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Classification of periodontal diseases

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Introduction

The term periodontal diseases has had somewhat differing connotations over time, as discussed by Löe in the preceding chapter. A continuing concern in classification is whether to include only diseases that have primary manifestation and etiology in the periodontium or whether to also include periodontal manifestations of systemic diseases. Similarly, there may be questions about the propriety of including other conditions that present in the periodontium but do not involve primarily the marginal tissues. Regardless of academic considerations for such distinctions, clinicians must account for all potential abnormalities when formulating a differential diagnosis. The classification presented in this chapter therefore is meant to be relatively inclusive rather than restrictive.

It is also based on certain other principles, including that: a) the periodontal diseases that progress from the marginal gingiva are infectious diseases (47), that is, they are caused by bacteria (148); b) inflammatory conditions restricted to the gingiva itself fit within the defining term gingivitis, whereas inflammations extending deeper to involve periodontal ligament, cementum or alveolar bone fit within the term periodontitis (124); and c) although both gingivitis and periodontitis of local origin can be influenced in their expression by systemic conditions and some gingival abnormalities may be caused primarily by systemic conditions, no periodontitis has been documented to be purely of systemic origin (47). Finally, this classification accepts occlusal trauma (and its synonyms for the changes that occur in the periodontium subsequent to abnormally large forces transmitted to it through the teeth) as a physiological adaptation rather than a disease (32). It is thus not included as an entity in the classification.

Actually formed in many ways by numerous investigators and authors over a number of years, the classification presented (Table 1) is only slightly modified from that published earlier in *Advances in Dental Research* (124). The text below follows the outline of Table 1.

Gingivitis

Gingivitis may be divided into 3 general groups: one that has as primary cause bacteria that colonize the gingival sulcus and adjacent tooth surfaces, one that additionally is necrotizing and one that is not plaque-related and does not begin marginally.

Bacterial plaque-related gingivitis starts near the coronal extent of the gingiva, because that is where the etiological bacteria are located. More apical extension of the inflammation in this type of gingivitis usually occurs only as the disease becomes more severe because it is not treated over time. Only in its most severe expressions or when severity is aggravated by a coexistent systemic condition does plaque-related gingivitis include clinical manifestations all the way from the gingival margin to the mucogingival junction. Gingivitis that is not plaque-related, on the other hand, usually has a more generalized expression because the causes are either systemic or are distributed with no particular relationship to the gingival sulcus or margin.

Gingivitis, plaque bacterial, non-aggravated

Gingivitis caused by bacterial plaque is the most prevalent form and the most common periodontal disease (110). Plaque bacterial etiology was convincingly demonstrated by the classical studies of experimental gingivitis in humans (89, 157), which have been duplicated many times. These studies showed that, in otherwise healthy people, gingivitis always develops when plaque accumulates and is always reversed by removing the plaque. These basic findings are so reproducible that the model is used to test the effectiveness of antigingivitis agents in clinical trials (128).

Table 1. A classification of periodontal diseases

- Gingivitis
  - Gingivitis, plaque bacterial
    - Non-aggravated
    - Systemically aggravated
      - Related to sex hormones
      - Related to drugs
      - Related to systemic disease
  - Necrotizing ulcerative gingivitis
    - Systemic determinants unknown
    - Related to HIV
  - Gingivitis, non-plaque
    - Associated with skin disease
    - Allergic
    - Infectious
- Periodontitis
  - Adult periodontitis
    - Non-aggravated
    - Systemically aggravated
      - Neutropenias
      - Leukemias
      - Lazy leukocyte syndrome
      - AIDS
      - Diabetes mellitus
      - Crohn's disease
      - Addison's disease
  - Early-onset periodontitis
    - Localized early-onset periodontitis
      - Neutrophil abnormality
    - Generalized early-onset periodontitis
      - Neutrophil abnormality
      - Immunodeficient
    - Early-onset periodontitis related to systemic disease
      - Leukocyte adhesion deficiency
      - Hypophosphatasia
      - Papillon-Lefèvre syndrome
      - Neutropenias
      - Leukemias
      - Chédiak-Higashi syndrome
      - AIDS
      - Diabetes mellitus type I
      - Trisomy 21
      - Histiocytosis X
      - Ehlers-Danlos syndrome (Type VIII)
    - Early-onset periodontitis, systemic determinants unknown
  - Necrotizing ulcerative periodontitis
    - Systemic determinants unknown
    - Related to HIV
    - Related to nutrition
  - Periodontal abscess

