Aggressive periodontitis: case definition and diagnostic criteria

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HISTORICAL BACKGROUND

Terminology and classification

Before addressing the case definition and diagnostic criteria of aggressive periodontitis it is useful to provide a brief review of the historical events pertaining to the terminology of this disease. The classification and terminology of periodontal diseases have evolved in tandem with the advancement in the understanding of the pathogenesis of these diseases. During the 19th century and the first half of the 20th century the prevailing view of what we now classify as chronic periodontitis was that it was a noninflammatory disease (57). The pathogenesis of periodontitis in adults was viewed as principally the development of a pathological pocket and alveolar bone atrophy attributed mainly to trauma from occlusion, while local inflammation and bacterial infection were viewed as playing only a secondary role (30, 31). Furthermore, it has long been recognized that destructive periodontal disease may also develop in children and young adults, and although the phenotype of this early-onset form is clinically different from that of the adult form, both forms were considered manifestations of a degenerative, noninflammatory disease (45). Based on histologic observations, Gottlieb (29, 31) used the term ‘diffuse atrophy of the alveolar bone’ to describe the disease, and he hypothesized that it was caused by a ‘lack of an effective cementum barrier’, which he called ‘cementopathia’, that may lead to gingival recession, alveolar bone loss and pathological pocket formation (32).

In 1942, Orban & Weinmann (50) introduced the term ‘periodontosis’ to describe severe periodontal disease in young individuals. A 1950 report by the American Academy of Periodontology defined periodontosis as a ‘degenerative non-inflammatory destruction of the periodontium originating in one or more of the periodontal structures, characterized by migration and loosening of the teeth in the presence or absence of secondary epithelial proliferation and pocket formation or secondary gingival disease’ (45). The terms ‘juvenile periodontitis’ and ‘early-onset periodontitis’ were introduced in 1969 (19) and 1989 (11), respectively, and were widely used during the last three decades of the 20th century. The latter terms were readily adopted because they portray the early-onset development of the disease and its occurrence in younger age groups. Other terms were proposed to describe the disease, such as ‘precocious advanced alveolar atrophy’ (48) and ‘precocious periodontitis’ (64), but were not widely adopted.

In the 1999 Classification Workshop of the American Academy of Periodontology (12), a consensus report adopted the term ‘aggressive periodontitis’ as a new name for this unique disease classification, replacing the term ‘early-onset periodontitis’ (43). For consistency, in this article, the term ‘aggressive periodontitis’ is used when citing classic literature that previously used synonymous terms of this disease.

Case definition by Baer, in 1971

Baer (15) defined aggressive periodontitis as ‘a disease of the periodontium occurring in an otherwise healthy adolescent, which is characterized by a rapid loss of alveolar bone around more than one tooth of the permanent dentition’. He proposed the following seven criteria to define the disease.

• Early onset of the disease during the circumpuberal period (between 11 and 13 years of age).
• A distinctive radiographic pattern depicting vertical alveolar bone loss at the first permanent molars and at one or more incisor teeth. Notably, Baer described criteria for a ‘classical’ case of aggressive periodontitis and variant criteria for atypical cases of aggressive periodontitis. Accordingly, a ‘classical’ or typical case of aggressive periodontitis would show an arc-shaped loss of alveolar bone, extending from the distal surface of the second bicuspid to the mesial surface of the second molar. Furthermore,
the bone loss at the posterior teeth occurs bilaterally, and the left and right sides of the jaw may be depicted as mirror images of each other. On the other hand, atypical cases of aggressive periodontitis also occur, and the pattern of bone loss in these cases differs from that found in the classical case. For instance, atypical cases of aggressive periodontitis may show bone loss at only one proximal surface of a first molar, or that only the molars are affected and not the incisors. Baer believed that the variations in the clinical features of aggressive periodontitis are caused by the variability in the phase of disease development and whether the disease is diagnosed at an early phase or an advanced phase. Baer deemed the occurrence of a pattern of bone loss localized to one proximal surface of the first molar in multiple arches as an initial stage in the development of the disease, or an ‘incipient’ localized case. Subjects with advanced disease may show a generalized, severe, horizontal bone loss.

