

CHAPTER 2.

PERIODONTAL DISEASES

Section 1. Gingivitis and Periodontitis

DEFINITIONS

Inflammation: A localized protective response elicited by injury or destruction of tissue, which serves to destroy, dilute, or wall off both the injurious agent and the injured tissue. A cellular and vascular reaction of tissues to injury.

Gingivitis: Inflammation of the gingiva.

Periodontitis: Inflammation of the supporting tissues of the teeth. Usually a progressively destructive change leading to loss of bone and periodontal ligament. An extension of inflammation from gingiva into the adjacent bone and ligament.

Adult Periodontitis: A form of periodontitis that usually has an onset beyond age 35. Bone resorption usually progresses slowly and predominantly in the horizontal direction. Well-known local environmental factors are prominent and abnormalities in host defense have not been found.

Juvenile Periodontitis: May be generalized or localized; onset during the circumpubertal period; familial distribution; relative paucity of microbial plaque; less acute signs of inflammation than would be expected based upon the severity of destruction; may be associated with abnormalities in leukocyte chemotaxis and bacteriocidal activity.

Prepubertal Periodontitis: May be generalized or localized; onset between eruption of the primary dentition and puberty; may affect the primary and mixed dentition; characterized by severe gingival inflammation, rapid bone loss, tooth mobility, and tooth loss.

Refractory Periodontitis: Includes patients who are unresponsive to any treatment provided—whatever the thoroughness or frequency—as well as patients with recurrent disease at single or multiple sites.

The common forms of gingivitis and periodontitis are inflammatory processes initiated by bacterial plaque. Bacteria in the gingival crevice have been portrayed as an indigenous flora that trigger a self-destructive inflammatory response or as lethal pathogens which invade the host tissues to spark episodic bursts of disease activity. Current evidence suggests that bacterial products penetrate intact sulcular epithelium to initiate inflammation. Substantial evidence exists that bacteria can invade the host tissues as well.

There are multiple defense mechanisms in the gingival sulcus: 1) the primary line of defense by polymorphonuclear leukocytes (PMNs) can form a wall between plaque

and the epithelium; 2) the epithelial barrier is permeable and the site of ulceration, an early and important event in the development of gingivitis; 3) saliva, which contains secretory IgA, leukocytes, and lysozymes, aids host defense; 4) gingival fluid may flush substances from the pocket and contains PMNs and plasma factors, such as complement, non-specific opsonins, and immunoglobulins; and, 5) finally, the high rate of tissue turnover in the sulcus is protective (Page, 1986; Miyasaki, 1991).

GINGIVITIS

Etiology (See Page, 1986, for review)

Overwhelming evidence suggests that microbial plaque near the cervical region of the teeth causes gingivitis (Løe et al., 1965; Page, 1976; Moore et al., 1982). Healthy gingiva sulci typically contains a flora of *Streptococcus* and additional species including *Actinomyces*, *Veillonella*, and *Capnocytophaga*. *Streptococci* and *Actinomyces* may comprise over 85% of the microbial flora in health (Slots, 1979; Moore et al., 1982). Gingivitis has been characterized by a shift from a *Streptococcus*-dominated plaque to an *Actinomyces*-dominated plaque. Developing gingivitis has been associated with increased numbers of *A. israelii* and *Bacteroides*, especially *Porphyromonas gingivalis*. Gingivitis has also been associated with an increase in motile bacteria and spirochetes (Listgarten et al., 1978). Moore et al. (1982) described a great deal of individual variation in the development of gingivitis flora and reported a progression of species colonizing in a sequential matter in gingivitis. They associated gingivitis with specific *Actinomyces*, *Streptococcus*, *Fusobacterium*, *Veillonella*, and *Treponema*. Savitt and Socransky (1984) found *Eikenella corrodens*, *Fusobacterium*, and *C. gingivalis* elevated in gingivitis. *Prevotella intermedia* has been associated with pregnancy gingivitis (Kornman and Loesche, 1980).

Keratinized tissue (attached gingiva) is not an essential prerequisite to the maintenance of periodontal health when dental plaque is controlled (Kennedy et al., 1985). Malposed teeth only weakly correlate with gingivitis. A high sucrose diet may increase gingivitis (Sidi and Ashley, 1984).

Initiation

The initiation of the disease process is multifactorial. Currently, more than 40 components of gingival crevicular fluid (GCF) have been studied to determine their role in the pathogenesis of the disease process. Schwartz et al.

(1972) suggested that endotoxin penetrated healthy, intact crevicular epithelium. Labeled endotoxin was observed primarily in a gradient adjacent to the basal epithelium in the histologic sections examined in this study. Caffesse and Nasjleti (1976) suggested that bacterial hyaluronidase might act as a promoting agent for the penetration of bacterial collagenase through intact gingival epithelium. Hyaluronidase penetrated intact sulcular epithelium and also acted as a "spreading factor," widening the intercellular spaces and facilitating the penetration of labeled collagenase which failed to penetrate intact crevicular epithelium when used alone.

Most collagenase in the sulcus appears to originate from the host (Christner, 1980). Collagenase activity is present in the gingival tissue and in GCF in spontaneously occurring and experimental gingivitis in humans, and the amounts increase almost linearly with increasing severity of inflammation (see Page, 1992, for review). Activities similar to cathepsins B, D, H, and L are present in inflamed gingival tissue and in GCF harvested from inflamed sites (Kunimatsu et al., 1990). Neutral proteases resembling elastase, trypsin, chymotrypsin, and glycyloprolyl dipeptidase that can degrade non-collagenous matrix components have been recovered in GCF from inflamed sites with elastase activity being the highest activity observed (Cox and Eley, 1989).

Alkaline phosphatase activity has been associated with bone metabolism and neutrophilic granulocytes (Ishikawa and Cimasoni, 1970). B-glucuronidase and arylsulfatase (Lamster et al., 1985, 1986; Oshrain et al., 1984) levels are associated with inflammation, probing depth, and alveolar bone loss. Cytokines, specifically IL-1 α and IL-1 β are present in inflamed gingival tissue (Masada et al., 1990).

Mechanisms

Indirect mechanisms (host response) combine with the direct mechanisms (bacteria and their products) to determine the intensity of the inflammatory reaction (Genco, 1992). Bacterial products penetrate or adhere to tissues and induce a host response by activating complement and causing migration of PMNs (Miyasaki, 1991). Antibodies and cytokines (called acute phase proteins or C-reactive proteins) dramatically increase in inflammation. When bound to bacteria, C-reactive proteins promote binding to complement, which stimulates phagocytes to engulf bacteria (Kinane et al., 1992). Complement is activated in the classical pathway by antigen-antibody and is activated directly via the alternate pathway by bacterial components like LPS (Montgomery et al., 1986; Monefeldt and Tollefsen, 1993). Complement activation results in consequent release of C3A and C5A which trigger mast cells to degranulate and release histamine, in turn, increasing vascular permeability. The increased vascular permeability together with leucocyte emigration leads to stasis and inflammatory exudate from the vessels (Genco, 1992). C3A and C5A and bacterial product FMLP are chemoattractants for neutrophils (Schen-

kein, 1992). In turn, stimulated neutrophils release products which mediate damage to host tissues (Altman, 1992).

Crevicular epithelium may become more permeable with inflammation (Thilander, 1968). Thilander studied gingival biopsies from 12 gingivitis patients using transmission electron microscopy (TEM) and reported: 1) slight changes with dilation of vessels, focal edema, and increased epithelial spaces; 2) moderate changes in which intermediate and tight junctions in the epithelium were lost, areas of basement membrane were missing, and leukocytes appeared to be migrating between the epithelial cells; and 3) marked changes where cytoplasmic changes suggested degeneration.

The Initial Lesion (Experimental Histology)

The pathogenesis of inflammatory periodontal disease remains remarkably consistent with the model of Page and Schroeder (1976). In this model, gingivitis is represented by the initial, early, and established lesion (Page, 1986). The initial lesion is a histological entity which would most likely correlate with a preclinical gingivitis. The initial lesion appears 2 to 4 days after plaque accumulation in previously healthy gingiva and is localized to the gingival sulcus, including the junctional epithelium and the most coronal part of the connective tissue (rarely more than 5% to 10% is involved). Characteristics of the initial lesion include: 1) vasculitis subsequent to the junctional epithelium; 2) extravascular fibrin and serum protein; 3) loss of perivascular collagen; 4) increased migration of leukocytes into the junctional epithelium and sulcus; 5) alteration of the coronal part of the junctional epithelium; and 6) increased crevicular fluid. Exacerbations of acute inflammation may be associated with abscess formation or disease progression (Page, 1976).

The Early Lesion (Experimental Histology)

Clinically, the early lesion correlates with early gingivitis. The early lesion appears 4 to 7 days after plaque accumulation and is characterized by a dense lymphoid infiltrate. Characteristic features include: 1) features of initial lesion are present and progress; i.e., GCF increases with inflammation and crevicular leukocytes peak at 4 to 7 days; 2) collagen loss increases and may reach 60% to 70% in the inflamed tissue; 3) cytoplasmic alterations appear in resident fibroblasts; 4) lymphoid cells accumulate subjacent to the junctional epithelium and make up approximately 75% of the infiltrate (approximately 5% to 15% of the total connective tissue is infiltrated); and 5) basal cells of the junctional epithelium begin to proliferate. Lymphoid cells have a non-specific affinity for inflamed tissue. Cellular hypersensitivity may play a role in the early lesion (Page, 1976).