Although plaque-related gingivitis is caused by bacteria, and the composition of the associated flora differs from that associated with health (100, 101), the composition of required flora is not very specific (100, 120, 121). Thus, bacteriological diagnosis of gingivitis is not a very useful concept (123). The diagnosis is basically made clinically.

Clinically, gingivitis typifies inflammation of any integumental surface. The normal, firm, regular contour of gingiva has changed to one that is swollen to various degrees from edema and from fibrosis in many longstanding cases or in certain cases modified by systemic conditions. In light-skinned people, the normal pink color changes to red or blue-red. In dark-skinned people, the color changes may not be so obvious but, depending on the intensity of the normal pigmentation, may be observable as deep blue-red discoloration together with the edema that is detectable by palpation. The earliest changes from normal may not be visible, but the enhanced vascular permeability is expressed in gingival crevicular fluid, which can be collected at the gingival margin (42).

The earliest histological signs of gingivitis are those of a mild acute inflammation (10), an increased proportion of the junctional epithelium occupied by polymorphonuclear leukocytes (135) and significant destruction of the collagen immediately subjacent to the junctional epithelium (134). Page & Schroeder (114) described further histopathological changes, moving through predominance of lymphocytes and then plasma cells in the extravascular cellular infiltrate as the severity and longevity increase. Clearly, chronic gingivitis in adults is generally dominated by plasma cells and B cells (79, 114). In children, however, gingivitis is generally dominated by T-lymphocytes (1, 93, 137). In the description by Page & Schroeder (114), the progression to plasma cell domination was thought to occur in a matter of a few weeks at most. They termed that stage the established lesion, which followed the lymphocyte-dominated early lesion, which in turn followed the initial lesion dominated by polymorphonuclear leukocytes. That staging provided an excellent context for relating histopathological changes to probable pathogenetic mechanisms. More recently, however, it has become clear that conversion from early to established lesions has neither a consistently short nor a reproducible time frame. Gingivitis can remain lymphocyte-dominated for quite a long time (at least months as opposed to weeks) (17, 18).

Although some people question whether gingivitis should be considered a periodontal disease, since it alone does not cause loss of significant amounts of periodontal support or tooth mortality, most people conclude otherwise (111, 120). A remaining clinical frustration, however, is that there are no currently

established means to differentiate stable gingivitis from gingivitis that is progressing or will progress to destructive periodontitis (80, 115). Even biopsy does not produce enlightenment in this critical question. Although conversion from T cell domination to B cell domination has been suggested to be the critical event for progression (138), there are many instances of longstanding, B cell-dominated gingivitis that have not progressed to periodontitis (111).

The essential features of plaque bacterial gingivitis, then, are relatively nonspecific bacterial causation, clinical signs of inflammation, limitation to gingiva, uncertainty as to progression and reversibility by removal of the bacterial cause. Bacterial plaque-related gingivitis can be prevented by preventing accumulation of bacterial plaque (121).

Gingivitis, plaque bacterial, systemically aggravated

There is no requirement for an abnormal systemic condition to act as a co-factor for gingivitis to be produced. On the other hand, the clinical expression of gingivitis can be markedly altered by the existence of systemic conditions (48). Some such factors enhance risk for progression to periodontitis, but some systemic factors alter expression of gingivitis without presenting deficits of host response for resisting periodontitis. The former include blood dyscrasia, such as neutropenia, whereas the latter include sex hormones, certain drugs and some other systemic diseases. If these increase the risk for periodontitis, it is only because of greater plaque accumulation resulting from morphological gingival changes, which make cleanliness more difficult.