- A rapid rate of disease progression. Baer estimated that, typically, an affected tooth can lose 75% of the alveolar bone support at one or more root surfaces within 5 years of disease initiation. In some atypical cases of aggressive periodontitis, however, alveolar bone loss progresses only to a certain point and then may remain quiescent for many years.
- The disease affects only the permanent dentition. The primary teeth are not affected and are not prematurely exfoliated because of destructive periodontal disease.
- The amount of local etiologic factors is not commensurate with the severity of periodontal destruction. Gross deposits of dental calculus are uncommon in most cases of aggressive periodontitis, and in the early stages of the disease the gingiva has a normal clinical appearance with no clinical signs of gingival inflammation. However, dental plaque is present on the root surfaces of the affected teeth. Some patients do have poor oral hygiene and detectable plaque and calculus. Clinical signs of gingival inflammation are seen in subjects with advanced disease.
- Predominance in female subjects. Baer reported that cases of aggressive periodontitis have a female to male ratio of approximately 3:1.
- The disease has a familial pattern.

Case definition in the 1999 American Academy of Periodontology workshop

In 1999 the American Academy of Periodontology organized a workshop to propose a new classification of periodontal diseases and conditions (12). In this workshop a subcommittee recommended that the term ‘aggressive periodontitis’ should be used, and classified the disease into localized and generalized forms (43). According to this report, the following features are common to the localized and generalized forms of aggressive periodontitis.

- Patients are clinically healthy, except for the presence of periodontitis.
- Rapid attachment loss and bone destruction.
- Familial aggregation.

Secondary features that are often, but not always, present include the following.

- The amounts of microbial deposits are inconsistent with the severity of periodontal tissue destruction.
- Elevated proportions of *Actinobacillus actinomyctemcomitans* (now termed *Aggregatibacter actinomycetemcomitans*).
- Elevated proportions of *Porphyromonas gingivalis* in some populations.
- Phagocyte abnormalities.
- A hyper-responsive macrophage phenotype, including elevated levels of prostaglandin E2 and interleukin-1β.

The following additional specific features were proposed for defining the localized and generalized forms.

Localized aggressive periodontitis.

- Circumpubertal onset.
- Localized first molar/incisor presentation with interproximal attachment loss on at least two permanent teeth (one of which is a first molar) and involving no more than two teeth other than first molars and incisors.
- Robust serum antibody response to infecting agents.

Generalized aggressive periodontitis.

- Usually affecting persons under 30 years of age, but patients may be older.
- Generalized interproximal attachment loss affecting at least three permanent teeth other than first molars and incisors.
- Pronounced episodic nature of the destruction of attachment and alveolar bone.
- Poor serum antibody response to infecting agents.

A perspective on previous and current case definitions

Early reports published before 1970 did not present detailed diagnostic criteria of aggressive periodontitis, except for severe loss of periodontal tissue at a young age. On the other hand, the criteria proposed
by Baer (15) constituted the first well-defined case definition of aggressive periodontitis as a distinct clinical entity, and these criteria were invaluable to clinicians and scientists in the diagnosis of patients. However, some of the parameters used in Baer’s case definition of aggressive periodontitis were not based on sound evidence. More details on this subject are presented later in this article.

The case definition of ‘early-onset periodontitis’ was recommended in the 1989 World Workshop by the American Academy of Periodontology (11) because one of the hallmarks of this disease is its commencement at an early age. However, this case definition had a key shortcoming, in that the term ‘early-onset’ is broad, and as such, was inclusive. Hence, this new term conveyed that the classification may also include other destructive forms of periodontal disease that may develop in children. For instance, young individuals showing localized, incipient lesions with attachment loss, although not fully matching Baer’s criteria of typical lesions, were also classified in the early-onset periodontitis classification, albeit subclassified as ‘incidental attachment loss’ (44) or ‘incidental early-onset periodontitis’ (5, 6). There is evidence that some subjects showing incidental attachment loss may progress to aggressive periodontitis, whereas other subjects may not (17). Furthermore, some studies have also included in the disease category of ‘early-onset periodontitis’ destructive forms of periodontitis that are merely oral manifestations of systemic diseases (66) because these forms are usually manifested in children. Hence, the term ‘early onset’ may have caused some confusion leading to misclassification issues.

The 1999 American Academy of Periodontology consensus report on aggressive periodontitis (43) recommended that age at the time of disease presentation should not be used as a criterion for the case definition of this disease. Nonetheless, the consensus report used age as a descriptor in the subclassification of cases of aggressive periodontitis. For instance, the subclassification ‘localized aggressive periodontitis’ was defined as having a circumpubertal onset; and ‘generalized aggressive periodontitis’ was described as affecting persons under 30 years of age, but that patients may be older. Hence, the 1999 consensus report was ambivalent regarding the relevance of age for the case definition of aggressive periodontitis. The report also proposed certain other criteria based on immunological profiles. Accordingly, localized aggressive periodontitis was defined as having the specific feature of a ‘robust’ serum antibody response to infecting agents, whereas generalized aggressive periodontitis was defined as having a poor serum antibody response to the pathogens. It is interesting to note, however, that the literature contains inconclusive evidence of the relationship between the serum antibody response to infecting agents and the classification of aggressive periodontitis (7, 20, 72). Therefore, it may be concluded that, at the present time, the use of the criterion of associations of certain immunological profiles in the case definition of aggressive periodontitis is not warranted.

