Acute periodontal lesions

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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 because of the associated pain. In addition, and in contrast to most other periodontal conditions, 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 In spite of this, the available scientific knowledge on these conditions is limited and is based on somewhat outdated literature.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, although 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, mucocutaneous disorders, or traumatic and allergic lesions. This article provides an overview and updates of existing information on acute conditions affecting the periodontal tissues, including abscesses in the periodontium, necrotizing periodontal diseases and other acute conditions.

Abscesses in the periodontium

Definition of periodontal abscess

Abscesses in the periodontium are odontogenic infections that may be caused by pulp necrosis, periodontal infections, pericoronitis, trauma or surgery (109). Odontogenic or dental abscesses are classified, according to the source of infection, 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 localized accumulation of pus located within the gingival wall of the periodontal pocket’ (130) (Fig. 1).

Classification of periodontal abscesses

Different criteria have been used to classify periodontal abscesses.

Location

Abscesses can be classified as gingival or periodontal abscesses (110). A gingival abscess is a localized painful swelling that affects only the marginal and interdental gingiva and is normally associated with subgingivally impacted foreign objects. These conditions may occur in a previously healthy gingiva (7). A periodontal abscess is a localized painful swelling that affects deeper periodontal structures, including deep pockets, furcations and vertical osseous defects, and is usually located beyond the mucogingival line. Histologically, both lesions are identical, but a gingival abscess affects only the marginal soft tissues of previously healthy sites, whilst a periodontal abscess occurs in a periodontal pocket associated with a periodontitis lesion (76).

Course of the lesion

The course of the lesion can be acute and chronic. An acute periodontal abscess usually manifests symptoms such as pain, tenderness, sensitivity to palpation and suppuration upon gentle pressure. A chronic abscess is normally associated with a sinus tract and it is usually asymptomatic, although the patient can experience mild symptoms (250). A localized 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.

**Number of abscesses**

The number of periodontal abscesses (single and multiple) has also been used for classification purposes (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, in medically compromised patients and in patients with untreated periodontitis after systemic antibiotic therapy for nonoral reasons (125, 126, 321). Multiple abscesses have also been described in a patient with multiple external root resorptions (339).

**Type of etiological factors**

A periodontal abscess is usually associated with a previously existing periodontal pocket, although it can also develop in the absence of a pocket (130). Thus, different types of abscesses may be considered, as related to their etiological factors; this classification will be described in the section on etiology.

**International Workshop for a Classification of Periodontal Diseases and Conditions**

According to the *International Workshop for a Classification of Periodontal Diseases and Conditions* (year 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 (which 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’ (Fig. 2).

**Clinical significance of periodontal abscess**

A common periodontal emergency

Periodontal abscesses represented ca. 14% of all dental emergencies in a study in the USA (7). In general practices in the UK, 6–7% of the patients treated in 1 month suffered from a periodontal abscess, which was the third most prevalent infection that demanded 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, a periodontal abscess was detected in 37% of the patients and in 3.7% of the teeth followed for 5–29 years (mean 12.5 years) (209); in the Nebraska prospective longitudinal study, 53% of the patients followed for 7 years had a periodontal abscess, and 85% of these abscesses were associated with teeth treated only with coronal scaling. Sixteen out of 27 abscess sites had initial probing pocket depths deeper than 6 mm, and in eight sites probing...
pocket depths were 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 because of the presence of furcation, and complex anatomy and root morphology. However, one case series suggested that the mandibular anterior incisors were the most frequently affected teeth (149).

**Tooth loss**

Periodontal abscesses may lead to tooth loss, especially if they affect teeth with pre-existing moderate to severe attachment loss, as occurs during supportive periodontal therapy in patients with severe chronic periodontitis. In fact, periodontal abscess has been considered as the main cause for tooth extraction during supportive periodontal therapy (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 supportive periodontal therapy 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). Taking these reports into account, it has been suggested that when a periodontal abscess is encountered in patients receiving supportive periodontal therapy, early diagnosis and adequate therapy are crucial to preserve the prognosis of the affected tooth (294).

**Association 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 during therapy or related to an untreated abscess. During the treatment of an abscess, the concomitant bacteremia may lead to colonization of pathogenic microorganisms in other body sites and to the development of different infections, such as pulmonary actinomycosis (315), a brain abscess containing *Prevotella melaninogenica* and other *Prevotella* spp. (103), or a total knee arthroplasty infection (330). It has been suggested that the risk of bacteremia during abscess drainage may be reduced if a needle aspirate of the abscess contents is obtained before the procedure (99, 265).