Gingivitis related to sex hormones. Case reports and clinical studies long ago established that pregnancy can be associated with aggravated gingivitis and also sometimes localized proliferations known as pregnancy "tumors" (50). Quite clearly, however, they are not neoplasms but rather instances of exaggerated inflammation, conditioned by the altered hormonal balances of pregnancy. Similar phenomena may be found following the use of oral contraceptives (116). The clinical severity of generalized gingivitis is usually greater in pregnant than in nonpregnant women (86) but is not associated with more destructive periodontitis (30, 99). The effects seem to be mediated primarily by the effects of progesterone on the microvasculature of inflamed connective tissue (66, 77).

Gingivitis related to drugs. The expression of gingivitis can be modified by some relatively commonly used medicines, especially certain agents for treatment of convulsive disorders, some cardiovascular drugs and certain immunosuppressants. The modification consists of a hypertrophy of the connective tissue elements of the gingiva (primarily collagen), so that the gingiva appears swollen or overgrown (64). The amount of associated inflammation is a function of the accumulation of bacterial plaque.

The prototypical gingival hypertrophy-producing central nervous system agent is phenytoin (or diphenylhydantoin). About half of patients who chronically take phenytoin develop the gingival overgrowth (117).

Hypertrophy-producing cardiovascular agents are primarily calcium channel blockers, such as nifedipine (106) and oxodipine (107). Some other calcium channel blockers also are associated with gingival overgrowth (35, 49).

The immunosuppressant cyclosporin represents the other major class of drug associated with gingival hypertrophy (37). As for the other drug-induced gingival overgrowths, good plaque control can reduce the severity (139).

Gingivitis related to systemic disease. Modifying conditions other than the above can result from some systemic diseases. This especially may be suspected when gingival inflammation is more severe, particularly in children, than would be expected from the amount of plaque. Among the possibly offending conditions are blood dyscrasia, such as leukemia (12, 119) and granulomatosis (31). Late effects of vitamin C depletion also include increased gingival bleeding (76).

Necrotizing ulcerative gingivitis

Necrotizing ulcerative gingivitis has long been recognized as a form of periodontal disease (52, 118, 133). Ulcerated gingival margins and papillae, the latter resulting in a punched-out appearance interdentally, inflammation and pain, are presenting signs. Lymphadenopathy, elevated temperature, malodor and a pseudomembrane over affected areas of the gingiva are variable findings.

In early descriptions, necrotizing ulcerative gingivitis was described as associated with a bacterial fusospirochetal complex. Indeed, spirochetes invade the necrotic tissue and beyond in necrotizing ulcerative gingivitis (84). However, cultural studies of associated plaques have found *Treponema* and *Seleno-*

monas species along with "*Bacteroides*" (now *Porphyromonas* or *Prevotella*), *Fusobacterium* sp. and others (90), not clearly different from the bacterial associations with other forms of gingivitis (100) or periodontitis (104). Rather than a unique bacterial infection, necrotizing ulcerative gingivitis seems to be a manifestation of mixed bacterial infection modified by particular systemic determinants.

Necrotizing ulcerative gingivitis, systemic determinants unknown. Necrotizing ulcerative gingivitis is traditionally associated with mental or physical stress (13, 52, 53, 133, 142, 149). The precise associations and mechanisms by which stress results in the necrosis remain elusive to proof. Conceivably, neuroimmunological mechanisms are involved, but there is no direct evidence for this as yet. At the present time, it is probably safest to conclude that, in all but the instance described immediately below, the precise systemic modification is unknown.

Necrotizing ulcerative gingivitis related to human immunodeficiency virus (HIV). Ulcerative lesions of the gingiva resembling necrotizing ulcerative gingivitis can be found in some cases diagnosed as acquired immunodeficiency syndrome (AIDS) (166). Some reports suggest that HIV infection should be suspected when the signs of necrotizing ulcerative gingivitis are present (129).