PARAMETERS FOR THE CASE DEFINITION OF AGGRESSIVE PERIODONTITIS

Age of onset of disease

Among early reports, Seidler et al. (58) described 35 subjects, 14–30 years of age, with advanced periodontal disease and noted that the clinical periodontal features and other demographics of these subjects were different from the destructive periodontal disease that is diagnosed in older adults. These investigators wrote: ‘This discovery was startling, the more so when it was compared with statistics comprising older patients with comparable periodontal disease’ (58). Seidler and colleagues (58) called this disease ‘precocious advanced alveolar bone destruction’ and concluded that its onset is around puberty, or slightly later. Baer (15) also believed that aggressive periodontitis commences at the circumpubertal period, between 11 and 13 years of age. Several other studies support the hypothesis that the onset of aggressive periodontitis is around the circumpubertal period. Large population surveys found cases of aggressive periodontitis with age of onset as young as 12–14 years (9, 25, 26, 65), and clinical studies in periodontal patients report cases of aggressive periodontitis with an age of onset as young as 10–14 years (18, 27, 35, 54, 60).

Notably, in all these studies – epidemiologic or clinical – the reported age is the age at disease presentation (i.e. when the person is diagnosed as having aggressive periodontitis). However, judging from the amount of periodontal tissue loss that is often present, in virtually all of these subjects the periodontal destruction may have commenced earlier, sometimes several years before diagnosis of the disease. Hence, in these studies there is always a discrepancy between the age of onset of aggressive periodontitis and the age at disease presentation, with the actual age of onset substantially preceding that at diagnosis. This
discrepancy may be partly attributed to validity and precision issues of the methods of disease detection currently available (1, 22). More about this parameter is discussed later in this article.

Permanent vs. primary teeth

The issue of the age of onset of aggressive periodontitis also hinges on whether or not the primary teeth are affected in this disease, and this issue has often been overlooked. Baer (15) contemplated that aggressive periodontitis is a disease of the permanent dentition and it does not cause premature exfoliation of the primary teeth. It should be noted, however, that Baer did acknowledge that this disease may also have an onset during the period of mixed dentition, and therefore some of the primary teeth, particularly the primary second molars, may develop alveolar bone loss as a result of periodontitis.

During the early 1960s, Jamison (36) surveyed 5- to 14-year-old children in the city of Tecumseh, Michigan, and reported that approximately one-quarter of the children had destructive periodontal disease around the deciduous teeth. It has been estimated that approximately 71% of all cases of aggressive periodontitis show alveolar bone loss affecting the primary dentition, and bone loss affecting the mixed dentition is present in 86% of the subjects (24).

Very often, young children with destructive periodontal disease are not diagnosed at an early phase of disease development and therefore, in these subjects, the actual age of onset is unknown. There are reports of children as young as 7 and 8 years of age who showed clinical and radiographic signs of periodontal destruction at some or all of their primary teeth and who subsequently developed aggressive periodontitis at their permanent teeth (23, 46, 49). A study of a large group of 13- to 19-year-old individuals with aggressive periodontitis retrospectively assessed radiographs taken when the subjects were 5–12 years of age. The results showed that approximately half of the children had alveolar bone loss at their primary teeth (61). These studies suggest that in a large percentage of cases of aggressive periodontitis the age of onset of the disease may be during the mixed dentition (7–12 years of age), and in these individuals the disease may affect both the primary and the permanent teeth. However, it may be worth remarking that the latter studies did not report that the alveolar bone loss had caused an early exfoliation of the involved primary teeth, and, as such, Baer’s contemplation, that aggressive periodontitis does not typically cause premature exfoliation of the primary teeth, may be valid.

There have been case reports of prepubertal children with severe periodontal disease leading to exfoliation of the primary teeth (13, 16, 63), and based on these reports ‘prepubertal periodontitis’ was proposed as a distinct clinical entity in the early 1980s (51). However, the clinical criteria of aggressive periodontitis are, to a large extent, distinguishable from those of prepubertal periodontitis. Hence, compared with aggressive periodontitis, prepubertal periodontitis has an earlier disease onset (i.e. during or immediately after the eruption of the primary teeth), is characterized by early exfoliation of the primary teeth and is usually associated with some systemic defects, such as a functional defect in neutrophils or monocytes (51). There is evidence suggesting that prepubertal periodontitis is a genetically heterogeneous disease, and that in some families it just represents a partially penetrant Papillon–Lefèvre syndrome (34). For these reasons, the term ‘prepubertal periodontitis’ is no longer recognized as a distinct clinical classification, and prepubertal children with severe periodontitis who are diagnosed with systemic disorders are currently classified in the disease category ‘Periodontitis as a Manifestation of Systemic Disease’ (12).