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

**Etiology, pathogenesis and histopathology of periodontal abscess**

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

In periodontitis, a periodontal abscess may represent a period of disease exacerbation that is favored by the existence of tortuous pockets, the presence of furcation involvement (Fig. 3) or a vertical defect, in which marginal closure of the pocket may lead to spread 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 defence, could result in a diminished capacity to drain the increased suppuration. Among periodontal abscesses in periodontitis patients, different subgroups can be distinguished:

- after nonsurgical 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 pockets, whilst 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 of an untreated periodontitis (74) (Fig. 4).
- acute exacerbation in refractory periodontitis (97).
- acute exacerbation in supportive periodontal therapy, as described previously (55, 209, 294).

![Fig. 3. Periodontal abscess with the presence of furcation involvement.](image-url)
systemic antimicrobial intake without subgingival debridement. In patients with severe periodontitis this may also cause abscess formation (125, 126, 321), probably related to an overgrowth of opportunistic bacteria (125).

Periodontal abscesses can also occur in previously healthy sites (i.e. nonperiodontitis periodontal abscesses) owing to impaction of foreign bodies or to alteration of the root surfaces:

- different foreign bodies have been described to be associated with the development of a periodontal abscess, for example: an orthodontic elastic (250); a piece of dental floss (5); a dislodged cemental tear (124); a piece of a toothpick (100); or pieces of nails in subjects with nail-biting habits (304). 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 by different factors: perforation by an endodontic instrument (4); cervical cemental tears (124, 146); external root resorption (339); an invaginated tooth (60); or a cracked tooth (116).

In the development of a periodontal abscess, the first step may be the invasion of bacteria into 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, 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 focus, their virulence and the local pH (an acidic environment will favor the activity of lysosomal enzymes) (76).

The histopathology of periodontal abscess lesions was described following evaluation of biopsies retrieved from 12 abscesses (76), observing 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 neutrophils and lymphocytes present in an area of destroyed and necrotic connective tissue.
- a destroyed and ulcerated pocket epithelium.

In seven biopsies analyzed using electron microscopy, gram-negative bacteria were found to invade the pocket epithelium, and the affected connective tissue formed a mass of granular, acidophilic and amorphous debris.

**Microbiological findings**

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

The most prevalent bacterial species identified in periodontal abscesses, using culture-based or molecular-based diagnostic techniques, is *Porphyromonas gingivalis*, with a range in prevalence of 50–100% (82, 123, 128, 149, 224, 321, 327) (Fig. 5). Other strict anaerobes frequently detected include *Prevotella intermedia*, *Prevotella melaninogenica*, *Fusobacterium 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 abscesses is not different from the microbiota of chronic periodontitis lesions. It is polymicrobial and dominated by non-motile, gram-negative, strictly 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 types of abscesses, except for those associated with systemic antibiotic intake for nonoral reasons in patients with periodontitis (125, 126, 321): in these abscesses, similarly to other abscesses in periodontitis, periodontal pathogens were present, although opportunistic bacteria were also detected, especially *Staphylococcus aureus*, leading the authors to suggest that this type of abscess could be considered as a superinfection.

**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 (ranging from light discomfort to severe pain, tenderness of the gingiva, swelling, tooth mobility, tooth elevation and sensitivity of the tooth to palpation) has been described to be associated with an abscess (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 (Fig. 6), which 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 or increased tooth mobility (123, 128, 300).

The radiographic examination may reveal a normal appearance, or some degree of bone loss (as most abscesses will occur in a pre-existing periodontal pocket).

Periodontal abscesses may be associated with elevated body temperature, malaise and regional lymphadenopathy (128, 145, 300), and 30% of the patients may have elevated numbers of blood leukocytes (128).

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

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

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

**Treatment of a periodontal abscess**

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

**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 the body, 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 drainage. If the abscess is associated with a foreign-body impaction, the object must be eliminated through careful debridement (5), although it may no longer be present.

Systemic antimicrobials may be used as the sole treatment, as initial treatment or as an adjunctive treatment to drainage. Systemic antimicrobials as the sole or as initial treatment may only be recommended if there is a need for premedication, if the infection is not well localized or if adequate drainage cannot be ascertained (176). As an adjunctive treatment, systemic antimicrobials should be considered if a clear systemic involvement is present (7, 176).

The duration of therapy and the type of antibiotic is also a matter for discussion, including the recommendation of shorter courses of therapy (176, 202). However, the available scientific evidence on the efficacy of these therapies is very limited, with only two prospective case series and two randomized clinical trials. Smith & Davies (300) evaluated incision and drainage of the abscess, together with adjunctive systemic metronidazole (200 mg, three times daily for 5 days), followed by a delayed periodontal therapy, in 22 abscesses for up to 3 years. Hafström et al. (123) 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. Herrera et al. (129) compared azithromycin (500 mg, once per day for 3 days) vs. amoxicillin plus clavulanate (500 + 125 mg, three times daily for 8 days), with delayed scaling (after 12 days), in 29 patients with abscesses followed for 1 month, and concluded that both protocols were similarly effective. Eguchi et al. (82) compared irrigation with sterile physiological saline and 2% minocycline hydrochloride ointment vs. irrigation with sterile physiological saline without the local antibiotic, in 91 patients for 7 days.