The Established Lesion (Experimental Histology)

Chronic clinical adult gingivitis correlates with the established lesion which occurs 2 to 3 weeks after the beginning of plaque accumulation. The key feature of the

established lesion is the presence of plasma cells. The lesion is centered around the bottom of the sulcus and relatively confined; features of earlier lesions persist. The predominant immunoglobulin is IgG with a small but significant amount of IgA and rarely IgM. Characteristics include: 1) persistence of the manifestations of acute inflammation; 2) continued loss of connective tissue: fibrosis and scarring may also occur; 3) predominance of plasma cells without appreciable bone loss; 4) extravascular immunoglobulins; and 5) the proliferation, apical migration, and lateral extension of the junctional epithelium. Early pocket formation may or may not occur. The established lesion may remain stable for extended periods of time (Page, 1976).

Seymour (1983) conducted an experimental gingivitis study with dental students. The students ceased all forms of oral hygiene for 21 days and had biopsies taken from each first molar at 0, 4, 8, and 21 days. There was an association between the formation of plaque and the development of gingivitis. A lymphocyte-dominated lesion developed between 4 and 7 days and continued up to day 21. A plasma cell lesion did not develop within this time period. The lack of plasma cells in experimental gingivitis is also supported by the work of Brex et al. (1988).

Quirynen et al. (1991) also conducted an experimental gingivitis study to quantify the influence of gingival inflammation on the rate of plaque formation. Plaque was found to accumulate at a significantly greater rate when gingival tissues were already inflamed; initially inflamed tissues had a 29% greater extension of plaque than initially healthy tissues.

Effects on Cementum

In a TEM study, Selvig (1966) examined 9 extracted teeth from patients and reported early changes which included an increase in small diameter collagen fibrils, presence of microfibrils, and a loss of functional orientation in the periodontal ligaments (PDL) opposite the cementum. Below the epithelial attachment there was a complete destruction of collagen and Sharpey's fibers accompanied by leukocyte infiltration. In the area of fiber dissolution, crystals in the outer layers of cementum were decreased in number and size. Loss of mineralization ranged from 4 to 18 μm . Above this region there was a zone of epithelial attachment to cementum. Degradation of collagen was felt to precede apical migration of epithelium on cementum.

Gingivitis and Gingival Recession

Gingival recession and clefts may form in some sites due to inflammation. Epithelial proliferation in the presence of inflammation may lead to anastomoses between the crevicular and mucosal epithelium in a susceptible site with subsequent recession.

Surgical procedures, trauma, and orthodontics may lead to the resorption of thin alveolar bone (as thin as 0.15 mm) creating conditions favorable for recession. A narrow width (thickness) of attached gingiva and prominent roots may

represent susceptible sites for recession due to inflammation (Novaes et al., 1975).

Prepubertal Gingivitis

A 21-day experimental gingivitis study comparing 6 children (age 4 to 5 years) with 6 dental students (age 23 to 29 years) indicated that preschool children developed gingivitis less readily than adults. Children developed significantly less gingival exudate and bleeding units (8.6% versus 43.9%) than adults at day 21 in teeth with the same plaque index. Crevicular leukocytes increased in children, but to a lesser degree than adults. These results were interpreted to suggest a different vascular response between children and adults and a relatively similar cellular response (Mattsson, 1978).

Subsequent studies suggest that in childhood, there is no clear-cut age at which the gingival reaction to bacterial irritation becomes similar to that observed in adults. Instead, gingival activity seems to increase gradually from early childhood to adult age (Mattson and Goldberg, 1985).

Longhurst et al. (1977) reported markedly fewer plasma cells in inflamed gingival tissue from young children than from adults. Morphologically the lesions consisted of approximately 70% lymphocytes, between 11% and 26% macrophages, and fewer numbers of polymorphonuclear leukocytes and plasma cells (Seymour et al., 1981).

High levels of spirochetes ($> 2\%$) were observed only in the prepubertal group (Wojcicki et al., 1987). A study by Moore et al. (1987) also indicated that the young children had fewer cultivable spirochetes than adults. Significant increases in subgingival spirochetes occurred when bleeding upon probing was observed as a sign of inflammation (Armitage et al., 1982). Therefore, a possible correlation exists between fewer spirochetes and a lower incidence of gingivitis found in prepubertal children.

Significance of Gingivitis

(See Page, 1986, for review.) Gingivitis does not necessarily progress to periodontitis. Initially, gingivitis was considered physiologic. In the 1950s and 1960s, the concept that untreated gingivitis progressed to periodontitis emerged. Observations by Marshall-Day et al. (1955) that gingivitis without evidence of bone loss was confined to a younger age group, and bone loss without clinical evidence of gingival disturbance was rarely observed strengthened this view. Suomi et al. (1971) found a loss of epithelial attachment at a rate more than three and one-half times higher in a group with greater gingival inflammation scores. In a longitudinal study of a Sri Lankan population with chronic gingivitis, Loe et al. (1986) reported 89% of the subjects developed periodontitis. However, episodic bursts of attachment loss were observed which did not correlate with clinical gingivitis (Haffajee et al., 1983).

Ranney (1986) suggested that gingivitis, at least as detectable histologically, has not been ruled out as a necessary

TABLE 1. IMMUNOLOGIC FINDINGS OF IMPORTANCE IN THE DIAGNOSIS OF DESQUAMATIVE GINGIVITIS

Underlying Disease	Tissue: Pattern of Immune Deposits	Sera: Types of Antibodies
Pemphigoid, all forms	Epithelial intercellular deposits (100%)	Intercellular antibodies of epithelium (over 95%)
Bullous pemphigoid	Basement membrane zone (100%)	Basement membrane (97%)
Cicatricial pemphigoid	Basement membrane zone (97%)*	Basement membrane (23%)
Lichen planus	Globular deposits (cystoid bodies) in epidermis and dermis (97%) Fibrin deposits along basement membrane	None
Psoriasis	Stratum corneum deposits	None are specific for psoriasis
Other (hormonal, etc.)	Negative or few cystoid bodies	Negative

*Figures in parentheses represent percentage of patients with the respective findings (Nisengard, 1981).

precursor of periodontitis, but it does not invariably progress to periodontitis. He also suggested certain measures of host response (e.g., antibody and PGE₂ in GCF) merit attention as possible predictors of clinical outcome. Waerhaug (1980) observed that inflammation arising from periodontal pockets may affect the deeper supporting structures without being clinically evident in the superficial structures. Is this periodontitis without a pre-existing gingivitis? Only in the immediate sense, since the pocket historically derived from a gingival inflammation. Gingivitis may be considered site specific because averaged measures have little meaning, although Moore et al. (1982) failed to find site specificity in the composition of the flora. When all the data are considered, the most likely interpretation is that gingivitis is a disease; most gingivitis lesions are transient or persistent, but not progressive. However, a small proportion can and does progress to periodontitis.

Desquamative Gingivitis

Desquamative gingivitis is characterized by desquamation or sloughing of the gingival epithelium, leaving an intensely red surface. Sloughing of the epithelium is due to vesiculation and should be considered a sign rather than a disease.

McCarthy et al. (1960) studied 40 cases of desquamative gingivitis over a 12-year period and carefully re-evaluated the existing literature. They concluded that chronic desquamative gingivitis was actually a manifestation of several diseases and therefore had multiple etiologies. Nisengard et al. (1981, 1987) reviewed the manifestations and treatments of these lesions. Approximately 75% of desquamative gingival lesions are dermatologic diseases, with cicatricial pemphigoid and lichen planus comprising over 95% of the dermatoses group. The remaining 25% of desquamative gingival lesions are either of idiopathic origin or can be associated with an endocrine imbalance, aging, chronic infection, or abnormal response to bacterial plaque (Table 1). Most patients are middle-aged and approximately 80% are females. Diagnosis is based on the clinical exam, histology, and immunofluorescence (IF) (Nisengard, 1975). Two types of IF are of prime value for lesions of desquamative gingivitis:

Direct IF. This type detects in vivo bound immunoglobulins and complement in a biopsy specimen by incubating the specimen with fluorescein-labeled antibodies to IgG, IgA, and IgM.

Indirect IF. This type detects serum antibodies and is accomplished by incubation of serum on sections of monkey esophagus with fluorescein-labeled anti-human immunoglobulin.

Pemphigus Vulgaris. Pemphigus vulgaris can involve the skin and mucous membranes. It is seen primarily in older patients of Jewish race and Mediterranean origin. Biopsy and histological examination reveal acantholysis and intraepithelial clefting (Lever et al., 1975). Treatment generally consists of systemic steroids, 40 mg prednisone every other day, with or without immunosuppressant therapy. Referral to a dermatologist is recommended.