On the other hand, there are indications (71) that the disease category classified previously as localized prepubertal periodontitis (51) may indeed be a severe form of aggressive periodontitis. A case report described a medically healthy patient diagnosed with prepubertal periodontitis at age 10 years; the patient then developed localized aggressive periodontitis at 13 years of age, and the disease subsequently progressed to generalized aggressive periodontitis (59). Hence, there is evidence that in certain individuals with severe aggressive periodontitis, periodontal tissue loss may commence at a prepubescent age, and that an early age of onset may suggest a more severe form, and possibly a larger component of systemic etiology.

Pattern of attachment loss and alveolar bone loss

Another key feature of aggressive periodontitis is that the patients exhibit periodontal attachment loss at multiple teeth and the tissue loss occurs bilaterally (14, 15, 58). In the permanent dentition the disease usually starts at the proximal surfaces of the permanent first molars and/or incisors, and therefore the loss of periodontal support around these teeth is
often more pronounced than around other teeth. At the initial stage of the disease the tissue loss may be too small to be detected using current examination methods (1, 22). Early lesions may be identified as loss of periodontal tissue localized to only one or a few teeth (Fig. 1). The diagnosis of the disease during the period of the mixed dentition poses particular challenges (15) because of the biological processes that take place locally during the normal exfoliation of the primary teeth. Furthermore, during this period eruption of the permanent teeth also occurs, and the associated bone remodeling may mask the diagnosis of pathologic bone loss that is associated with periodontitis. For these reasons, incipient disease often remains undetected in children during the mixed-dentition age.

Radiographically, at the early stage of development of aggressive periodontitis, the periodontal lesions often show a vertical pattern of alveolar bone loss at the proximal surfaces of the permanent first molars (28, 35) (Fig. 1). Also, the incisors are often affected, although the bone loss here is usually horizontal because the alveolar bone is thinner than at the proximal surfaces of molars. In typical cases the bone defects around the first molars are arc-shaped and affect all first molars (Fig. 2), and may extend from the distal surface of the second premolar to the mesial surface of the second molar (Figs 3 and 4). The alveolar bone defects are usually similar on the right and left sides of the mouth, and this has been referred to as a ‘mirror-image’ pattern (15). However, there are variances from this typical pattern. For instance, some subjects with aggressive periodontitis may show significant bone loss around the incisors, and only moderate bone loss around the molars; whereas other subjects with aggressive periodontitis may show involvement of only the molars with little or no involvement of the incisors. In advanced cases of aggressive periodontitis the bone loss may be generalized and show a horizontal pattern (Fig. 5).

The distinction between aggressive periodontitis and chronic periodontitis is straightforward, particularly when adequate radiographic images of the case are available for assessment. Consider the patient depicted in Fig. 6. A radiographic examination of a 20-year-old person revealed a vertical bone lesion at
the mesial surface of the mandibular right first molar (Fig. 6), and a clinical examination found attachment loss of 6 mm at the same site. However, local etiologic factors were present at the site of the bone lesion. In addition, no other sites had clinical attachment loss or radiographic bone lesions in this person. Hence, one may infer that in this individual the bone lesion is probably incidental to the presence of local factors, and that these radiographic (Fig. 6) and clinical criteria do not match the case definition of aggressive periodontitis.

Rate of disease progression

When diagnosed with aggressive periodontitis, patients typically show a pronounced loss of periodontal attachment on multiple teeth (58). Moreover, although the precise age when the tissue loss

Fig. 3. Radiographs of the 16-year-old patient with aggressive periodontitis shown in Fig. 9. There is vertical bone loss at the first molars and a ‘mirror image’ pattern of bone loss.

Fig. 4. Radiographs of the 18-year-old patient with aggressive periodontitis shown in Fig. 7. Most of the teeth show bone loss, and the most profound bone loss affects the incisors and the first molars.

Fig. 5. Radiographs of a 20-year-old patient with aggressive periodontitis showing generalized alveolar bone loss.
commenced is often unknown, judging from the amount of tissue lost and the number of years since the affected teeth erupted in the mouth, it can be inferred that the rate of attachment loss and alveolar bone loss is high. Based on this, it has been estimated that in a typical case of aggressive periodontitis the rate of bone loss is three to four times higher than the rate of progression of chronic periodontitis (15).