Gingivitis, non-plaque

Two features distinguish gingival inflammation not caused by plaque bacteria from that which is: failure of the gingivitis to resolve with excellent mechanical or chemical plaque control; and gingivitis that is caused by factors other than plaque often has no predilection for the gingival margin as compared with the attached gingiva and may not start at the margin. Inflammation in such instances may be evenly distributed apicocoronally, although this can vary according to whether the cause is systemic or local.

Gingivitis associated with skin disease. The gingiva can be inflamed because of a disease that affects skin as well as gingiva. Gingiva may be the primary involvement in such cases, but generally there are manifestations elsewhere on the integument. Conditions in this category include lichen planus, mucous membrane pemphigoid, pemphigus and other vesiculobullous disorders, including oral manifestations of epidermolysis bullosa and ectodermal dysplasia.

The gingiva may also be the seat of desquamative or highly inflamed lesions associated with hormonal changes related to menopause or other imbalance of ovarian hormones (62).

Gingivitis, allergic. Instances of diffuse, velvety-appearing gingivitis extending from the gingival margin to the mucogingival junction have been associated with contact allergies to the constituents of chewing gum (70). Additionally, ingredients in toothpaste (73) and foodstuffs (136) have been indicated as sources of gingivitis-producing allergens. One should suspect that additional agents sometimes may be involved in clinical allergic inflammation.

Gingivitis, infectious. Nearly any external infective agent may occasionally have the gingiva as a locus of infection. When the agent is a virus, the lesion is usually vesicular, at least on primary manifestation. The most frequent offender is probably herpesvirus I, although others may be represented. Bacterial species that are not normally present in plaque, and yeasts, such as *Candida albicans,* can cause gingival lesions.

Periodontitis

As distinguished from gingivitis, periodontitis is inflammation that extends to periodontal structures beyond the gingiva, producing a loss of the connective tissue attachment of the teeth. There appear to be multiple forms of periodontitis that have differences among them in etiology, natural history, progression or response to therapy. The Consensus Report related to diagnosis from a workshop in 1989 sponsored by the American Academy of Periodontology (33) recommended a classification containing 5 primary forms of periodontitis. One of these included 3 sub-forms. This classification by the Academy extended a departure from earlier classifications that listed periodontitis as a single entity, as exemplified by some textbooks from the 1970s (54, 56).

A recognition that there are multiple forms of periodontitis suggests a need for differential diagnosis among the different forms. This is not really straightforward, because differentiating criteria have not been discretely associated with individual forms, at least not to the extent that adequate specificity and sensitivity are provided. Nonetheless, it is apparent that sufficient differences in natural history and associated factors do exist to justify preliminary division of forms.

Adult periodontitis, non-aggravated

The most prevalent form of periodontitis, adult periodontitis, has its earliest significant expression in the adult years (81), generally becoming clinically significant after age 30. Its expression does not depend on systemic abnormality. Periodontitis undoubtedly requires a precursor gingivitis, but animal (78) and human studies (8, 85) indicate that not all gingivitis progresses to periodontitis. Adult periodontitis has a rather slow net rate of progression (87). Longitudinal measurements with conventional probes in the early 1980s led to conclusions that progression was primarily one of starts and stops, with net loss of attachment accruing from short bursts of activity (55). Similar measurements with more sensitive tools, however, indicate that much of the progression cannot be differentiated from slow, continuous loss, although discrete episodes may occur (68).