Bullous Pemphigoid. Bullous pemphigoid was described as a distinct clinical and histopathologic entity by Lever (1953). The site of the bullae is in the subepidermal region. Lesions are commonly observed on the skin and intraoral lesions are rare.

Cicatricial Pemphigoid. Cicatricial pemphigoid or benign mucous membrane can involve the oral mucosa, the conjunctiva of the eye (symblepharon), and other mucous membranes and skin. They are characterized by subepithelial bullae and basement membrane deposits of IgG and complement. Treatment can consist of nothing for the asymptomatic, topical steroids for mild localized cases, or systemic steroids in more severe cases. Referral to an ophthalmologist is recommended (Nisengard and Neiders, 1981).

Lichen Planus. Lichen planus lesions may manifest as a desquamative lesion in keratotic, erosive, or atrophic forms of the disease (Jandinski et al., 1976). Direct IF shows cystoid bodies of IgG, IgM, and complement in dermis and epidermis. Fibrin deposits can be found along the basement membrane and a degeneration of the basal epithelium with "saw tooth" rete ridges. Treatment is usually with topical steroids.

Psoriasis. Psoriasis presents as skin lesions that are papules covered with silvery scales. Microscopically there is hyperkeratosis, acanthosis, and elongation of the rete ridges and dermal papillae. Several reports suggest that psoriatic

plaques involve an autoimmune mechanism. Direct IF may show antibody and complement bound to stratum corneum antigen. Treatment is with topical steroids.

HIV-RELATED PERIODONTAL DISEASE

Oral Signs and Symptoms

One of the most common features of HIV disease is oral candidiasis. Four major types of candidiasis may be seen in HIV disease: pseudomembranous, hypertrophic, atrophic (erythematous), and angular cheilitis. Silverman et al. (1986) reported that 56% of healthy homosexual males had cultivable oral *Candida*; prevalence among AIDS-Related Complex (ARC) and AIDS patients was 93% and 70% respectively. The presence of a *Candida* infection may be predictive of AIDS. Klein et al. (1984) compared 22 adults with unexplained oral candidiasis, reversed T4:T8 ratios, and generalized lymphadenopathy with 20 similar patients who had lymphadenopathy and reversed T4:T8 ratios, but did not have oral candidiasis. Over 50% (13/22) of subjects with candidiasis developed AIDS in a median of 3 months compared to 0/20 patients without candidiasis who were followed for a median of 22 months. Dentists should be aware of the possible implications of oral candidiasis in otherwise clinically healthy individuals. Viral lesions are commonly associated with HIV disease (Greenspan, 1988). Common lesions include oral papillomas, condyloma acuminatum, and focal epithelial hyperplasia, all of which are associated with human papillomaviruses (HPVs). Lesions of recurrent herpes simplex virus are also seen. Herpes zoster (caused by varicella) may also be encountered.

Oral hairy leukoplakia (HL) is a white lesion found primarily on the lateral borders of the tongue. HL was first discovered in 1981 in male homosexuals and has been seen in members of all other risk groups (Greenspan, 1988). Virtually all patients with HL are antibody-positive for HIV. The lesions may also be seen on the buccal/labial mucosa. The surface may be smooth, corrugated, or markedly folded, and does not rub off. HL is probably a virally induced lesion; in fact, Epstein-Barr virus has been detected in biopsies of HL. Silverman et al. (1986) found HL in 28% of 375 homosexual males. Over 50% of patients with HL may go on to develop AIDS.

Oral lesions associated with HIV include recurrent aphthous stomatitis, salivary gland enlargement, and thrombocytopenic purpura (Greenspan, 1988).

The most common AIDS-associated neoplasm is Kaposi's sarcoma (KS), a malignancy arising from lymphatic or vascular endothelium (Greenspan, 1988). According to the Centers for Disease Control and Prevention (CDC), 34% of patients with AIDS have KS. Other studies report an incidence of up to 80%. Intraoral lesions may occur alone or in combination with skin, lymph node, or visceral lesions. They may be blue, red, or purple in color and may be flat or raised, solitary or multiple. The most common oral lo-

cation for KS is the hard palate, although lesions may occur on the gingiva, buccal mucosa, tongue, and soft palate. On the gingiva, KS may cause diffuse swelling resembling severe gingivitis. Cytomegalovirus (CMV) is commonly associated with KS in HIV-positive subjects. The exact relationship between CMV and KS has not been determined.

Non-Hodgkins lymphoma is another common HIV-associated neoplasm (Greenspan, 1988). It can occur anywhere in the mouth, presenting as a painless swelling which may or may not be ulcerated.

Tuberculosis is another increasingly prevalent infection in those with AIDS.

Over the past several years, an increased incidence and severity of periodontal disease in HIV-infected homosexual males has been observed. These diseases do not respond well to conventional therapy and often progress very rapidly (Winkler et al., 1988). HIV-associated gingivitis (HIV-G) is characterized by generalized gingival swelling and spontaneous bleeding. Necrosis of marginal and papillary gingiva may be seen, and necrosis may extend well into the attached gingiva (Winkler et al., 1988). This lesion has shown a clinical representation described as being "half moon" in appearance at the gingival margin. Frequently, an overlying *Candida* infection is observed, and successful resolution of the gingivitis may be dependent upon successful treatment of the candidiasis. The most characteristic features of HIV-associated periodontitis (HIV-P) are rapid destruction of the periodontal supporting apparatus and severe soft tissue necrosis. In some HIV-P lesions, more than 90% of the attachment can be destroyed in as little as 3 to 6 months, resulting in early tooth loss (Winkler et al., 1988). Soft tissue necrosis, ulceration, and cratering are often seen immediately adjacent to regions of rapid bone loss. Another distinguishing feature of HIV-P is severe pain, commonly described as a "deep aching" bone pain. Interestingly, the pain often precedes the clinical presentation of HIV-P (Winkler et al., 1988).

Microbiologic assessment of HIV-G and HIV-P shows an increase in *Candida albicans*, *Prophyromonas gingivalis*, *Fusobacterium nucleatum*, *Eikenella corrodens*, *Actinobacillus actinomycetemcomitans*, and *Wolinella* species compared to controls (Murray et al., 1988). The microbiota associated with HIV-G and HIV-P are similar to those seen in classic periodontitis sites. Interestingly, there is a high prevalence of these organisms in HIV-G. This suggests that HIV-G may be a precursor to HIV-P and that early treatment of the HIV-G lesion may prevent the rapid destruction of periodontal support seen in HIV-P. Winkler and Robinson (1992) note that the organisms in HIV-P are similar to adult periodontitis except that *C. albicans* and *Campylobacter rectus* are present in higher proportions.

HIV-seropositive homosexual males have significantly higher antibody titers to *A. actinomycetemcomitans*, *E. cor-*

rodens, *F. nucleatum*, *P. gingivalis*, and *P. intermedia* than do HIV-seronegative homosexuals and heterosexuals (Murray et al., 1988).

In a study of 75 HIV-infected individuals (Barr et al., 1992A), only 1% of 218 cultured whole salivas presented cell-free infectious virus. The authors concluded that potential transmission of HIV infection by saliva is unlikely.

Periodontal Management

A widely used treatment for periodontal lesions in HIV+ individuals involves gross scaling to remove visible plaque and calculus deposits and debridement of necrotic tissue when present (Winkler and Robertson, 1992; Grassi et al., 1988). Access for both debridement and for topical antimicrobial therapy is aided by the fact that probing depths are often minimal in the necrotizing ulcerative periodontitis lesion. During debridement, povidine-iodine irrigation has been used for its antiseptic and anesthetic effects (Winkler and Robertson, 1992; Grassi et al., 1988).

Antibiotics should be used with caution due to the increased risk of overgrowth of *Candida albicans* and other microflora associated with HIV infection. To prevent overgrowth of opportunistic microorganisms, the use of a concurrent antifungal agent has been recommended. Narrow spectrum antibiotics, such as metronidazole which leave much of the Gram-positive flora unperturbed, have also been recommended to prevent *Candida* overgrowth in the management of periodontal lesions in HIV+ individuals (Winkler and Robertson, 1992).

Following initial debridement, follow-up visits are necessary in order to thoroughly remove plaque, calculus, and other deposits and to provide strict plaque control instruction. Home use of an antimicrobial mouthrinse such as chlorhexidine has been shown to be an effective therapeutic aid in reducing the acute symptoms of periodontitis in HIV+ patients and in preventing the recurrence of these lesions (Grassi et al., 1988). Clinical case reports and controlled studies have shown this therapy to be generally effective in reducing the acute symptoms of periodontitis in HIV+ individuals and in halting the progression of the necrotic lesion. The response to therapeutic intervention may, however, depend upon the patient's current HIV stage, intake of systemic medication to treat the HIV infection itself (e.g., zidovudine [AZT], intake of antibiotics, and oral habits (e.g., tobacco smoking).

Scully and McCarthy (1992) emphasize the need for early diagnosis and assessment every 3 months. Local debridement and topical application of antimicrobials such as povidone-iodine or chlorhexidine is beneficial. Yeung et al. (1993) compared the rate of progression of periodontitis between a group of asymptomatic HIV-seropositive men and a healthy control group. HIV-infected patients with pre-existing periodontitis tended to experience a greater rate of attachment loss over time compared with controls.