Albandar (3) conducted a longitudinal follow-up study, using clinical and radiographic measurements, in a large group of 14-year-old schoolchildren. He found that all children who were diagnosed with aggressive periodontitis at 14 years of age showed disease progression when they were re-examined at 15 years of age; and approximately half the proximal surfaces of the permanent first molars in these children had experienced 1–2 mm of alveolar bone loss during the 1-year follow-up period. In the 1986/1987 National Survey of the Oral Health of US Children, Brown and co-workers (17) identified 13- to 20-year-old subjects with aggressive periodontitis, and these subjects were later re-examined clinically when 19–26 years of age. During the 6-year follow-up period the periodontal status of these subjects had continued to deteriorate and the severity of the disease had increased. The mean attachment loss over 6 years was 0.45 mm (0.08 mm/year) in the group of subjects with localized aggressive periodontitis, and was 1.12 mm (0.19 mm/year) in the group of subjects with generalized aggressive periodontitis. In contrast, the rate of attachment loss in male subjects with chronic periodontitis has been estimated to be 0.05 mm/year (55). This shows that the rate of attachment loss in aggressive periodontitis is higher than that in chronic periodontitis.

On the other hand, Gunsolley et al. (33) performed a 3- to 4-year follow-up study in a group of patients with aggressive periodontitis and reported that the mean attachment loss during the study was 0.24 mm (or 0.08 mm/year) for ‘untreated’ subjects with localized aggressive periodontitis and 0.27 mm (or 0.07 mm/year) for subjects with generalized aggressive periodontitis (total for treated and untreated). The group studied by Gunsolley et al. (33) were patients attending a dental clinic and their mean age was 25 years (localized aggressive periodontitis) and 30 years (generalized aggressive periodontitis), whereas the group studied by Brown et al. (17) were 13–20 years of age and were identified in a population survey. This, and other differences in measurement methods, may partly explain the difference in the rates of attachment loss observed between the two study groups.

Notably, in aggressive periodontitis not all periodontal sites show continuous, quantifiable disease progression. The study by Brown et al. (17) showed that approximately 30% of mesial sites and 15% of buccal sites showed attachment loss of ≥2 mm over a

Fig. 6. Radiographs of a 20-year-old subject showing a vertical bone lesion and deposits at the mesial surface of the mandibular right first molar. No other sites with significant bone loss can be identified on these radiographs. In this subject the radiographic and clinical features do not match the case definition of aggressive periodontitis.
duration of 6 years. Albandar et al. (2) examined a group of patients with aggressive periodontitis, annually, over a 3-year period, and detected a continuous progression of alveolar bone loss at some, but not all, sites. Mros & Berglundh (49) re-examined a group of 14- to 19-year-old patients with localized aggressive periodontitis following a baseline examination and periodontal treatment, and found that half of the group showed extensive or limited recurrence of the disease, whereas the rest of the subjects did not show further loss of periodontal attachment. Hence, in aggressive periodontitis the rate of disease progression varies between subjects, and between different sites within the same subjects.

**Presence of local etiologic factors**

Typically, patients with aggressive periodontitis show smaller amounts of local factors, such as dental plaque and supragingival calculus, than do patients with chronic periodontitis with comparable periodontal destruction (Figs 7 and 8). Baer (15) stated that in aggressive periodontitis there is a lack of a relationship between local etiologic factors and the amount of periodontal destruction. Seidler et al. (58) did not describe the status of the local factors in their patients, but judging from the radiographs depicted in their paper there were no gross calculus deposits on the involved teeth in the subjects illustrated. Figures 7 and 8 depict cases of aggressive periodontitis in which the patients show an insignificant amount of supragingival dental plaque or calculus on their teeth.

The periodontal destruction in aggressive periodontitis is initiated by the interaction between pathogenic microorganisms and the host immune system (41, 56), and this interaction is influenced by many local and systemic factors (10). Although the pathogenesis and mechanism of tissue loss are similar in chronic and aggressive periodontitis (62), the effect of host factors is markedly more pronounced in the latter disease. For instance, there is strong evidence for a familial aggregation of aggressive periodontitis (47), and several genetic factors that may increase the risk for developing the disease have been identified (68). In contrast, in chronic periodontitis local factors play a major role, with a less significant role for host factors (8). Indeed, the significance of factors other than dental plaque and calculus in the pathogenesis of aggressive periodontitis is

![Fig. 7. Clinical photographs of a 18-year-old patient with aggressive periodontitis. The radiographs of this patient are shown in Fig. 4.](image)

![Fig. 8. Clinical photographs of a 17-year-old patient with aggressive periodontitis. The radiographs of this patient are shown in Fig. 10.](image)
manifested by the early onset of periodontal tissue loss, even though many affected subjects show minimal amounts of local etiologic factors (15, 58).