Surgical procedures have also been proposed, mainly for abscesses associated with deep vertical defects (158) or in cases occurring after periodontal debridement in which residual calculus is present subgingivally after treatment (74). A case series evaluating a combination of an access flap with deep scaling and irrigation with doxycycline is also available and reports ‘good results’, but scientific data were not provided (316).

After drainage and debridement the patient should be recalled 24–48 h after treatment to evaluate the resolution of the abscess (Fig. 7A,B) and the duration of the intake of antimicrobials. 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 immediate drainage is not possible or a systemic affect is evident, therapy with systemic antimicrobials...
should be considered. The drug with the most appropriate profile is metronidazole (normally prescribed for acute conditions at 250 mg, three times daily). Azithromycin (500 mg, once per day) and amoxicillin plus clavulanate (500 + 125 mg, three times daily) 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 a residual lesion

As most periodontal abscesses occur in a pre-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 already within the active phase of therapy, the periodontal therapy should be completed once the acute lesion has been treated. In patients receiving supportive periodontal therapy, careful evaluation of the recurrence of the abscess should be made, as well as assessment of the tissue damage and how this affects tooth prognosis.

Summary

Abscesses in the periodontium are important because 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 types of abscess have been identified, mainly classified by their etiological factors because there are clear differences between those affecting a pre-existing periodontal pocket and those affecting healthy sites.

For the management of this condition, rapid and accurate diagnosis (mainly based on clinical features) and provision of early therapy are mandatory. Therapy for the acute condition should be based on drainage and debridement, with evaluation of the need of systemic antimicrobial therapy based on local and systemic factors. When the supporting tissues have been destroyed to the 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 has been controlled, as most abscesses are found in patients with untreated periodontitis, thus needing periodontal therapy.

Necrotizing periodontal diseases

Definition

Necrotizing periodontal diseases are a group of infectious diseases that include necrotizing ulcerative gingivitis, necrotizing ulcerative periodontitis and necrotizing stomatitis. However, it has also been suggested that these conditions may represent different stages of the same disease because they have similar etiologies, 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 (Fig. 8).

Necrotizing ulcerative gingivitis has been diagnosed for centuries but referred to by various names, such as Vincent’s disease, trench-mouth disease, necrotizing gingivo-stomatitis, fuso-spirochaetal stomatitis, ulcerative membranous gingivitis, acute ulcerative gingivitis, necrotizing ulcerative gingivitis and acute necrotizing ulcerative gingivitis (21, 138, 152, 269). Necrotizing ulcerative periodontitis 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 necrotizing ulcerative gingivitis and necrotizing ulcerative periodontitis. More recently, the terms necrotizing gingivitis and necrotizing periodontitis have been used instead of the terms necrotizing ulcerative gingivitis and necrotizing ulcerative periodontitis (138). The simpler terms necrotizing gingivitis and necrotizing periodontitis adequately describe these diseases and these terms will be used in the rest of the text.

Fig. 8. Multiple gingival crater formation. The clinical scenario includes rapid progression and severe periodontal destruction.
Classification of necrotizing periodontal diseases

According to the location of the tissue affected by the acute disease process, necrotizing periodontal diseases 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: when 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

Necrotizing periodontal diseases are considered to be among the most severe inflammatory conditions associated with oral biofilm bacteria (138). Therefore, it is important to control predisposing factors, and once the disease has developed, to act quickly in order to limit its progression and exacerbation.

The prevalence of necrotizing periodontal diseases in systemically healthy populations has not been adequately established because most studies have focused on a specific group of patients with clear predisposing factors, such as military personnel (141, 248), students (108, 188, 307), patients positive for HIV (136, 137) 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 epidemiologic information. A high prevalence of necrotizing gingivitis (14%) was observed in different populations (including military groups) during the Second World War (12, 138) and a moderately high rate (2.2%) was observed in populations in North America in the 1950s (122). After the Second World War, the prevalence clearly decreased in developed countries and currently the prevalence is low.