Adult periodontitis is caused by local environmental factors constituted by the associated bacterial flora and retentive factors for bacteria (23, 81). Enumeration of specific bacterial species has been considered as a potential tool for differential diagnosis among periodontal diseases. Cultural methods are probably not worth considering for this type of diagnosis for a variety of reaons, but reliable, rapid means of identifying some species are becoming available. These include indirect immunofluorescence microscopy (167) and nucleotide probes (130). Detection of some species, for example, *Porphyromonas gingivalis,* indicates a high probability that periodontitis is present, as judged by the usual clinical signs (25, 167, 159). However, there is also a high probability that periodontitis is present when the test is negative (167, 169). *P. gingivalis* is also found in other forms of periodontitis in proportions that do not provide a basis for differentiation from adult periodontitis (101, 145). What may be needed are tests for whether the disease is progressing or will initiate or progress in the future. Unfortunately, the results to date do not show consistently significant associations of given species with episodes of progression (104, 123). This leaves differentiation of adult periodontitis from other forms of periodontitis at the present time to history or observation with respect to approximate age of onset and relatively slow net rate of progression.

Adult periodontitis, systemically aggravated

Although there are no apparent systemic prerequisites for adult periodontitis, its expression can be modified to more rapid progression or different clinical appearance by coexistence of systemic abnormality (47). Such conditions include those listed in Table 1 under adult periodontitis (diabetes mellitus, Crohn's disease, Addison's disease and several leukocyte abnormalities) but may also include conditions listed lower in Table 1 under systemic disease-related early-onset periodontitis if they happen to manifest in adult life in particular cases.

Early-onset periodontitis

There are many published observations of severe periodontal destruction occurring in the early twenties, teens or before. Such cases are increasingly being designated early-onset periodontitis to distinguish them from adult periodontitis (23, 124). The American Academy of Periodontology's 1989 classification of periodontitis (33) divided early-onset periodontitis into prepubertal periodontitis, juvenile periodontitis and rapidly progressive periodontitis. Two of these, prepubertal periodontitis and juvenile periodontitis, were further subdivided into localized and generalized forms, whereas rapidly progressive periodontitis was not subdidived by intraoral distribution of affected sites. The classification in Table 1 reduces early-onset periodontitis to 2 categories, localized and generalized. This includes cases referred to in the literature variously as juvenile periodontitis, localized juvenile periodontitis, generalized juvenile periodontitis (158), rapidly progressive periodontitis (109), severe periodontitis (21) or prepubertal periodontitis (113), because of current uncertainties of other reasonable dividing lines. A national survey in the United States provided an estimate for the incidence of early-onset periodontitis at 1.5 cases per 1000 person-years at risk (88).

Longitudinal observations in the absence of any conventional oral hygiene or dental care have revealed a relatively small subset (8%) that experienced extremely rapidly progressive disease and could represent early-onset periodontitis, in contrast to the majority (81%), which probably represented adult periodontitis (87). Given the widely accepted view that the etiology of all periodontitis is bacterial (97), the vastly different rates of progression suggest that there may be corresponding etiological or mechanistic differences between early-onset periodontitis and adult periodontitis, either in the causative bacteria or in the effectiveness with which the host resists the infection.

Localized early-onset periodontitis

A number of reports document cases that have severe periodontal destruction essentially limited to first molars and incisors. This localized pattern can persist into the mid- to late twenties or later in at least some cases (124). Such a clinical pattern has often been referred to as localized juvenile periodontitis, or simply juvenile periodontitis. Usually in such studies, involvement of 1–2 teeth other than first molars or incisors is allowed within the disease definition (21, 158). The probable reason that the localization is to first molars and incisors is that these are the teeth with greater probability for being at risk when the disease started, as other permanent teeth were not yet erupted.

Although most definitions of juvenile periodontitis have limited it to circumpubertal onset, case reports trace periodontitis from prior to puberty to a postpubertal diagnosis of localized juvenile periodontitis (22, 143). Other descriptions of periodontitis affecting the deciduous or mixed dentition also suggest the probability of progression to localized or generalized juvenile periodontitis or rapidly progressive periodontitis (24, 29, 34, 63, 152). Cases in the youngest individuals observed within the rapidly progressive subset in Sri Lanka reported by Löe et al. (87) generally had lesions confined to first molars and incisors, but by age 20 to 30 they were characterized by a generalized pattern of destruction. Other studies of combined localized and generalized cases of early-onset periodontitis have also found age distributions that suggest spread from the former to the latter with time: generalized cases are older than localized cases (9, 21, 65, 131). Given a sufficient number of cases of early-onset periodontitis, essentially every possible number of involved teeth can be seen (122).