The deposition of dental plaque is a prerequisite to the initiation of the local inflammation and the ensuing host response leading to periodontal tissue loss (40). Among the pioneers who investigated the role of dental plaque in the pathogenesis of periodontitis, Waerhaug (69) studied autopsy specimens from subjects with aggressive periodontitis and showed that subgingival plaque is always associated with attachment loss in these subjects, and also noticed the presence of a severe chronic inflammation in the soft tissue bordering upon the plaque. In addition, Waerhaug (70) examined extracted teeth from patients with aggressive periodontitis and found no accumulation of subgingival plaque and no loss of periodontal attachment at tooth sites where there had been adequate supragingival plaque control. In both studies Waerhaug remarked that the subgingival plaque was very thin and had only occasionally calcified to form dental calculus. These findings suggest that the presence of a microbial insult is a prerequisite to the occurrence of attachment loss in aggressive periodontitis, although alone it does not fully explain the amount and rate of tissue loss in the affected subjects.

It is also noteworthy that the criteria proposed by Baer did not suggest that local factors were totally absent in aggressive periodontitis. Rather, he contemplated that the amount of periodontal destruction usually is not commensurate with the amount of local factors observed (15). The amount and the rate of formation of dental plaque and calculus vary between individuals (37). The lack of a correlation between the amount and the rate of tissue loss, and the amount of local factors, is an observation suggesting that other etiologic factors probably play a more significant role in the development of the disease. However, this observation should not be used as an exclusion criterion in the diagnosis of the disease because, for various reasons, the amounts of dental plaque, calculus and other local etiologic factors vary between patients. Indeed, large population studies suggest that local factors are prevalent in some patients with aggressive periodontitis and that these factors increase the risk of aggressive periodontitis development in these populations (4, 65). Cappelli et al. (21) surveyed schools in San Antonio (Texas, USA) and showed a high prevalence of poor oral hygiene and dental calculus in the study population, including subjects diagnosed with aggressive periodontitis.

**Systemic diseases**

An important feature of aggressive periodontitis is that the subjects are healthy and not inflicted with a debilitating systemic disease that affects their general health and predisposes to periodontal destruction. There is ample evidence suggesting that host factors play a key role in the predisposition of individuals to aggressive periodontitis (41), and notwithstanding the advancement in the understanding of the disease pathogenesis, these factors are yet to be clearly defined. Patients who have periodontal breakdown associated with a systemic disease that enfeebles their health and well-being and contributes to periodontal destruction are not classified in the aggressive periodontitis category. In the 1999 American Academy of Periodontology classification this group is termed Periodontitis as a Manifestation of Systemic Diseases (12) and includes several disorders (see Khocht & Albandar (38) for a detailed description).

**Sex ratio**

Baer (15) postulated that the female to male ratio of cases of aggressive periodontitis was 3:1, and he proposed this feature among the other criteria for defining aggressive periodontitis as a distinct clinical entity. However, the literature reveals inconsistent findings, with some studies showing comparable prevalence rates in male subjects and female subjects, whereas other studies show higher rates in either male subjects or female subjects (6, 65). Undoubtedly, the prevalence ratio among the two sexes is a descriptive variable, and if proven relevant it may be useful in the assessment of the risk predisposition to the disease. However, this descriptor is not useful as a diagnostic criterion of aggressive periodontitis because it is not exclusive.

**Familial pattern**

Baer (15) described a pattern where aggressive periodontitis tends to cluster within families. Findings in other studies corroborate the familial pattern of this disease (47, 52). Several mechanisms of increased predisposition to the disease by genetic factors have been proposed (39, 42, 68). While the familial pattern of the disease is an important feature that suggests a genetic predisposition, it is a generic factor that is too broad to be used in a case definition at present. Future advancement in the understanding of the genetic predisposition to aggressive periodontitis
may allow for the inclusion of specific genetic profiles in future case definitions.

### Subclassification of aggressive periodontitis

Aggressive periodontitis occurs in two forms: a localized form that mainly affects the permanent first molars and incisors; and a generalized form that involves most or all of the permanent teeth (15). Opinions vary as to whether these are two forms of the same disease, or whether they represent two distinct diseases. There is evidence that, at least in some cases, the localized form progresses to a generalized form when the affected individuals become older (17, 59), and in other cases the two forms overlap. On the other hand, a clinical study by Gunsolley et al. (33) found that patients with different forms of the disease responded differently to periodontal treatment, in that patients with the localized form were stable after treatment, whereas patients with the generalized form continued to lose periodontal attachment and teeth.