Atypical periodontal lesions observed in HIV+ individuals are often superimposed on conventional periodontitis. In previous studies, the relationship of HIV+ status and severity of periodontitis is unclear. For example, some studies report no direct correlation between the relationship of pocket depth or plaque index with HIV staging (Friedman et al., 1991; Gornitsky et al., 1991). In other studies, attachment loss was greater in later stages of HIV infection (Lucht et al., 1991; Klein et al., 1991) especially when CD4 counts fell below 200 (Barr et al., 1992B). In HIV+ individuals, the prevalence and severity of common forms of periodontal disease such as chronic inflammatory periodontal disease (adult periodontitis) may vary between risk groups due to other factors such as oral hygiene levels, smoking habits, medications, etc.

PERIODONTITIS

Classification: In July 1989, the *Proceedings of the World Workshop in Clinical Periodontics* recommended the following classification of periodontitis:

- I. Adult Periodontitis
- II. Early-Onset Periodontitis
 - A. Prepubertal Periodontitis
 1. Generalized
 2. Localized
 - B. Juvenile Periodontitis
 1. Generalized
 2. Localized
 - C. Rapidly Progressive Periodontitis
- III. Periodontitis Associated with Systemic Disease
- IV. Necrotizing Ulcerative Periodontitis
- V. Refractory Periodontitis

Pathogenesis of Pocket Formation

Changes associated with gingivitis in the periodontal tissues comprise a mixture of resolution and repair that are mostly reversible unless tissue necrosis occurs (Gillet et al., 1990). Pocket development between the tooth surface and gingiva with apical displacement of the junctional epithelium (JE) comprise the first indications of destructive disease (Gillet et al., 1990). Replacement of JE by pocket epithelium results in a thickening of the epithelium and rete ridge development (Muller-Glauser and Schroeder, 1982). The epithelium may become micro-ulcerated and allow penetration of bacteria or bacterial products which could overwhelm the host defenses and lead to a burst of disease activity (Gillet et al., 1990). The initial junctional epithelium defect is within the JE rather than at the JE/tooth interface (Takata and Donath, 1988). The epithelium will grow down the connective tissue/tooth interface to form a long JE. Epithelium along the cementum/soft tissue interface can prevent the establishment of connective tissue reattachment and result in an irreversible change (Gillett et al., 1990).

Lesions of Periodontitis

Page (1976) characterized the histopathological features of periodontitis as:

1. Predominance of plasma cells;
2. Continuing loss of collagen subjacent to the pocket epithelium with fibrosis at more distant sites;
3. Formation of periodontal pockets;
4. Presence of cytopathically altered plasma cells in the absence of altered fibroblasts;
5. Extension of the lesion into alveolar bone and PDL with significant bone loss;
6. Conversion of bone marrow distant from the lesion to fibrous connective tissue; and
7. Widespread manifestation of inflammatory and immunopathologic tissue reaction.

Clinically, periodontitis ranges from periodontal pocket formation, suppuration, fibrosis, destruction of alveolar bone and PDL, mobility, and drifting to eventual tooth exfoliation. Generally, the lesion of periodontitis resembles the established lesion described by Page (1976) with the spread of inflammation into the surrounding tissues with accompanying alveolar bone loss. Bone destruction usually begins along the crest of the interdental septum around communicating blood vessels. Periods of acute exacerbation with pus and abscess formation and periods of quiescence occur.

Distinguishing Periodontitis from Gingivitis

Moskow and Polson (1991) reexamined previous morphologic descriptions of gingival and periodontal inflammation based on a light microscopic study of 105 gingival biopsies and 350 autopsy and surgically-retrieved jaw sections. Clinically normal and marginally inflamed gingiva demonstrated more widespread distribution of inflammatory cells (neutrophils, lymphocytes, and plasma cells) than has usually been reported. A definitive pattern of inflammatory cell type in association with various clinical patterns of soft tissue or osseous destruction could not be established. The character of the cellular infiltrate in both gingivitis and periodontitis was variable and did not seem to be part of a logical consistent progression as Page and Schroeder (1976) described. There did not appear to be a specific cell type characteristic for each "stage" of disease progression. Moskow and Polson (1991) noted that bone changes can occur long before there is any evidence of attachment loss. Internal buttressing of the crestal alveolar bone was a common finding prior to any resorption of the alveolar crest as a result of inflammation. Spread of inflammatory infiltrate into crestal marrow spaces and into the PDL was observed without evidence of gingival fiber destruction. Thus features of the classic advanced lesion were observed prior to the classic early lesion. Since bone changes can occur at a very early stage in the development of the inflammatory lesion, the distinction between gingivitis and periodontitis

may not be possible. Intact transeptal fibers were always present over crestal alveolar bone even in the presence of significant osseous resorption (Moskow and Polson, 1991).

Progression to Experimental Periodontitis

In a study by Lindhe et al. (1975), 10 inbred beagle dogs who were brushed twice daily and given a weekly prophylaxis did not subsequently develop periodontitis. Eight of 10 dogs that accumulated plaque on a soft diet developed periodontitis with a loss of attachment of 2.9 mm at 48 months and progressive radiographic bone loss first evident at 24 months. Upper premolars and molars were affected most. These findings suggest that periodontitis might be prevented by removing calculus and providing oral hygiene; gingivitis can proceed to periodontitis; however, 2/10 untreated dogs and some sites did not progress, suggesting variability in host susceptibility.

Spread of Inflammation

Weinmann (1941) studied autopsy histological sections (patients were 14 to 74 years) and observed inflammation following blood vessels into bone marrow spaces while the PDL was generally free of inflammation. Resorption of the alveolar crest generally began on the periosteal side. Akiyoshi and Mori (1967) studied a young autopsy patient using light microscopy and radiographs and concluded that inflammation extends through transeptal fibers along blood vessels directly to interdental canals of the alveolar crest and also indirectly to the alveolar crest via the PDL. In early marginal periodontitis, resorption occurred from the endosteal side of the crest.

Macapanpan et al. (1954) used a rat model (35 rats) with a rubber dam inserted between the upper right first and second molars to determine the effects of trauma on the spread of inflammation up to 72 hours. The authors reported that tension to the PDL reduced resistance to direct infiltration of inflammatory cells from an existing gingivitis, but trauma alone did not cause periodontitis since sites under tension, away from the rubber dam site, were not affected.

Initiation of Active Periodontitis

Allenspach-Petrzilka and Guggenheim (1983) used TEM to examine gingival tissue from 2 female patients with chronic periodontitis and pockets of > 8 mm. The authors reported bacteria in the intercellular spaces of the pocket epithelium and in microabscesses in the underlying connective tissue. Bacteria were observed in the more apical parts of the pocket in the absence of inflammatory tissue. Bacterial invasion leading to focal necrosis or microabscesses might explain the cyclic nature of periodontitis. Listgarten (1986) suggested that increased plaque mass or a reduced host defense might precipitate episodes of periodontal destruction.

Untreated Periodontal Disease

Becker et al. (1979) studied 30 patients (25 to 71 years) initially identified as having periodontal disease who subsequently refused treatment but agreed to a second examination 18 to 115 months after the first (mean 3.72 years). Probing depths, mobility, and radiographs were compared. Untreated patients had a mean tooth loss of 0.36/patient/year, after eliminating 22 teeth initially considered hopeless and 1 patient who lost 25 teeth (the loss rate including the "hopeless" teeth was 0.61 teeth/year). Molars showed the greatest percentage loss. All patients manifested radiographic evidence of progressive bone loss. Increases in probing depth varied from 0.24 mm to 2.46 mm/year, with the greatest increase observed at the lingual interproximal sites.

Goodson et al. (1982) examined 22 patients (at least 20% of pockets 4 mm in depth) monthly for an average period of 13 months (9.3 to 23 months) and monitored attachment loss using regression analysis. Eighty-three percent (83%) of the sites remained unchanged; 5.7% became significantly deeper; and 11.5% became shallower. About one-half of the sites which lost attachment showed spontaneous recovery to the original depth. Deeper sites showed more variability. Attachment loss varied among individuals, with some subjects gaining or losing 4 to 5 mm/year. The findings suggested a dynamic condition of disease exacerbation and remission.

Lindhe et al. (1983) reported on 64 Swedish patients (16 to 64 years, mean 40.5 years) monitored at 3 and 6 years without periodontal therapy who had few sites over 5 mm (0.25%) and a second group of 36 American patients (13 to 63 years, mean 34.3 years) who were followed for 1 year at bimonthly intervals. The Swedish group lost 0.82 ± 0.87 mm the first 3 years and 0.45 ± 0.84 mm the second 3 years. In the American group, 3.2% of the sites lost > 2 mm and 4.3% sites gained > 2 mm attachment over 1 year. These data also suggested rapid loss at some sites rather than progressive bone loss. Also, sites with more advanced attachment loss were not more prone to additional destruction. However, the monitored sites might be affected by bacterial inoculation or redistribution.

