, graft versus host disease or some systemic conditions (10, 75, 80, 147, 169, 233, 246).

Pemphigus is a severe autoimmune muco-cutaneous disease, with a chronic and aggressive progression, characterized by the destruction of the intercellular adhesion systems between keratinocytes, leading to intra-epithelial bulla formation (39, 170, 221, 288). Among the different clinical forms, only the vulgaris and the vegetans can affect the oral mucosae, although the latter is very infrequent. Pemphigus vulgaris is more frequent in women, 40-60 years of age, with a Mediterranean or Jewish background. Skin lesions are more frequent, but in 50% of the cases oral lesions may precede the skin lesions (295). Intraoral lesions if affecting the gingiva appear as desquamative gingivitis (86). Diagnosis may be difficult and will be based on histology and immune-fluorescence (48, 87, 212, 230, 282, 286, 288, 296).

Pemphigoid includes a group of autoimmune muco-cutaneous diseases, either affecting the skin (bullous pemphigoid and gestational herpes) or the mucosae (benign mucous membrane pemphigoid or cicatricial pemphigoid). In the latter, the autoimmune reaction affects the basal membrane (sub-epithelial bulla), frequently occurring in women older than 50 years, presenting oral lesions in more than 90% of the cases. These lesions are usually located in the gingiva, later spreading to neighboring tissues or other sites. Gingival tissues are affected in 40-100% of the cases, as desquamative gingivitis including periods of exacerbation and remission (19, 31, 170, 239, 274, 285).

Other muco-cutaneous conditions, characterized as vesicle-bullous conditions, include: linear IgA disease, bullous epidermolysis, erythema multiforme and lupus erythematosus. When affecting the gingival, they manifest as desquamative gingivitis and the differential diagnosis should be based on histological or laboratory grounds, as well as the involvement of other body sites or organs (13, 50, 94, 200, 225, 310, 323, 331).

Allergic reactions

Allergy is an abnormal reaction of the human body, responding exaggeratedly after a contact with a foreign substance or product (allergen), which will not induce a similar reaction in other individuals (3, 27, 44, 72, 195, 228). Food products, including fruits, seafood, nuts or some vegetables, induce most allergic reactions; however, some medicines, including antibiotics (e.g. penicillin) or non-steroidal anti-inflammatory drugs (e.g. acetyl-salicylic acid) can be very relevant (15, 17, 23, 42, 46, 70, 72, 112, 179, 228, 235). Other potentially allergenic products are haptens, which needs to be linked to proteins in order to become allergens, and are very relevant in dentistry since they include some metals and dental materials (3, 41, 72, 73, 164, 169, 173, 203, 217), topical anesthesia, oral hygiene products ingredients (161), as well as components of rubber dam, latex examination gloves and cosmetics (16, 45, 79, 169, 180, 208, 277, 297). Allergies in the mouth may have different clinical manifestations ranging from the typical urticarial reaction to angioedema, although they do not normally affect the gingival tissues (27, 159, 205).

Exudative erythema multiforme is a disseminated hypersensitivity reaction, which may affect the majority of the human systems and even compromise the patient's life (3, 24, 29, 34, 47, 58, 81, 93, 98, 107, 167, 260, 270, 279, 306). An inductor or precipitating factor is normally present, including herpes simplex virus infections, drugs such as sulphamide, penicillin or salicylate, or gastro-intestinal conditions, including Crohn disease and ulcerative colitis (29, 190, 270). Clinically, it may affect skin and mucosae, with minor and major (also known as Steven Johnson syndrome) forms, and it is characterized by bullae formation (24, 34, 47, 93, 143, 190, 223, 260). The diagnosis is mainly clinical and, when affecting gingival tissues, differential diagnosis with other conditions that manifest as desquamative gingivitis should be considered (24, 47, 144). In mild cases, topical corticoids, analgesics and a soft diet may be sufficient. In severe cases, systemic corticoids are the first option, and in refractory cases the treatment is with azathioprine or dapsone (144, 192, 223, 232).