It has been suggested that localized aggressive periodontitis has a younger age of onset and shows a strong serum antibody response to infecting agents, whereas patients with the generalized form are older and have a poor serum antibody response to infecting agents (43). However, the evidence supporting these recommendations is scanty and inconclusive (7, 20, 72). Furthermore, the data showing a progression, in certain subjects, from localized to generalized aggressive periodontitis at older age (17, 59) do not support this postulate. More research is needed to demonstrate whether these two forms are different diseases or are different forms of the same disease.

Figure 2 illustrates a subject with localized aggressive periodontitis, and Fig. 5 illustrates a subject with generalized aggressive periodontitis. However, often the distinction between the localized and generalized forms of aggressive periodontitis is clinically unfeasible, particularly at the advanced stage of the disease when more teeth are involved with periodontal destruction. Three such cases are illustrated in Figs 3, 4, 7–10. In all of these three subjects with aggressive periodontitis the early phase of the disease was characterized by clinical attachment loss and alveolar bone loss confined to the incisors and first molars, and as the disease progressed most of the teeth became involved with periodontal tissue loss. This lack of distinctive clinical features of the two forms of the disease, particularly as the disease progresses, is a source of ambiguity for the classification of subjects.

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**Fig. 9.** Clinical photographs of a 16-year-old patient with aggressive periodontitis showing pronounced gingival inflammation. The radiographs of this patient are shown in Fig. 3.

**Fig. 10.** Radiographs of the 17-year-old patient with aggressive periodontitis shown in Fig. 8.
into localized or generalized disease groups, and this has a profound bearing on the validity of studies that use these subclassifications. On the other hand, there is little evidence that the localized and generalized disease groups are mutually exclusive clinical entities.

CASE DEFINITION OF AGGRESSIVE PERIODONTITIS

If at all possible, the case definition of aggressive periodontitis should be based on the presence of distinctive clinical signs of the disease and the diagnosis of its causal factors. However, given the present status of our understanding of the etiology of this disease, specific etiologic factors that have high validity and that can be reliably measured have not yet been identified. Hence, the current case definition relies to a large extent on the case history and on clinical and radiographic findings.

Key diagnostic criteria of aggressive periodontitis include an early age of onset, involvement of multiple teeth with a distinctive pattern of periodontal attachment and bone loss, a relatively high rate of disease progression and absence of systemic diseases that compromise the host's response to infection. The following distinctive criteria are recommended for the case definition.

- An early age of onset, usually before 25 years of age. The age of onset may be a predictor of the severity of this disease, so the younger the age of onset, the more severe the disease that may develop.
- Loss of periodontal tissue occurs at multiple permanent teeth. The tissue loss occurs because of a microbial infection.
- The periodontal destruction is detectable clinically and radiographically. Typically, the lesions are depicted radiographically as vertical bone loss at the proximal surfaces of posterior teeth because the alveolar bone is thicker at the posterior region than anteriorly. The pattern of bone loss is usually similar bilaterally. In advanced cases the lesions may be depicted radiographically as a horizontal loss of the alveolar bone.
- There is a relatively high progression rate of periodontal tissue loss.
- The primary teeth may also be affected, although early exfoliation of these teeth due to periodontal tissue loss is not common.
- The patients are systemically healthy. Aggressive periodontitis may occur in different forms. In the localized form, tissue loss usually starts at the permanent first molars and/or incisors (Fig. 2), and with increasing age tissue loss may affect the teeth adjacent to the first molars and incisors. Localized aggressive periodontitis may remain localized, but more often it progresses by involving other teeth, and at the advanced stage it presents a clinical picture similar to that of generalized aggressive periodontitis (Figs 4, 9 and 10). In generalized aggressive periodontitis, tissue loss may also commence at the permanent first molars and incisors because these are the first teeth to erupt, and the disease progresses rapidly so that most or all of the permanent teeth become involved with severe attachment and bone loss (Fig. 5). The rate of disease progression in the generalized form of aggressive periodontitis may be higher than in the localized form.

Multiple etiologic factors are often involved in the pathogenesis of aggressive periodontitis. Insofar the young age of onset is an indication of a significant contribution of host factors and perhaps of other nonplaque-related etiology. Younger age of onset may suggest a higher contribution of nonplaque etiologic factors. Similarly, higher rates of disease progression and early exfoliation of the primary teeth may suggest a higher contribution of host factors and, at present, a poor prognosis of disease treatment and control. Future advancements in understanding the disease pathogenesis may help define case definitions of this disease that take into consideration specific etiologic factors.