Necrotizing periodontal diseases have been described in young people from both developed and developing countries (12). In North America and Europe, these diseases have been studied mostly in groups of subjects in their late teens to mid-20s. In 326 North-American students in the 1960s (108), the prevalence of necrotizing periodontal diseases ranged from 2.5% to 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 of necrotizing periodontal diseases is higher than in developed countries, 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 of age (249). In South Africa, 3.3% of subjects 3–48 years of age, presented with necrotizing gingivitis; 73% of these subjects were 5–12 years of age and most were of a low socio-economic class (20). In Nigeria, the prevalence of necrotizing gingivitis ranged between 1.7% and 15% in children of 2–6 years of age, and was 27.2% in children with severe malnutrition (12, 88, 292). In Kenya, 0.15% of patients who attended the Nairobi Hospital during one year were diagnosed with necrotizing gingivitis and 58.5% were younger than 11 years of age (155). In spite of these figures, subjects of any age may be affected.

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

Necrotizing periodontal diseases can progress rapidly and cause severe tissue destruction. It is therefore important for these conditions to be managed promptly because there is evidence proving that necrotizing periodontal diseases can be controlled by adequate periodontal treatment combined with effective oral-hygiene measures and control of predisposing factors (152). However, patients with necrotizing gingivitis are frequently susceptible to future disease recurrence, mostly as a result of the difficulties in controlling predisposing factors as well as the difficulty in achieving proper supragingival biofilm control, in part because of the sequelae of these diseases, including the presence of gingival craters (196).

Necrotizing gingivitis 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 disease into a generalized disease (Fig. 9). Necrotizing gingivitis may also progress apically, evolving into necrotizing periodontitis (Fig. 10). In fact, necrotizing periodontitis can be the result of one or various episodes of necrotizing gingivitis, or it can be the result of a necrotizing periodontal disease affecting a site with pre-existing periodontitis (227).
Necrotizing periodontal diseases can also become chronic, with a slow reduction in their symptomatology and progression, and 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 patients with AIDS or with severe malnutrition, necrotizing gingivitis and necrotizing periodontitis 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 to the compromised host immune response, leading to extensive bone destruction and the presence of large osteitis lesions and oral-antral fistulae (335). Necrotizing stomatitis has common features with cancrum oris or Noma. Some investigators suggest that Noma is a progression of necrotizing stomatitis affecting the skin, whereas others believe that necrotizing stomatitis and Noma are two distinct clinical entities. Noma is a destructive gangrenous disease affecting the facial tissues. It is associated with high rates of mortality and morbidity (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 necrotizing gingivitis, 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**

Necrotizing periodontal diseases are caused by infectious agents, although predisposing factors, such as a compromised host immune response, are the main factors facilitating bacterial pathogenicity. This bacterial etiology was already demonstrated by Plaut in 1894 and by Vicent in 1896 (269), as microscopic examination of plaque samples 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, knowledge of the pathogenesis of these diseases is limited because 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 the connective tissue (181), as well as to release endotoxins that may cause periodontal tissue destruction through the activation or modification of the host response.

Necrotizing gingivitis lesions show a distinct pathology under light microscopy (181), with the presence of an ulcer within the stratified squamous epithelium and the superficial layer of the gingival connective tissue surrounded with a nonspecific acute inflammatory reaction. Four areas 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 high number of leukocytes, especially neutrophils, and numerous spirochetes of different sizes and other bacterial morphotypes located between the host cells.
the necrotic zone, containing disintegrated cells, together with medium- and large-size spirochetes and fusiform bacteria.

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

Microbiology of necrotizing periodontal diseases

A similar composition of the microbiota associated to necrotizing periodontal diseases has been observed in different studies, including Treponema spp., SeIEnomonas spp., Fusobacterium spp. and P. intermedia. Other microorganisms have also been described, although these were defined as ‘variable’ flora and were not present in all cases (187). As this typical microbiological description can also be detected in healthy, gingivitis or periodontitis sites, the use of microbiological testing does not provide relevant diagnostic information (67, 152).

In HIV-positive patients with necrotizing periodontal diseases the microbiological findings are also non-specific (204, 266, 338), except in regard to the counts of yeasts (namely, Candida albicans), the presence of herpes viruses (62, 272, 338, 340) or the detection of superinfecting bacterial species, such as enteric bacteria including Enterococcus avium, Enterococcus faecalis, Clostridium clostridioforme, Clostridium difficile, Mycoplasma spp. and Klebsiella pneumoniae (258, 340). Most recently, with the use of molecular technologies (PCR), some bacterial species (including Eubacterium saphenus, Eubacterium saburreum, Filifactor alocis, Dialister spp. and Porphyromonas endodontalis) were found to be frequently associated with necrotizing periodontal disease lesions, whilst 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 (including human cytomegalovirus) in necrotizing periodontal diseases (78, 273). In children with necrotizing gingivitis in Nigeria, in addition to the presence of cytomegalovirus 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 for necrotizing periodontal disease are those that alter the host immune response, although usually more than one factor is necessary for initiating the disease (138). In a study in the USA, the most important factor was HIV infection. In non-HIV patients, the most important factors were a previous history of necrotizing periodontal disease, poor oral hygiene, inadequate sleep, unusual psychological stress, poor diet, recent systemic diseases, alcohol abuse, tobacco smoking, Caucasian ethnicity and age below 21 years (140).