Socransky et al. (1984) have suggested a random burst model for periodontitis. The continuous destruction model is challenged by four major lines of evidence: 1) attachment loss rates have been noted which are too fast or too slow to fit a linear progressive model; 2) a large number of sites appear not to be changing; 3) animal studies indicate that disease progression is not continuous in all sites; and 4) severe changes in a specific site are soon brought under control by as yet unknown mechanisms. The authors indicate that sequential (monthly) attachment level measurements have shown that 5.7% sites have probeable attachment gains while 2.8% have losses which ranged from 2 to 5 mm in some sites. Over 6 years, 12% of the sites lost over 2 mm;

40% of these sustained loss in the first 3 years, and half of the sites with no loss in the first 3 years showed loss in the second 3 years.

REFRACTORY PERIODONTITIS

Refractory periodontitis has been variably described. Kornman et al. (1991) referred to treated adult patients who failed to respond to therapy as having refractory periodontitis. Patients who had responded favorably to therapy and then demonstrated signs of disease reactivation were classified as having relapsing (recurrent) periodontitis. Recurrent periodontitis may also apply to disease recurrence in sites without good plaque control or maintenance. Magnusson et al. (1989) described patients who had further disease progression despite good plaque control, treatment by periodontal surgery, tetracycline therapy, and maintenance recalls as refractory. The *Proceedings of the World Workshop in Clinical Periodontics* described refractory periodontitis as disease in multiple sites in patients which continue to demonstrate attachment loss after apparently appropriate therapy. These sites presumably continue to be infected by periodontal pathogens.

Etiology

A patient may be "refractory" to periodontal therapy for several reasons including: 1) inadequate or inappropriate therapy; 2) inadequate maintenance; 3) inadequate plaque control; 4) systemic disease; 5) transient defect in immune response; (6) inadequate or inappropriate immune response; or 7) persistence of periodontal pathogens. Genetic contribution and implications in refractory periodontitis are unknown.

MacFarlane et al. (1992) reported a strong association between a peripheral blood PMN defect and refractory periodontitis. In a retrospective search for associated environmental variables, they found that 90% (28 of 31) of the refractory patients were smokers, demonstrating that local effects of tobacco smoke may compromise the PMN, and should be viewed as an epigenetic factor in periodontitis.

Microbiology

Walker and Gordon (1990) reported *Prevotella intermedia* and *Porphyromonas gingivalis* were the predominant cultivable species in active sites of 24 patients with refractory periodontitis. Magnusson et al. (1991) studied 21 patients who had further disease progression despite treatment by periodontal surgery, tetracycline therapy, and maintenance recalls. This group reported that the microflora found in active sites did not reflect that found in other studies, being predominantly Gram-positive with little of the traditional periodontal pathogens. Large and small motile rods were more frequently associated with active disease. Subjects showed elevated IgG titers to known pathogens, suggestive of prior exposure; however, authors were unable to isolate those species from the pocket. Inability to culture

these specific organisms could be due to the extensive antibiotic, surgical, and non-surgical therapy these individuals received resulting in eradication of the pathogen. The authors postulate that Gram-positive organisms may have become pathogenic and responsible for disease progression in this set of subjects (Magnusson et al., 1991). Conversely, it may be that no specific bacteria are responsible for this disease pattern. Walker et al. (1993) demonstrated that at least 2 patterns or rates of attachment loss may be associated with refractory periodontitis and that each pattern may be indicative of a different flora. The pattern associated with a relatively rapid loss of attachment was characterized by a Gram-negative flora which contained spirochetes, *P. intermedia* and *Fusobacterium* species. A slow, continuous rate was associated with a predominantly Gram-positive flora containing a high proportion of *S. intermedius* and/or a *S. intermedius*-like organism.

Treatment

Treatment for recurrent periodontitis should rely upon conventional periodontal therapy emphasizing good plaque control and maintenance. Treatment for refractory periodontitis may additionally include the following regimens:

Scaling and Root Planing and Amoxicillin/Clavulanate. Magnusson et al. (1989) studied 10 patients who continued to exhibit attachment loss after tetracycline and periodontal surgery. Patients were treated with scaling and root planing and amoxicillin/clavulanate (250 mg TID for 2 weeks). Clinical parameters improved in the first 3 months and were maintained for 12 months post-therapy.

Scaling and Root Planing and Clindamycin. Gordon et al. (1990) evaluated 30 patients with a disease progression (> 3 mm attachment loss) following treatment (scaling and root planing, surgery, and tetracycline). Patients were treated with scaling and root planing and clindamycin (150 mg QID for 7 days). Therapy decreased the annual disease rate (active sites/year) from 8.0% to 0.5%. Clindamycin, in conjunction with periodontal scaling, was effective in suppressing or eliminating the Gram-negative components of the microbiota associated with deep active sites refractory to conventional therapies (Walker and Gordon, 1990).

Several findings suggest that the sequential use of multiple antibiotic agents may offer greater promise as an adjunctive treatment approach for the management of recurrent and/or progressive periodontitis than a single antibiotic regimen.

Scaling and Root Planing with Amoxicillin plus Metronidazole. van Winklehoff et al. (1992) tested 4 deep sites in each of 118 patients positive for *Actinobacillus actinomycetemcomitans* (40 were refractory patients). After therapy consisting of scaling and root planing and metronidazole (250 mg)/amoxicillin (375 mg) TID for 7 days, the organism was eradicated in 114/118. In addition, 34/67 sites were negative for *Prevotella intermedia* and 30/34 were negative for *Porphyromonas gingivalis*.

Amoxicillin/Clavulanate Potassium and Doxycycline. Matisko and Bissada (1993) studied 11 patients with recurrent/progressive periodontitis and demonstrating subgingival infection with *A. actinomycetemcomitans* and/or *P. gingivalis*. Patients receiving doxycycline, 200 mg the first day and 100 mg for 4 days thereafter, and then amoxicillin/clavulanate potassium, 500 mg 3 times daily for 5 days, produced significant improvement. A beneficial and positive effect was evidenced by the gain in probing attachment level and reduction in probing depth for up to 25 weeks.

Combination Therapy. Collins et al. (1993) described the clinical and microbiological features of 30 refractory patients and their response to a combined local and systemic therapy at 6 weeks and 3 years following treatment. The treatment consisted of a 2-week regimen of amoxicillin/clavulanate potassium in conjunction with professional, intramuscular delivery of povidine iodine, and chlorhexidine mouthwash rinse BID. A majority (87%) of the patients had favorable clinical responses to the treatment. It was effective at reducing probing depth, with a 56% decrease in the number of pockets greater than 6 mm at 6 weeks. This was accompanied by an overall gain of ≥ 1 mm of probable attachment gain in 45% of all sites. The clinical effects persisted at 34.4 months with an attachment gain of ≥ 1 mm in 41.2% of sites. These data suggest that this combination therapy is an acceptable, non-invasive alternative for the management of these patients.

By analyzing the results of subgingival microbial samples sent to a diagnostic microbiological laboratory, Listgarten et al. (1993) observed that a substantial number of microorganisms associated with refractory periodontitis are variably resistant to commonly-used antibiotics. Diagnostic microbiology was considered an essential adjunct to the therapist faced with periodontal lesions refractory to conventional treatment.

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Section 2. Early Onset Disease

Children are generally susceptible to the same periodontal maladies that affect adult segments of the population. However, certain disease entities warrant special attention due to their increased incidence and predilection in younger age groups. Knowledge and conceptual understanding of periodontal disease affecting children is ongoing and progressive. Advancing insights into the genesis and progression of these diseases mandate continual update and awareness by the periodontal therapist since this will assuredly impact on diagnosis as well as current and future approaches to management.

DEFINITIONS

Early Onset Periodontitis: Age of onset is usually prior to 35 years; rapid rate of progression of tissue destruction, manifestation of defects in host defense; and composition of the associated flora different from that of adult periodontitis.

According to Page et al. (1983A), prepubertal periodontitis is a genetic-based periodontitis of unknown prevalence

affecting a prepubertal population during/after eruption of the primary dentition. Two forms have been described:

1. Generalized periodontitis (GPP): Acute fiery-red proliferative gingival inflammation (affecting marginal/attached gingiva) accompanied by rapid destruction of alveolar bone; affects all deciduous teeth and possibly the permanent dentition; peripheral white blood cell counts are markedly elevated with profound functional defects of PMNs and monocytes—no PMNs are found in the gingiva. Oral manifestations are frequently accompanied by otitis media, infections of the upper respiratory tract.

2. Localized periodontitis (LPP): Limited (undetermined) pattern of less rapid periodontal involvement with little/no gingival inflammation; PMNs/“or”/monocytes have functional defects. Recurrent otitis media and other infections are infrequent findings.

The term juvenile periodontitis (JP) was introduced by Butler (1969) and replaces the previously used term periodontosis.

JP, as defined by Baer (1971), “is a disease of the periodontium occurring in an otherwise healthy adolescent which is characterized by a rapid loss of alveolar bone about more than one tooth of the permanent dentition. There are two basic forms in which it occurs. In one form of the disease (localized), the only teeth affected are the first molars and incisors. In the other, more generalized form, it may affect most of the dentition. The amount of destruction is not commensurate with the amount of local irritants present.”