Contact allergy of intraoral location is an ill-defined entity (3, 27, 72, 73), normally associated with drugs (antimalarial, non-steroidal anti-inflammatory, antihypertensive or anti-diabetic medications) or metals (especially amalgam (41, 169, 208), gold (334), nickel (73), or other dental materials, including acrylic resins or dental composites (6, 164, 173, 203, 217, 277) (Figure 6). Contact allergies associated with toothpaste, mouth rinse or chewing gum are rare (16, 79, 161, 180, 297). The lesions are usually not clinically distinguishable from a tooth-related irritation or trauma (73, 305, 329). Symptoms include burning, itching or stinging feeling and the lesion is often defined as a liquenoid reaction (165, 206). The clinical aspect of intraoral contact allergies includes erythematous and edematous gingival tissues, sometimes with ulcers and whitish areas. The same lesions can be observed on the lip, buccal or lingual mucosae. Diagnosis, therefore, is often difficult, with a need to find a direct association between the clinical lesions and the exposure to allergen. The most important therapeutic measure is to remove the allergen, although this is not always easy, and sometimes it will not solve the case, including cases of wrong diagnosis (16, 79, 161, 180, 297).

Traumatic lesions

The clinical presentation of lesions associated with physical and chemical agents will depend of the aggression, being either direct or indirect. The effect of a direct action depends on the type of agent, the time of action and the extension of mucosa affected. Indirect effects appear as color alteration, erythema, erosion, ulcer, gingival enlargement, hemorrhage or dysgeusia (59, 236, 259).

Among traumatic lesions, iatrogenic lesions are relevant in dentistry, produced during a therapeutic intervention or as the result of the therapy (Figure 7). They are normally considered as treatment complications, since dental instruments and chemical products can cause injuries or burns, including lesions in the gingival tissues (8, 59, 71, 105, 112, 220, 236, 247, 251, 259, 276, 277, 290, 305).

Physical (mechanical and thermal) injury

Physical mechanical injuries may appear as erosions or ulcers, associated with gingival recession. But also can be observed as hyper-queratosis, vesicles or bullae, sometimes in combination with other oral lesions on lips, tongue or teeth; they may be asymptomatic, but they can also induce intense, localized pain at the area of the lesion. The correct diagnosis is based not only on the clinical aspect, but also on the identification of the noxious agent, and for that, patient collaboration is crucial (148, 182, 236, 259, 305).

Physical mechanical injuries are most frequently caused by traumatic accidents, but they can also be related to incorrect oral hygiene habits and para-functions (182, 238, 242, 301). If the physical trauma is limited, but continuous over time, the gingival lesion will be frictional hyper-queratosis that may lead to a leukoplasic lesion. If the physical trauma is more aggressive, superficial laceration or a more severe tissue loss can be produced, eventually resulting in gingival recession (Figure 8). As an example, the use of an abrasive dentifrice and vigorous horizontal brushing will result in an ulcer or an erosion in the gingiva, frequently leading to tooth abrasion (182, 301). The use of dental floss can also result in gingival ulceration or inflammation, especially at the most coronal part of the interdental papilla (142).

Some physical traumatic lesions are self-induced and they are named as self-induced gingivitis, patomimias, factitious lesions or artifact (14, 30, 37, 77, 120, 121, 244, 308, 309). Lesions present as ulcers in the gingival margin, associated with gingival recession; patients are frequently children or teenagers, sometimes associated with psychological conditions. There is a clear tendency for recurrence, and the traumatic agent can be the fingers, nails or different instruments (pencil, pen...) (69, 166, 253, 259).

Another group of physical traumatic lesions are related to dental fractures or root rests, orthodontic or prosthetic appliances and oral piercing (56, 148, 174, 175). Normally, they are observed as ulcers or erosions, but dental or periodontal abscesses can be triggered, as well as chronic infections such as sub-prosthesis palatitis or lesions as fissured epulis. Frictional hyper-queratosis can also occur. In addition, the risk of pre-cancer or carcinoma lesions is present, especially if other factors (infection, irritation, chemicals...) act also over the traumatized area.

Ionizing radiations may also cause physical injuries in the gingival tissues (320). This type of lesion is observed after irradiation therapy as part of the head-and-neck cancer treatment. The gingival tissues show mucositis, with erythema, followed by epithelial necrosis with whitish plaques, which leaves bleeding surfaces after dislodging (283).

Lesions related to hot, cold or electrical trauma are not frequent, although burns caused by very hot food or liquids may need emergency consultation (35, 219, 220, 236). The patient will feel pain in the affected area, which appears with erythema or desquamated, sometimes with vesicles, erosions or ulcers. Normally, diagnosis is straightforward (Figure 9).