Systemic conditions

Conditions that impair the host immune response favor necrotizing periodontal diseases. Infection with HIV or with diseases affecting leukocytes (e.g. leukemia) are among the most important predisposing factors. Other systemic conditions that have shown a positive association with necrotizing periodontal diseases include malnutrition, measles, chickenpox, tuberculosis, herpetic gingiva-stomatitis, malaria, or even diabetes, which was identified in a study of Chilean adolescents (188).

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

- in HIV-positive patients, necrotizing periodontal diseases are more frequent and show faster progression, although no differences have been detected between the characteristics of the disease in HIV-negative and HIV-positive patients. It has been suggested that HIV-positive patients have a higher tendency for recurrence and a 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 necrotizing gingivitis and necrotizing periodontitis (113, 303) and therefore the diagnosis of necrotizing periodontal disease 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 a predisposing factor for necrotizing periodontal diseases (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 inverted proportion in the ratio of helper T-lymphocytes/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 situations of acute stress have been associated with necrotizing gingivitis (140, 152, 291). Certain situations may predispose individuals to necrotizing periodontal disease, such as military personnel in wartime, new recruits for military services, drug-abusers during abstinence syndrome, students during examination periods and patients with depression or other psychological conditions (108, 122, 248). During these stress periods, not only is the immune response 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 reductions of the gingival microcirculation and salivary flow and increases in the serum and urine levels of 17-hydroxycorticosteroid, which are associated with an alteration in the function of polymorphonuclear leukocytes and lymphocytes, or even with an increase in the levels of periodontal pathogens, such as P. intermedia (187). Higher urinary levels of 17-hydroxycorticosteroid have been reported in patients with necrotizing gingivitis than in healthy or treated patients; in addition, the former group demonstrated statistically significant higher levels of anxiety, depression or emotional alteration (138). Patients with necrotizing gingivitis also had polymorphonuclear leukocytes with altered functions because their bactericidal, phagocytic and chemotactic capacities were depressed (63).

Inadequate oral hygiene, pre-existing gingivitis and previous history of necrotizing periodontal disease

Plaque accumulation has been considered a predisposing factor for necrotizing periodontal disease (140, 152), although it may also be a consequence of the presence of ulcers and crater lesions that may limit toothbrushing as a result of pain. Necrotizing periodontal disease usually occurs over a pre-existing periodontal disease, usually chronic gingivitis (248) (Fig. 11). In one study, 28% of the patients with necrotizing periodontal disease reported a history of painful gingival inflammation and 21% showed lesions compatible with previous necrotizing periodontal disease (140).

Alcohol and tobacco consumption

Smoking is a risk factor for necrotizing periodontal disease (152, 153, 264) and, in fact, most HIV-negative patients diagnosed with necrotizing periodontal disease were smokers (108, 248, 307). The mechanisms explaining this association are probably related to the effect of smoking on inflammation and the tissue response, because smoking interferes with both polymorphonuclear leukocyte and lymphocyte function and nicotine induces vasoconstriction in gingival blood vessels.

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

Young age and ethnicity

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

Diagnosis of necrotizing periodontal diseases

The diagnosis of necrotizing periodontal diseases is based mainly 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 necrotizing periodontal disease 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 and have a 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 (Fig. 12). In necrotizing gingivitis, gingival bleeding is a frequent finding, and it is usually spontaneous or occurs after minimal contact (Fig. 13). Pain normally has a rapid onset and occurs with different degrees of severity, depending on the severity and extent of the lesions. The bouts of pain increase with eating and with oral hygiene practices and is normally the reason for the patient’s consultation.

Other less common findings include the presence of:

- pseudomembrane over the necrotic area. The pseudomembrane consists of a whitish/yellow-colored meshwork, 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 this is not an exclusive sign of necrotizing gingivitis.
- adenopathies, which are usually found in the most severe cases of disease. 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 necrotizing gingivitis occurs in necrotizing periodontitis, but in addition, in necrotizing periodontitis the following characteristics may be present:

- necrosis affects the periodontal ligament and the alveolar bone, leading to loss of attachment. As there is concomitant necrosis of the soft tissue, the presence of pockets is not an usual finding (Fig. 14).
- as the disease progresses (Fig. 15), the interdental papilla is divided into a buccal part and a lingual/palatal part, with a necrotic area in the middle, known as the interproximal crater. If the craters are deep, the interdental crestal bone becomes exposed and denuded. 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 the buccal or lingual/palatal parts of the 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. These lesions are of greater severity in patients with severe systemic compromise, including patients with AIDS and patients with severe malnutrition (335).