Page et al. (1983A) define rapidly progressive periodontitis (RPP) as a distinctive form of periodontitis affecting young individuals ranging in age from puberty to 35 years; characterized by acute and quiescent phases and an inconsistently generalized pattern of distribution. The active phase is characterized by marginal proliferative gingivitis and severe rapid bone loss which may be followed by spontaneous cessation and resolution of gingival inflammation. Systemic findings (e.g., weight loss, mental depression, and malaise) may be present, and the authors have reported functional defects in the PMNs or monocytes in approximately 83% of affected individuals studied.

JUVENILE PERIODONTITIS

Clinical Features

Affected individuals are considered healthy adolescents despite reports of abnormal PMN and/or monocyte dysfunction. Localized JP (LJP) patients characteristically do not manifest a predisposition for disseminated infection. Prevalence ranges from 0% to 17% (average, 0.10% to .25%) with differences attributed to varying criteria, geographics, and a diverse data base. Studies suggest increased incidence in blacks when compared to Caucasian populations (Burmeister et al., 1984). Although a higher incidence of JP is reported in circumpubertal females, occurrence of disease among sexes becomes more equally distributed with

increasing age, suggesting earlier occurrence among females (Hormand and Frandsen, 1979). Age criteria (12 to 20 years) for JP differ among investigators, but generally entail a circumpubertal onset with an upper age limit of 22 years.

Prevalence of JP has also been reported by Bial and Mellonig (1987), who radiographically evaluated 49,380 male naval recruits for evidence of JP. They reported a prevalence of 0.36% for this condition in their population. Melvin et al. (1991) screened 5,013 naval recruits for JP and reported a prevalence of 0.76% in their population. Prevalences of JP varied considerably between racial groups. Blacks had a much higher JP prevalence (2.1%) than Caucasians (0.09%), and black males had a higher prevalence (3.81%) than black females (1.99%). The overall male to female ratio of JP was found to be 1.1:1.0; however, when race was considered, the female to male ratio of black recruits versus Caucasian recruits was 0.52:1 and 4.3:1, respectively.

Löe and Brown (1991) reported and estimated prevalence of JP in U.S. school children age 14 to 17 years, using the National Institute of Dental Research national survey. Estimated prevalence of localized JP was 0.53% and generalized JP was 0.13%. In LJP, first molars were most commonly affected (40%), followed by second molars (21%) and incisors (10%). Attachment loss was widely distributed in GJP, with 37% of premolars and 33% of molars affected. The percent of adolescents with LJP increased until age 16, while the percent with GJP did not increase after age 15. Males were slightly more likely to have LJP and GJP, with blacks more likely than whites to have either disease. Black males were 2.9 times more likely to have LJP than black females, with the reverse true for whites. Hispanics were 2.4 times more likely to have LJP than non-Hispanics.

Cogen et al. (1992) retrospectively determined the prevalence of destructive periodontal disease in the deciduous dentition of children who later were diagnosed with LJP in their permanent dentition. Examination of the mixed dentition radiographs of 14 black children revealed that 12 had radiographic evidence of LJP in the mixed dentition. Seven of the 14 patients had radiographs of the deciduous dentition, of whom 5 patients had evidence supporting the diagnosis of LJP which involved the deciduous dentition. Sjodin et al. (1993) examined radiographs of the primary and permanent dentition of JP patients for evidence of primary dentition bone loss. Patients of the same age without radiographic evidence of bone loss were used as controls. Forty percent (40%) of all JP patients showed bone loss in the primary dentition as compared to 5% of the controls, and 31% of the JP patients had calculus in the primary dentition compared to 5% of the controls. First molars were most commonly affected followed by central incisors.

JP has historically been clinically associated with a paucity of bacterial plaque, so much so that some authors have stated that “local irritants must not be commensurate with

bone loss" (Baer, 1971). Burmeister et al. (1984) consistently reported positive correlations between plaque presence and degree of destruction in JP. It must be emphasized that whether bacterial plaque is clinically visible or not, it is always associated with JP. In the majority of LJP patients, subgingival calculus is not present (Lindskog and Blomlof, 1983). LJP progresses 3 to 4 times the rate of adult periodontitis (Baer, 1971); a progression rate of 5 $\mu\text{m}/\text{day}$ has been suggested on the basis of retrospective study (Waerhaug, 1977).

Etiology

Areas of etiologic commonality of JP can be identified in the periodontal literature. A full spectrum of correlative significance may be gleaned, but perspectives should be maintained. Factors include developmental (embryogenic) disorders, deciduous patterns of exfoliation, hyperocclusion, systemic abnormalities, qualitative defects of periodontal tissues, genetic predisposition, and microflora.

Developmental (Embryogenic) Disorders. Hiatt and Burrow (1965) proposed that neural crest alterations (virus induced?) could affect ectodermal/mesodermal stem derivatives and thus periodontium and epidermis. Their observations are more consistent with Papillon-Lefevre syndrome.

Deciduous Patterns of Exfoliation. McMillan (1976) suggested that distal root flare/resorption of the deciduous second molar may result in bone resorption at the mesial of the permanent first molars. Could all four first molars be affected simultaneously? What about incisors?

Hyperocclusion. The occlusal relationship in affected patients should be evaluated and adjusted as necessary (Ramfjord, 1952; Evian et al., 1982). In the genesis of JP, excessive occlusion may be a contributing factor as opposed to a primary cause; it should be adjusted if deemed excessive.

Systemic Factors. Factors associated with JP are numerous and range from chemical imbalance (Ross et al., 1958) to psychiatric factors (Gonzales, 1960). Suomalainen et al. (1991) investigated the origin of collagenase in the gingival crevicular fluid (GCF) of 6 JP and 6 adult periodontitis (AP) patients with no history of prior treatment. Results indicate that GCF from AP patients degraded type I and II collagen at equal rates and markedly faster than type III collagen, whereas GCF from JP patients preferentially degraded type I and III over type II collagen. Type III collagen was degraded 4 times faster by JP GCF than by GCF from adult periodontitis patients. The substrate specificity of JP GCF was indicative of collagenases produced by fibroblasts, epithelial cells, and macrophages. It was postulated that *Actinobacillus actinomycetemcomitans* may increase local collagenase production in JP patients by a direct effect on resilient fibroblasts or epithelial cells. It should be recognized that several systemic diseases have oral manifestations consistent with the JP disease pattern;

however, these must be distinguished from JP forms described by Baer (1971) in which individuals do not manifest systemic disease. These diseases include Papillon-LeFevre syndrome (Gorlin et al., 1964), Down's syndrome (Saxen et al., 1977), cyclic neutropenia (Cohen and Morris, 1961), agranulocytosis (Bauer, 1946), Chediak-Higashi disease (Tempel et al., 1972), hypophosphatasia, and diabetes mellitus (Becks, 1941). These entities should be considered in a comprehensive differential diagnosis of JP.

Qualitative Periodontal Defects. These have principally focused on cemental hypoplasia. Originally termed deep cementopathia by Gottlieb (1923, 1928), more recent microscopic observations by Ruben and Shapiro (1978) and Lindskog and Blomlof (1983) support the existence of true cemental hypoplasia in healthy and diseased root surfaces of a limited number of LJP patients.

The Role of Genetics. The genetic role in JP is suggested by reports of familial occurrence (Saxen, 1980A, 1980B). Nishimura et al. (1990) reported the results of a family study of a mother and daughter with increased susceptibility to early-onset periodontitis. They concluded, after assessing microbiological, immunological, host defense, and genetic parameters, that both subjects had an identical condition and that these patients may provide a unique model for improving our understanding of host factors involved in periodontal disease. Transmission of JP has been thought to be through an x-linked mode. Hart et al. (1992) suggested that transmission is via autosomal dominant transmission. The rationale for the previous x-linked mode of inheritance is that: 1) the selection of families for study introduces a bias for females in that females are more likely than males to seek dental care (female ascertainment bias); 2) mothers are more completely studied than fathers because they are more likely to bring children to appointments; and 3) studies that have looked only at affected siblings and have excluded the proband have found an equal ratio of affected females and males.

Evidence supporting autosomal dominant transmission include reports of nearly equal numbers of males and females affected by JP and demonstration of male-to-male transmission of JP (Løe and Brown, 1991).

Microflora. This factor warrants further discussion. Bacteria are always present and may be considered categorically composed of supragingival plaque, attached plaque, unattached or loosely adherent plaque, epithelium-associated bacteria, connective tissue-associated bacteria, and alveolar-associated bacteria. Newman et al. (1976) and Newman and Socransky's (1977) contributions to this area literally provided the impetus for further progressive study. These authors described 5 original groups of bacteria from JP lesions, providing a true conceptual shift from a traditional degenerative based etiology to one based on microflora. While subsequent investigations have identified JP-associated bacteria, two stand out: *Actinobacillus actinomycetemcomitans* (Y-4) and *Capnocytophaga* (3 species

= ochracea, sputigena, and gingivalis). These organisms will briefly be discussed.