Although the American Academy of Periodontology designates factors as being potentially distinctive for the early-onset periodontitis forms they recommended (33), these factors have not been shown to discriminate with satisfactorily high sensitivity and specificity (124). The classification presented here accepts the possibility that localized and generalized early-onset periodontitis can represent the same disease etiologically or at least substantially overlap. In that view, the extent and severity of disease are a function of the relative effectiveness of defensive host response to a mixed infection.

Factors reported as being especially associated with localized juvenile periodontitis include high numbers of *Actinobacillus actinomycetemcomitans* in the associated flora, abnormalities of leukocyte chemotaxis, a reduced number of surface receptors for chemoattractant ligands and an abnormal amount of a cell-surface glycoprotein designated GP-110 on neutrophils. However, none of these parameters are exclusive to localized juvenile periodontitis. *A. actinomycetemcomitans* can be found in conditions other than juvenile periodontitis (15, 34, 36, 51, 59, 144, 168) and is not found in all cases of juvenile periodontitis (59, 91, 101, 108). High levels of serum antibodies to *A. actinomycetemcomitans* are associated with juvenile periodontitis (41, 83, 126, 162, 165), but such antibodies can also be found in significant though fewer cases of generalized early-onset periodontitis (2, 41, 126, 162). Also, serum antibody to *A. actinomycetemcomitans* is related to race independent of disease status (57).

Neutrophils from 70% to 80% of subjects clinically identified as having localized juvenile periodontitis exhibit subnormal chemotactic response as compared with simultaneously tested control subjects (26, 29, 75, 122, 150, 158). So also do fewer, but nonetheless a sizeable number of subjects that were diagnosed as generalized juvenile periodontitis, rapidly progressive periodontitis or other synonyms of generalized early-onset periodontitis (3, 122, 150, 158). Some studies, especially from northern Europe, did not find defective neutrophil chemotaxis in early-onset periodontitis (71, 72, 74, 127). A few reports of an associated defective monocyte chemotaxis exist, but the results are not consistent (3, 150).

The molecular marker GP-110 is associated more specifically with a defect in neutrophil chemotaxis than with a specified clinical pattern of destruction. That is, abnormally low GP-110 can be demonstrated on neutrophils from both localized and generalized cases of early-onset periodontitis, if these cases exhibit depressed chemotactic responses. Where chemotaxis is normal, GP-110 also seems normal, even if juvenile periodontitis is present (160, 161).

Generalized early-onset periodontitis

Some cases of early-onset periodontitis start with a localized pattern of destruction and apparently progress to generalized involvement with time. Yet other cases seem to start with a generalized pattern (122). Among the generalized cases, the American Academy of Periodontology recognizes a distinction between generalized juvenile periodontitis and rapidly progressive periodontitis based in part on age of onset (33). However, efforts to identify age of onset in studies of early-onset periodontitis have been unable

to do so, considering that age at diagnosis can differ substantially from age of onset (16, 92).

The prominence of pigmenting "*Bacteroides*" (now *Porphyromonas* (140) or *Prevotella* (141)) was cited as a feature of rapidly progressive periodontitis rather than the predominance of *A. actinomycetemcomitans* in the flora in juvenile periodontitis (presumably including generalized juvenile periodontitis) (33). However, in at least one extensive series of studies (101), "*Bacteroides*" *gingivalis* (*P. gingivalis*) was found in a higher mean percentage of the flora in localized juvenile periodontitis than in generalized early-onset periodontitis, and "*Bacteroides intermedius*" (*Prevotella intermedia*) also was among the most frequently occurring species in the subgingival flora of localized juvenile periodontitis. Black-pigmenting "*Bacteroides*" are, in fact, commonly found in the subgingival flora of all forms of periodontitis (38, 90, 101–104, 145, 153, 170). The differences in prevalence and numbers of these species are not consistent enough to be very useful for differential diagnosis among the different forms (123, 124).