Management of necrotizing periodontal diseases

Owing to the (previously listed) specific features of necrotizing periodontal disease (tissue destruction, acute course and 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: treatment of the acute phase; treatment of the pre-existing condition and corrective treatment of the disease sequelae; supportive or maintenance phase.

Treatment of the acute phase

There are two main objectives of therapy: to arrest the disease process and tissue destruction; and to control the patient’s general feeling of discomfort and pain that is interfering with nutrition and oral hygiene practices (138). 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 minimal pressure over the ulcerated soft tissues. The debridement should be performed daily, becoming 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 because brushing directly in the wounds may impair healing and induce pain. During this period the patient is advised to use chemical plaque-control formulations, such as chlorhexidine-based mouthrinses (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 local oxygen therapy, which may help to reduce, or even eradicate, microorganisms, resulting in faster clinical healing with less periodontal destruction (101).

In cases that show unsatisfactory response to debridement or show systemic effects (fever and/or malaise), the use of systemic antimicrobials may be considered. Metronidazole (250 mg, every 8 h) may be an appropriate first choice of drug because it is active against 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 because of the large numbers 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.

Treatment of the pre-existing condition

Necrotizing periodontal diseases normally occurs over a pre-existing chronic gingivitis or periodontitis infection. Once the acute phase has been controlled, treatment of the pre-existing chronic condition should be started, 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 involved systemic conditions.

**Corrective treatment of disease sequelae**

The correction of the altered gingival topography caused by the disease should be considered (Fig. 16) because gingival craters may favor plaque accumulation and disease recurrence. Gingivectomy and/or gingivoplasty procedures may be helpful for treatment of superficial craters; periodontal flap surgery, or even regenerative surgery, are more suitable options for deep craters (138).

**Supportive or maintenance phase**

During supportive or maintenance phases, the main goal is compliance with the oral hygiene practices (Fig. 17) and control of the predisposing factors.

![Fig. 16. Gingival craters are important sequelae because they can limit mechanical plaque control.](image)

**Specific considerations for HIV-positive patients**

HIV-positive patients may not be aware of their serologic status. The occurrence of necrotizing periodontal disease in systemically healthy individuals is suggestive of HIV infection and, therefore, the affected individuals should be screened for HIV (138, 140). The specific management of necrotizing periodontal disease in HIV-positive patients includes debridement of bacterial deposits combined with irrigation of the site with iodine-povidone, based on its hypothetic anesthetic and bleeding control effects (338), although no scientific studies are available to support this protocol (271, 336, 338). Careful consideration should be made regarding the use of systemic antimicrobials because of the risk of overgrowth of *Candida* spp. Metronidazole has been recommended for its narrow spectrum and 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 necrotizing periodontal disease (194). In nonresponding 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 conditions, leading to development of a customized periodontal treatment plan (266, 272, 338).

**Summary**

Necrotizing periodontal disease includes necrotizing gingivitis, necrotizing periodontitis and necrotizing stomatitis, and these may be considered as different stages of the same pathologic process. This group of diseases always presents three typical clinical features – papilla necrosis, bleeding and pain – which makes them different from other periodontal diseases. Although their prevalence is not high, their importance is clear because they represent the most severe biofilm-related periodontal conditions, leading to rapid tissue destruction. In their etiology, together with bacteria, numerous factors that alter the host response may predispose to these diseases, including HIV infection, malnutrition, stress or tobacco smoking.

Owing to their acute presentation, together with the associated pain and tissue destruction, treatment should be provided immediately upon diagnosis; this should include superficial debridement, careful
mechanical oral hygiene, rinsing with chlorhexidine and daily revisions. Systemic antimicrobials may be used adjunctively in severe cases or in nonresponding conditions, and the best option is metronidazole. Once the acute disease is under control, definitive treatment should be provided, including 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 considered based on the needs of the individual case.

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 responsible for emergency consultations.

The 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 establish the proper diagnosis, a clinical history, anamnesis and careful examination are mandatory because frequently there is a direct and recent relationship with the cause (68). In the following discussion, the lesions are classified according to their etiology because 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 uncommon. 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 gonococci, tularaemia or anthrax. In addition, the lesions present in the oral cavity may be a secondary location of generalized infectious disease, as in scarlatina, diphtheria, syphilis or tuberculosis.