Aa is a Gram-negative, non-motile capnophilic coccobacillus whose primary etiologic niche is the oral cavity; it is capable of seeding to distant sites, producing severe infection. Aa produces leukotoxin (PMN chemotaxis inhibiting factor); lymphocyte suppressing factor; lipopolysaccharide endotoxin; bone resorption-inducing toxin; acid/alkaline phosphatase; fibroblast inhibiting factor; collagenase; and epitheliotoxin (Zambon, 1985). This organism possesses tremendous destructive potential.

Aa has been observed in electron microscopic photomicrographs of gingival connective tissue of LJP lesions (Gillett and Johnson, 1982), suggesting tissue invasion. Mandell et al. (1987) identified Aa in all active sites and half of the inactive sites in 8 patients. All blood samples from each of these patients had elevated serum antibody to Aa.

Alaluusua et al. (1991) evaluated the possibility of intrafamilial transmission of Aa. Based on the prevalence and serotype distribution of Aa observed within the families studied, intrafamilial transmittance was suggested. However, since the data were cross-sectional, the direction of transmission could not be determined. The study also demonstrated that Aa does not colonize transiently, but shows persistent oral colonization.

The *Capnocytophaga* are Gram-negative, surface translocating (gliding motility) flexible rods that utilize a CO₂-based metabolism. Destructive potential is mediated by endotoxin, fibroblast proliferation-inhibiting factor and protease. *C. ochraceus* does not promote PMN chemotaxis and vascular exudation (Lindhe and Socransky, 1979), possibly accounting for the "facade" of clinical normalcy generally accompanying LJP. *C. sputigena* and *C. gingivalis* are extremely toxic organisms but thus far have not been specifically related to JP. Both produce a potent leukotoxin affecting PMN competence and have been shown to reduce PMN chemotaxis in vitro as a result of a post-receptor binding event (Shurin et al., 1979; Van Dyke et al., 1982A, 1982B). These, along with other organisms, such as *Eikenella corrodens* and black-pigmented *Bacteroides* species, may act synergistically with Aa to enhance tissue destruction in JP patients (Mandell et al., 1987; Kornman and Robertson, 1985).

Histopathogenesis

As recently as 1976, Waerhaug reported plaque-induced inflammation in LJP with plaque present within 0.2 to 1.1 mm of the epithelial cuff; a severe chronic inflammatory reaction and accompanying collagenolysis was noted in the adjacent connective tissue (CT). The presence of a broad zone of non-infiltrated CT between the inflammatory foci and the external tissue surface was deemed sufficient to mask visible signs of inflammation. No degenerative changes were observed. Numerous studies indicate that LJP

lesions are predominantly characterized by a plasma cell inflammatory infiltrate (cells with disrupted plasmalemma) and marked collagen loss (Daly et al., 1980; Seymour and Greaves, 1980; Liljenberg and Lindhe, 1980; Waldrop et al., 1981). This scenario is consistent with an intensive humorally mediated immunologic response (predominantly IgG) and has been documented by immunofluorescence and peroxidase-antiperoxidase methods. Elevated serum antibody (AB) to specific pathogens (e.g., Aa, Capno, Ec, and leukotoxin) associated with LJP have been documented (Ranney et al., 1982; Mandell et al., 1987; Vincent et al., 1987).

Numerous studies suggest that altered PMN function in LJP patients may contribute to early onset and progression (local effect?) of disease. Chemotactic defects in peripheral PMNs have been observed in approximately 73% of JP patients (Cianciola et al., 1977; Clark et al., 1977; Genco and Cianciola, 1977; Van Dyke et al., 1980, 1982A, 1982C, 1982D; and Ranney et al., 1981). Since PMNs are principally defensive cells, impaired PMN function may be expected to favor increased incidence and severity of periodontal disease. If a PMN defect does exist, why are affected individuals otherwise healthy? Clark et al. (1977) suggest that since the defect is generally limited in scope, infections in other body sites can mount a large enough response to overshadow "minor deficiencies" while bacteria implicated in periodontal disease cannot. One must also consider the possibility of a locally induced PMN (bacterial leukotoxin) defect in the case of periodontal disease. Wilton et al. (1977) found that crevicular PMNs differ functionally from peripheral blood PMNs in vivo. Murray and Patters (1980) noted significantly less phagocytic activity in crevicular leukocytes from rapidly progressing disease sites when compared to nondiseased sites of the same patients or cells from chronic periodontitis lesions. This suggests that PMN function may be diminished locally as a result of factors produced by plaque microorganisms.

Treatment

Rationale. Given that bacterial plaque is the primary etiologic factor of JP, therapeutic efforts should be directed toward its control. Since genetic and/or local PMN/monocyte deficits exist, chemotherapy to assist host response appears appropriate.

Prognosis. A prognosis is affected by 1) extent and location of bone loss (furcal invasion decreases success); 2) morphology of bony defect; 3) crown/root ratio; 4) degree of mobility; 5) occlusal factors; 6) oral hygiene efforts; and 7) general health and attitude of the patient.

Modalities. In a review article, Krill and Fry (1987) discussed the various therapeutic options available for treating localized JP. Options discussed encompassed the full range of therapy and included summary comments on early treatment methods, effectiveness of antimicrobials, non-surgical and surgical therapy, tooth transplantation, orthodontics, and adjunctive endodontics.

Non-Surgical Treatment

Plaque Control/Scaling-Root Planing. The therapist must be aware of limited access in cases of increasing probing depths, especially furcated teeth.

Antibiotics. Tetracycline (TCN) is currently the drug of choice in treatment of LJP. Both Aa and *Capnocytophaga* are sensitive to TCN, which can achieve gingival crevicular fluid (GCF) at levels 2 to 10 times greater than serum levels (Walker et al., 1981; Gordon et al., 1981A, 1981B). Slots et al. (1980A and 1980B) showed that 59 strains of Aa were sensitive to TCN at a concentration of 1 mg/ml. The two most frequently used dose-time regimens of TCN as an LJP treatment adjunct are: 250 mg QID x 14 days (start 1 to 2 days pretreatment) Slots et al. (1983), Lindhe and Liljenberg (1984), and Kornman and Robertson (1985) all suggest an extended regimen of 28 days. Novak et al. (1988) suggest non-surgical therapy in early LJP with a 3 to 6 week regimen of TCN and supragingival prophylaxis every 2 weeks for 3 months after TCN therapy.

Studies directed toward local delivery of TCN have been posed (Goodson et al., 1979, 1983, 1985; Goodson, 1985) with hollow fibers giving way to TCN-impregnated ethylene vinyl acetate. This approach delivers high concentrations (80 to 160 X GCF and 322 X blood levels versus systemic levels with a 250 mg dose) without systemic toxicity. Bacteriocidal potential is proportional to increasing dosage.

In summary, the advantages of TCN in LJP are: 1) broad spectrum-bacteriostatic antibiotic; 2) specific for LJP-associated pathogens (Aa, *Capnocytophaga*); 3) concentrated in GCF; 4) affinity for saliva-coated enamel and inflammatory tissue; 5) may suppress bone and fibrinolytic activity; 6) may inhibit collagenase activity, reducing the rate of collagen breakdown (Golub et al., 1985); and 7) is relatively nontoxic to a healthy host.

Doxycycline, a semisynthetic TCN, has been successfully used in conjunction with surgery in the treatment of LJP (Mandell et al., 1986; Mandell and Socransky, 1988). Additional benefits of doxycycline include: 1) lower dosage, taken BID instead of QID; 2) not inhibited with calcium (dairy products); 3) does not induce photosensitivity; 4) decreased gastrointestinal side-effects; and 5) excreted via liver rather than kidney.

The use of metronidazole (MET) in suppressing Aa was compared to TCN in a study by Saxen and Asikainen (1993). All patients received oral hygiene instructions and scaling and root planing. Nine patients were given 200 mg of MET TID for 10 days; 9 patients were given 250 mg of TCN QID for 12 days; and 9 patients received no medication. Clinical parameters improved for all groups, with radiographic evidence of new bone formation.

Metronidazole was thus more effective in the eradication of Aa than TCN. Tetracycline, however, was used for a shorter duration than recommended.

Occlusal Therapy. When occlusion is determined to be

a contributing factor in the presence of early onset disease, occlusal therapy should be initiated.

Orthodontic Treatment. Realignment and supereruption of affected teeth have been suggested by some authors (Evertt and Baer, 1964; Goldstein and Fritz, 1976) to level or eliminate defects in JP patients.

Surgical Treatment

Surgical approaches to JP management include: 1) modified Widman flap/flap curettage; 2) resective techniques; 3) regenerative procedures; 4) root resection/extraction; and, 5) autotransplantation. No single surgical modality will be applicable to every case of JP; treatment approaches must be selected on the basis of independent case analysis and thus individual patient need.