Antibody reactive with *P. gingivalis* has also been suggested as indicative of generalized rather than localized early-onset periodontitis (2, 39, 40), but the frequencies of such elevated antibody can be quite high among localized juvenile periodontitis cases (155). Using serum antibody reactivities against a panel of 22 bacterial strains, Gunsolley et al. (60) found that localized juvenile periodontitis cases could be differentiated using stepwise discriminate analysis from generalized early-onset periodontitis cases by antibodies reactive with strains of *A. actinomycetemcomitans, Fusobacterium nucleatum, Eubacterium brachy* and *P. gingivalis* considered together. None alone provided significant discrimination. The sensitivity for differentiating localized juvenile periodontitis from generalized early-onset periodontitis by the combination of antibody reactivities was 88%, and the specificity was 74%. The study found misclassification to be especially frequent in the generalized group, suggesting significant heterogeneity.

Thus, arguments can be made on both clinical and laboratory grounds for considering at least some cases, variously termed juvenile periodontitis, severe periodontitis, generalized juvenile periodontitis or rapidly progressive periodontitis, to be differing manifestations of the same disease. Additionally, family studies have found both generalized and localized cases within several individual sibships or families (16, 92). Given that early-onset periodontitis in general is somewhat rare, the co-occurrence of localized and generalized patterns of involvement in the same family should be highly unusual, if these patterns indeed represent independent diseases.

A case can be made for at least a significant subset of generalized early-onset periodontitis being related to an abnormality of immunological responsiveness (125). Indications for this include hyperresponsiveness to B cell mitogens (43, 147), depressed autologous mixed leukocyte culture reactions (151, 154) and a relative deficiency of certain expected antibody responses (45, 156). The clinical patterns of destruction found in a comparison of early-onset periodontitis subjects with and without antibodies to *A. actinomycetemcomitans* and *P. gingivalis* provide additional support for this line of thinking and for the possibility that the antibodies are indeed relatively protective against spread from localized to more generalized patterns (58, 125).

Early-onset periodontitis related to systemic disease

Several systemic disorders are accompanied by periodontitis or loss of teeth in childhood, including those listed in Table 1.

Leukocyte adhesion deficiency has particular relevance to 5 case reports that constituted the original rationale for the designation prepubertal periodontitis (113). The distribution of affected teeth among these 5- to 7-year-old children provided both localized and generalized patterns. All cases had some abnormality of leukocyte function. The severity, extent and rapidity of progression of the periodontitis correlated positively with the severity and frequency of other infections and the profundity of the functional leukocyte deficiency. Generalized prepubertal periodontitis had been seen by others in association with an autosomal recessive disorder that provided deficiencies of certain glycoproteins on the surface of leukocytes (6, 7). These molecules, Mac-1 (also the neutrophil iC3b receptor), lymphocyte function antigen-1 and another designated p150,95, collectively contribute to adhesion-dependent cellular functions (5). Page et al. (112) demonstrated abnormally low levels of adherence glycoproteins on cells from children with generalized prepubertal periodontitis, whereas adult subjects diagnosed with juvenile periodontitis, rapidly progressive periodontitis, adult periodontitis and normal control subjects had no such deficit. Waldrop et al. (163) described a family unit in which individuals homozygous for the Mac-1, lymphocyte function antigen-1 deficiency exhibited generalized prepubertal peri-

odontitis, whereas heterozygotes were periodontally normal or much less severely involved.