Both staphylococci and streptococci may cause oral infections with gingival involvement, leading to a lesion with a nonspecific 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. Treatment includes rehydration, rest and the prescription of systemic antimicrobials (154, 157, 160, 183). Stomatitis associated with S. aureus is characterized by bullous generalized dermatitis, with vesicles and desquamation, which affects the 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 with Neisseria gonorrhoeae, gonococcal lesions may develop as a result of direct contact. In the newborn, N. gonorrhoeae infection may occur through contact when passing through the birth canal. In adults, transmission may be bucco-genital and superficial lesions are found as white/yellowish plaques or pseudomembranes 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 generalized infectious diseases, syphilis may often affect the gingival tissues. Syphilis is caused by Treponema pallidum and may be difficult to diagnose because of similarities with other systemic conditions (96, 172, 256). Syphilis can be congenital or acquired. In acquired syphilis, the incubation period may vary from 12 to 40 days, and the lesions may follow different stages. In primary syphilis, the lesion is located at 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 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 uncommon and, when present in the oral cavity, it may affect the palate and the tongue (171). Differential diagnosis is critical and sometimes difficult. 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, the causal agent of oral and labial herpes lesions; herpes simplex virus type 2, associated with genital herpes; and varicella-zoster virus, responsible for varicella and herpes
Herpesviruses 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 of herpes simplex viruses and varicella-zoster virus is ganglions in the nervous system (66, 83, 84, 324, 337).

Varicella is the outcome of an infection with varicella-zoster virus and occurs after the initial 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 after appearance of 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 varicella-zoster virus from the regional sensitive ganglia is herpes zoster, which occurs especially in the elderly or associated with immune-depression. It may affect the trigeminal ganglion, with clinical manifestation preceded by pain or an itching feeling. Clinical lesions are vesicles surrounded by an erythematous halo, with a unilateral distribution; the vesicles break easily, forming erosive areas (214, 262, 312). Primary herpetic infection with herpes simplex virus type-1 is normally asymptomatic, 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 of age, with oral lesions in the form of ulcers or erosions, after the vesicles have broken (Fig. 18). Treatment may include antiviral agents and adequate nutritional support, mostly when pain compromises eating (66, 84, 216, 287, 324).

Recurrent herpetic infection with herpes simplex virus type-1 may be either intraoral or labial. Initial symptoms include local discomfort in the form of itching or stinging. The lesions develop as an erythema, and then a variable number of grouped vesicles break, forming an erosion in the oral mucosa, gingiva or the lip (Fig. 19). Lesions normally last for 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). As 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, cytomegalovirus and Coxsackie virus, are frequently transmitted via saliva and may result in specific oral manifestations: infectious mononucleosis (Epstein–Barr virus) or hand, foot and mouth disease (Coxsackie virus). Sometimes 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 acute conditions already discussed, viruses are associated with chronic conditions that may require emergency attention for complications during their development, trauma or unexpected findings, including viral warts 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 in the elderly (49, 118, 133, 229, 278, 328). Although their localized forms are usually not severe, it may spread and lead to more severe infections, such as esophageal 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 (Fig. 20), and these may be divided into host-related factors and local and environmental factors (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 common local and environmental factors include removable prostheses, systemic antimicrobials, corticosteroids and tobacco smoking (9, 49, 104, 114, 118, 134, 207, 275, 278, 314).

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

Gingival manifestations of systemic conditions

Mucocutaneous disorders

Mucocutaneous disorders represent a group of chronic autoimmune diseases that are 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 intraoral location, and also the skin or other mucosae (50, 310, 331).

Vesicle-bullous diseases usually present in the gingival tissues as desquamative gingivitis. This manifestation reflects the presence of epithelial desqua-
present in the gingiva, the lesions are usually observed as a desquamative gingivitis affecting the attached gingiva. 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 diagnostic criteria are not met, the lesions will be defined as lichenoid reactions (Fig. 23), normally associated with restorative materials, pharmaceutical drugs, graft vs. host disease or some systemic conditions (10, 75, 80, 147, 233, 246).