Use of the case definition in population surveys

The use of the case definition of aggressive periodontitis for the diagnosis of patients in the dental office is straightforward because clinical and radiographic assessments are readily available. On the other hand, population studies present a special challenge for the diagnosis of aggressive periodontitis. Surveys typically examine a large study sample in order to evaluate the health status of the population. The examinations and data collection are usually conducted under field conditions, and this may lead to partial examinations and/or less than optimal standardization of examination methods. Prospective surveys aimed at assessing the periodontal health of populations, particularly population studies in developing countries, often do not have access to radiographic diagnostic methods owing to limited resources. In addition, Institutional Review Board regulations may object to the use of radiographs or other diagnostic examinations for health-safety concerns or other motives. For these reasons, investigators often resort to clinical
measurements of attachment loss for monitoring the prevalence and severity of chronic and aggressive periodontitis. Clinical measurement of periodontal attachment is more invasive than measurements made on radiographs, and this may result in higher measurement errors. This is particularly true in children because of poor cooperation during the clinical examination. Moreover, the remodeling of alveolar bone during tooth eruption may also contribute to measurement errors in children.

Hence, the criteria of the case definition of aggressive periodontitis outlined above, although straightforward when used in the dental office, may not be well suited for large surveys, particularly those that do not gather adequate radiographic information. In those situations where only clinical measurements are available, the diagnosis of aggressive periodontitis may be less accurate than when both clinical measurements and adequate radiographs are available. Given the inherent limitations in the assessment of disease in surveys, it may be necessary to modify the diagnostic criteria when used in these surveys. However, the adjustment of the diagnostic criteria should be based on a thorough analysis of the measurement errors in the survey so that stringent clinical criteria may be used if the measurement errors are relatively high or if the age of the target population is considerably older than the circumpubertal age (65). However, one should bear in mind that although such a modification may potentially reduce the false-positive rate, it would also decrease the sensitivity of diagnosing true cases of disease (i.e. would increase the false-negative rate).

Concluding remarks and future considerations

Early age of onset, high rate of disease progression, involvement of multiple teeth with a distinctive pattern of periodontal tissue loss and absence of systemic diseases are key diagnostic criteria of aggressive periodontitis. In some patients, tissue loss may commence before puberty, whereas in most patients the age of onset is during, or somewhat after, the circumpubertal period. The literature lacks evidence of patients showing commencement of the disease during their late twenties or older. Cases of aggressive periodontitis are often diagnosed years after the onset of the disease, partly because current assessment methods detect established disease more readily and reliably than they detect incipient or initial lesions where the tissue loss is minimal and usually below the detection threshold of these methods. Hence, individuals in their late twenties or early thirties may also be diagnosed as having aggressive periodontitis if, at presentation, the severity and the pattern of periodontal tissue loss are consistent with an aggressive disease, suggesting that the loss had commenced at an earlier age.

The variability in the age of onset of aggressive periodontitis may be associated with the type and severity of etiologic factors. Hence, early age of onset may suggest a higher potency or high level of etiologic factors than late-onset disease. However, the presence of an etiologic factor is not sufficient to define a case if other clinical signs of disease are not present. Still, the presence of etiologic factors is a valuable determinant of increased risk of disease development.

At present, the diagnosis of aggressive periodontitis is achieved using case history, clinical examination and radiographic evaluation. Some of these methods are prone to relatively high measurement errors. In addition, these methods measure past disease history. Assessment methods that generate smaller measurement errors may contribute to an earlier detection of cases of aggressive periodontitis before significant tissue loss occurs. Also, clinical surveys in populations present a special challenge for the accurate diagnosis of cases of aggressive periodontitis (53).

Genetic predisposition plays a key role in the development of aggressive periodontitis and contributes to the early onset of tissue destruction, which is the hallmark of this disease. In susceptible individuals the presence and the intensity of other etiologic factors may determine the clinical features and the severity of the disease. For instance, the presence of specific periodontal pathogens subgingivally, together with one or more other risk factors, such as smoking and poor oral hygiene, will contribute to the onset of the disease at an early age, and may also lead to a more severe and/or generalized disease. On the other hand, individuals who are genetically predisposed but either do not harbor virulent periodontal pathogens or have only low levels of these microorganisms, and in addition lack other risk factors, may develop a localized form of aggressive periodontitis and the onset of the periodontal tissue loss may occur at an older age.

Future diagnostic methods of aggressive periodontitis should diagnose the disease early (67). These methods may entail the identification of key etiologic and risk factors, combined with a higher precision and early detection of initial lesions. Such
Methods may significantly enhance the predictive value of these tests and detect cases of aggressive periodontitis before significant tissue loss develops.

References