Hypophosphatasia is also a heritable molecular defect, specifically a quantitative deficiency of alkaline phosphatase, resulting in disturbed cementogenesis and resultant failure to provide periodontal attachment (14, 20). Papillon-Lefèvre syndrome includes hyperkeratosis of the palms and soles, sometimes calcification of the tentorium and choroid plexus and severe periodontitis in childhood (11, 19, 28, 46, 67, 95, 96, 132, 146). Other conditions in Table 1 are systemic diseases for which substantial literature exists to associate them with aggravation of periodontitis, often at a young age (47).

Early-onset periodontitis, systemic disease uncertain

If one accepts that juvenile periodontitis results because a systemic deficiency such as the neutrophil chemotactic defects allows progression of an infection that often, but not invariably, includes *A. actinomycetemcomitans*, and if one accepts that approximately 30% of juvenile periodontitis cases do not have a defect in neutrophil chemotaxis, then one must also allow for a group in which the systemic deficiency(ies) is (are) unknown. Similarly, many generalized early-onset periodontitis cases cannot be definitively associated with a specific systemic abnormality at present. Even though some of them have neutrophil defects and on average they have immunological abnormalities, the acknowledged heterogeneity within generalized early-onset periodontitis almost assures that there are additional explanations.

There are also a number of reported cases of periodontitis occurring prior to puberty with which no systemic abnormality has been identified. A recent, extensive review by Watanabe (164) identified 44 such case reports. Since the extent of investigation varied greatly among those reports, it is arguable whether systemic disease or abnormality was absent or simply undetected.

Necrotizing ulcerative periodontitis

Acute necrotizing ulcerative gingivitis with unknown systemic determinants or HIV-related as described previously can spread with time to a necrotizing periodontitis (4, 33). In conjunction with nutritional deprivation, the necrosis can extend to alveolar bone and extensive oral and facial soft tissue ulceration beyond the gingiva, a condition also known as noma or cancrum oris (44, 69).

Periodontal abscess

The periodontal abscess can be only a variant of any other form of periodontitis, consisting of an acute exacerbation of the pre-existing periodontitis. As such, it frequently provides the terminal event for the tooth (114). However, it can also occur as an acute event, stimulated by the forced introduction of foreign material or bacteria into the periodontal tissues. In such cases, it has its own natural history and response to therapy (98), justifying a separate designation in a classification scheme. The microbiology of periodontal abscess seems as varied as for periodontitis, suggesting that many of the species of the periodontal flora can participate in an abscess (105).

Other recently suggested entities

The American Academy of Periodontology's recommended classification (33) included a category called periodontitis associated with systemic disease. This category has large overlaps with others. Arguably, nearly all early-onset periodontitis fits this designation, because neutrophil defects are associated with many localized and generalized cases, and because immunological abnormality has been reported for groups of generalized early-onset periodontitis patients. Since it is clear that expression of all forms of periodontitis can be modified by some systemic diseases or abnormalities, it is probably better to consider them in that specific context, rather than treating them as a unique category.

The American Academy of Periodontology (33) suggested another category, refractory periodontitis, which was acknowledged to be heterogeneous, but was intended to designate patients who are unresponsive to treatment. Although such a grouping has utility in defining the study groups likely to exhibit a high rate of progression of disease (61, 94, 159), there are difficulties in separating refractory from recurrent disease. Also, the treatment that necessarily would precede the diagnosis cannot be standardized. Difficulty of treatment might be expected when there is an uncorrected systemic abnormality. In the context of disease classification or clinical diagnosis, refractory periodontitis seems inappropriate because of the heterogeneity and dependence on a treatment outcome.

Conclusion

The classification presented here is based on the concept that periodontal disease is the outcome of host-

parasite interaction (82). It considers the periodontal diseases to be infectious diseases unless otherwise specified and recognizes that their expression can be modified by factors other than the causative mixed bacterial infection. In most instances, variation in the extent or severity of disease can be understood as a function of a local infection in hosts having various degress of compromised resistance to infection or otherwise modified responsiveness. It is a classification that can evolve without drastic change in its fundamental structure. As new information becomes available, changes in the scheme would primarily be at the fourth level of specificity (Table 1).

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