Pemphigus is a severe, autoimmune mucocutaneous 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 common, but in 50% of the cases oral lesions may precede the skin lesions (295). Intra-oral 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 mucocutaneous diseases that affect either the skin (bullous pemphigoid and gestational herpes) or the mucosa (mucous membrane pemphigoid or cicatricial pemphigoid). In the latter, the autoimmune reaction affects the basal membrane (subepithelial bulla) and frequently occurs in women older than 50 years of age, presenting oral lesions in more than 90% of the cases. These lesions are usually located in the gingiva, later spreading to neighboring tissues or to 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 mucocutaneous conditions, characterized as vesicle-bullous conditions, include linear IgA disease, bullous epidermolysis, erythema multiforme and lupus erythematosus. When affecting the gingiva, they manifest as desquamative gingivitis and the differential diagnosis should be based on histologic or laboratory evidence, 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: an exaggerated response to a contact with a foreign substance or product (allergen) that does not necessarily 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 nonsteroidal anti-inflammatory drugs (e.g. acetylsalicylic acid) can also be responsible for allergic reactions (15, 17, 23, 42, 46, 70, 72, 112, 179, 228, 235). Other potentially allergenic products are haptens, which need to be linked to proteins in order to become allergens, and are very relevant in dentistry because they are present in some metals and dental materials (3, 41, 72, 73, 164, 169, 173, 203, 217), in topical anesthesia, in oral hygiene products (161), as well as in rubber dams, 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).

Erythema multiforme is a disseminated hypersensitivity reaction, which may affect the majority of 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; these include herpes simplex virus infections; drugs such as sulfamides, penicillin or salicylate; or gastrointestinal conditions, including Crohn’s disease and ulcerative colitis (29, 190, 270). Clinically, exudative erythema multiforme may affect the skin and mucosae, presents as minor and major (also known as Stevens–Johnson syndrome) forms and is characterized by bullae formation (24, 34, 47, 93, 132, 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 an intraoral location is an ill-defined entity (3, 27, 72, 73) and is normally associated with drugs (antimalarial, nonsteroidal anti-inflammatory, antihypertensive or antidiabetic medications) or metals (especially amalgam (41, 169, 208), gold (334) or nickel (73)), or with other dental materials, including acrylic resins or dental composites (6, 164, 173, 203, 217, 277) (Fig. 24). Contact allergies associated with toothpastes, mouthrinses or chewing gums 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, 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. Therefore, diagnosis is often difficult, with a need to find a direct association between the clinical lesions and the exposure to allergens. 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 incorrect diagnosis (16, 79, 161, 180, 297).

**Traumatic lesions**

The clinical presentation of lesions associated with physical and chemical agents will depend on wether the action of the agent is direct or indirect. The effect of a direct action depends on the type of agent, the length of exposure to the agent and the amount of surface 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 because they are produced during therapeutic intervention or as a result of the therapy (Fig. 24). They are normally considered as treatment complications because 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. However, they can also present as hyperkeratosis, vesicles or bullae, sometimes in combination with other oral lesions on the 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 in 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 parafunctions (182, 238, 242, 301). If the physical trauma is limited, but continuous over time, the gingival lesion will be frictional hyperkeratosis that may lead to a leukoplakic lesion. If the physical trauma is more aggressive, superficial laceration or more severe tissue loss can occur, eventually resulting in gingival recession (Fig. 25). For example, the use of an abra-
sive 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 are termed self-induced gingitivis, patomimias, factitious lesions or artifacts (14, 30, 37, 77, 120, 121, 244, 308, 309). Lesions present as ulcers in the gingival margin and are associated with gingival recession; patients are frequently children or teenagers, sometimes with psychological conditions. There is a clear tendency for recurrence, and the traumatic agent can be the fingers, nails or different instruments (pencil, pen, etc.) (69, 166, 253, 259).

Another group of physical traumatic lesions are related to dental fractures or broken teeth, orthodontic or prosthetic appliances and oral piercings (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 subprosthesis palatitis or lesions such as fissured epulis. Frictional hyperkeratosis can also occur. In addition, the risk of precancerous or carcinoma lesions is present, especially if other factors (infection, irritation, chemicals, etc.) also act over the traumatized area.

Ionizing radiation may cause physical injuries to 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 results in bleeding surfaces after dislodging (283).

Relevant lesions related to hot, cold or electrical trauma are uncommon, 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 is desquamated, sometimes with vesicles, erosions or ulcers. Normally, diagnosis is straightforward (Fig. 26).

Chemical and pharmacological injury

Numerous agents can induce chemical injury; these include acids and bases, medicines, alcohol and tobacco, and also lesions associated with the use of mouthrinses and dentifrices. Lesions may appear after direct contact of the agent over the mucosa, leading to a maculae, vesicles, erosions or ulcers, with different relevance, depending on the causal agent, the size of the lesion and the duration 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. However, they result in pain and in difficulties with oral hygiene practices. Infectious diseases, mucocutaneous diseases and traumatic or allergic lesions can be included among these conditions.

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

Many of these conditions have the appearance of an erythematous lesion, sometimes erosive, with pain induced by toothbrushing or chewing. The differential diagnosis is crucial 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. The proper differential diagnosis will lead to the appropriate therapeutic intervention.

References

Acute lesions

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