Chemical and pharmacological injury

Numerous agents can induce chemical injury, including acids and bases, medicines, alcohol, tobacco, and also lesions associated with the use of mouth rinses and dentifrices. Lesions may appear after the direct contact with the agent over the mucosa, leading to a maculae, vesicles, erosions or ulcers, with different extension and

relevance, depending on the causal agent, the extension of the lesion and the time of contact (8, 71, 105, 112, 276, 290).

Summary

This is a group of periodontal lesions, with acute onset, which are not etiologically associated with oral biofilm microorganisms. They however, result in pain and difficult oral hygiene practices. Among these conditions, infectious diseases, muco-cutaneous diseases and traumatic or allergic lesions can be listed.

In most cases, the gingival involvement is not severe, but it is important to be familiar with these lesions, since they may be frequent and may represent a reason for emergency dental consultations. In addition, some of them may be the first lesions of a severe systemic disease, as in muco-cutaneous diseases and they usually manifest with the characteristic gingival lesion of desquamative gingivitis.

Many of these conditions have the appearance of an erythematous lesion, sometime erosive, with pain induced by tooth brushing or chewing. The differential diagnosis is fundamental with special focus on the anamnesis and clinical history and progression of the lesions. Erosive lesions may be the result of direct aggressions, such as trauma or indirect reactive lesions related to dental or iatrogenic interventions. Similarly the proper differential diagnosis will lead to the appropriate therapeutic intervention.

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Figure 1. A periodontal abscess, manifesting as a localised purulent lesion within the gingival wall of the periodontal pocket.

Figure 2. Pericoronal abscess associated to the right lower third molar.

Figure 3. Periodontal abscess with the presence of furcation involvement.

Figure 4. Periodontal abscess in untreated periodontitis.

Figure 5. Microbiological sampling in a periodontal abscess.

Figure 6. Periodontal abscess demonstrating suppuration through the periodontal pocket.

Figure 7a. Periodontal abscess before treatment.

Figure 7b. Periodontal abscess, 12 days later, after treatment with azithromycin.

Figure 8. Multiple gingival crater formation. The clinical picture includes rapid progression and severe periodontal destruction.

Figure 9. Necrotic area in a localized papilla: necrotizing gingivitis starts at the interdental papilla and different degrees of destruction can be observed in different areas of the same mouth.

Figure 10. Necrotizing periodontitis: it can occur after numerous episodes of necrotizing gingivitis, or as a necrotizing disease over a pre-existing periodontitis.

Figure 11. Plaque and calculus accumulation in a chronic gingivitis patient: necrotizing periodontal diseases affect tissues already affected by chronic periodontal conditions.

Figure 12. Necrotizing gingivitis affects more frequently the lower anterior sextant.

Figure 13. Bleeding observed in necrotizing gingivitis: it can occur spontaneously or after a minimum stimulus.

Figure 14. Papilla destruction in necrotizing gingivitis: no pocket formation is observed due to the loss of soft tissues.

Figure 15. Crater formation and bleeding in a posterior area.

Figure 16. Gingival craters are important sequelae since they can limit mechanical plaque control.

Figure 17. Aesthetic consequences of necrotizing periodontal diseases: the best treatment is prevention by means of the control of the predisposing factors.

Figure 18. Herpetic gingivo-stomatitis: painful gingivitis with generalized vesicles in primary herpetic infection.

Figure 19. Recurrent herpetic infection: vesicles break, leading to erosive lesions. Gingival location is not infrequent.

Figure 20. Oral candidiasis oral: one of the predisposing factors is removable prosthesis and erythematous lesions are among the most frequent lesions.

Figure 21. Muco-cutaneous disorders: most of them may have oral and gingival, normally with a chronic evolution but also with acute periods.

Figure 22. Lichen planus: gingival involvement includes erosive lesions and reticular whitish lesions.

Figure 23. Lichenoid lesions: identical to lichen planus lesions, but clearly associated to a causative fact (such amalgam fillings), and disappearing after the elimination of the factor.

Figure 24. Iatrogenic lesions: gingival erosions.

Figure 25. Traumatic lesions: often self-inflicted, or associated to traumatic tooth brushing or incorrect oral hygiene habits.

Figure 26. Burning lesion: associated to very hot food intake, leading to lesions with vesicles that lead to erosive areas.

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