Modified Widman Flap (MWR)-Flap Curettage (FC). Lindhe and Liljenberg (1984) used MWF with TCN for 14 days to treat 16 LJP patients. When compared with patients treated for adult periodontitis (AP), at 6 months, the gain of clinical attachment was more pronounced in the LJP group (2.1 to 5.1 mm, LJP versus 2.1 to 3.3 mm, AP). At 12 months post-treatment, 6 LJP sites had recurrent lesions (bleeding, probing depths 3 mm) and were retreated; subsequent bone fill and clinical attachment were observed at 18 and 24 months. At the 5-year follow-up, the authors noted that clinical results remained unchanged from 6 months to 5 years with the exception of the 6 retreated sites. Barnett and Baker (1983) reported reduction of 5 to 8 mm pockets to 3 to 4 mm 1.5 months post-MWF (and TCN 1 gram/day for 14 days) surgery. Van Swol (1981) also reported rapid healing in LJP patients following MWF surgery.

Kornman and Robertson (1985) evaluated JP therapy clinically (bleeding/suppuration; probing depth; gingival retractability) and microbiologically (*Actinobacillus actinomycetemcomitans* (Aa); black pigmented *Bacteroides* [BPB]; surface translocating bacteria [STB]), comparing patient response to scaling and root planing (S/RP) alone, S/RP combined with 1 gram TCN/day for 28 days and MWF supplemented with 1 gram TCN/day for 28 days. Surgical therapy (MWF + TCN) resulted in pocket reduction, resolution of bleeding and suppuration, and dramatic reductions of BPB, Aa, and STB. These findings are consistent with those of Christersson et al. (1985).

Encouraging therapeutic results have been observed in JP lesions using MWF surgery supplemented with systemic TCN. Mandell et al. (1986) compared local TCN delivery via monolithic fibers, surgery (inverse bevel full thickness flaps without osseous recontouring) plus doxycycline (14 days) and doxycycline (14 days) without surgery in the treatment of LJP. Only the surgery-plus-doxycycline group was effective in suppressing or eliminating Aa.

Resective Techniques (Osteotomy-Osteoplasty). These are generally of limited value in management of JP lesions due to the severity of the disease. However, osseous resec-

tion may be useful as second stage procedures (post-grafting) in elimination of minor residual bony defects (Hoffman, 1983).

Regenerative Procedures. These are directed toward reconstitution of the periodontium in the face of severe disease. In theory, it would seem most applicable to JP, considering the exorbitant loss of attachment accompanying this disease. Regenerative response will depend on the magnitude and morphology of the osseous defects and the availability of graft materials, as well as their associated regenerative potential. Mattout and Roche (1984) used an iliac crest autograft in an 18-year-old JP patient, noting complete furcal fill and significant supracrestal repair. Yukna and Sepe (1982) and Mabry et al. (1985) used FDB allografts combined with TCN powder (4:1 ratio) supplemented with systemic TCN in management of LJP lesions. Mean fill of defects ranged from 61% to 80% using this therapeutic approach; "open-curettage" controls (Mabry et al., 1985) demonstrated 50% less defect fill.

Regenerative attempts offer therapeutic promise, but guidelines for treatment success must be realistic (50% bone fill; 75% bone fill). Procedures must be defined to the patient as to expectation and need for subsequent regenerative therapy or second stage surgical procedures.

Root Resection/Extraction. The therapist must weigh the impact of heroic therapy on adjacent teeth which may be potential abutments for a fixed partial denture. The objective is not carte blanc extraction, rather an attempt to provide esthetics, phonetics, and function commensurate with comprehensive dental health. It may be feasible to remove part of the diseased tooth (e.g., root resection, hemisection, etc.), bearing in mind that such therapy requires endodontic and often prosthodontic evaluation and support. Therapy should be kept in perspective during the course of comprehensive management of the JP patient.

Autotransplantation. This entails extraction of JP molars and replacement by autotransplanted third molars (Baer and Gamble, 1966; Borring-Moller and Frandsen, 1978). Donor: third molar, roots incompletely formed, < 90% developed; 2 to 3 mm apical to furca), atraumatically removed and placed in socket or stored in sterile saline. Recipient: mesial-distal width adjusted (polish; sodium fluoride treatment), granulation tissue left in site with alveolar alteration only as needed, intra-occlusion, nonrigid splinting and soft diet for 1 to 2 days. Root formation should continue with no root resorption, ankylosis, or pulpal necrosis.

Supportive Periodontal Treatment (SPT)

SPT, a *sine qua non* for successful periodontal therapy, is the dual responsibility of the therapist and patient. Following definitive treatment and post-treatment evaluation, the patient should be seen at 3-month intervals for SPT. The frequency of appointments may vary in accordance with the patient's needs. The SPT visit should include evaluation for signs of disease activity (bleeding and/or sup-

uration upon probing, increased probing depths, gingival atypia). Therapeutic attention should be directed to sites reflecting recurrence of disease or periodontal breakdown. Plaque control motivation should be assessed and monitored, with instructions tailored for individual patient needs.

PREPUBERTAL PERIODONTITIS

DEFINITION

Prepubertal Periodontitis: May be generalized or localized; onset between eruption of the primary dentition and puberty; may affect the primary and mixed dentition; characterized by severe gingival inflammation, rapid bone loss, tooth mobility, and tooth loss.

Features according to Page et al. (1983B):

1. Onset during or immediately after eruption of the primary teeth.
2. Prevalence unknown but probably rare.
3. Possibility of a genetic basis for some types.
4. Generalized form:
 - Extremely acute inflammation is present, with proliferation of gingiva;
 - There is very rapid destruction of the alveolar bone and gingiva;
 - Profound functional defects of peripheral blood neutrophils and monocytes are seen; neutrophils are absent from gingival tissue;
 - Peripheral blood white cell count is markedly elevated;
 - Otitis media and skin and upper respiratory infections are frequent findings;
 - Periodontitis may be refractory to antibiotic therapy; and
 - All primary teeth are affected; the permanent dentition may or may not be affected.
5. Localized form:
 - Only some teeth are affected; pattern of involvement not yet determined;
 - Gingival tissues may exhibit little or no inflammation;
 - Destruction is not as rapid as in the generalized form;
 - Functional defects are present in either neutrophils or monocytes, but not both;
 - Recurrent otitis media is not a frequent finding and usually there is no history of frequent infections; and
 - The disease is amenable to treatment by curettage and antibiotic therapy (Page et al., 1983A).

Watanabe (1990) reviewed diagnostic criteria, pathogenesis, and differential diagnosis of prepubertal periodontitis. Children with PP do not have neutropenia, agranulocytosis, aplastic anemia, or other traditional blood dyscrasias, and do not fit the diagnostic criteria for hypophosphatasia or Papillon-Lefèvre syndrome (PLS) (Page's definition did not exclude patients with these diseases). Es-

estimates of prevalence range from 0.84% to 26.9%. Variance in reported prevalence may depend on genetic factors, methodological factors, and the selection of non-random sample populations. In otherwise healthy children, PP may be caused by periodontopathic bacteria (*Actinobacillus actinomycetemcomitans*, *Prevotella intermedia*, *Porphyromonas gingivalis*, *Campylobacter* species, and *Eikenella corrodens* have been proposed). Susceptibility may be related to cementum defects, leukocyte chemotaxis dysfunction, and/or presence of bacteriophage.

Prichard et al. (1984) reported a case of prepubertal periodontitis affecting the deciduous and permanent dentition in a patient with cyclic neutropenia. This report illustrated the importance of obtaining a differential white blood cell count when diagnosing severe oral pathoses of obscure origin.

Several conditions exist that may lead to advanced periodontal deterioration in children. A differential diagnosis would include: hypophosphatasia, Papillon-LeFèvre syndrome, histiocytosis X, neutropenia, cyclic neutropenia, leukemia, diabetes mellitus, scleroderma, fibrous dysplasia, and acrodynia (Goepford, 1981). Page et al. (1983B) listed profound functional defects of peripheral blood neutrophils and monocytes in the features of prepubertal periodontitis. A partial list of neutrophil abnormalities that exhibit periodontal destruction includes: cyclic neutropenia, chronic familial neutropenia, hereditary neutropenia, agranulocytosis, chronic benign neutropenia, chronic idiopathic neutropenia, congenital agranulocytosis, chronic benign granulocytopenia, congenital neutropenia, atypical hereditary neutropenia, familial benign chronic neutropenia, and chronic neutropenia. Range of severity of neutropenia is categorized as mild = 1,000 to 2,000 cells/mm³; moderate = 500 to 1,000 cells/mm³; severe = less than 500 cells/mm³ (Kalkwarf and McLey, 1984).

Diseases Associated with Periodontitis in Prepubescent Children

Hypophosphatasia. An autosomal recessive or dominant disorder caused by low levels of alkaline phosphatase (3 types: infantile, childhood, and adult); mild forms may have no other clinical signs other than early exfoliation of deciduous teeth with minimal signs of inflammation. PMN defect reports are variable.

Papillon-LeFèvre Syndrome. An autosomal recessive trait that may be related to a generalized epithelial dysplasia; clinical features include palmar and plantar hyperkeratosis and periodontal destruction. PMN defects are controversial.

Neutropenia. A number of neutropenias exist; several manifest severe gingivitis with ulcerations, and a history of recurrent infections.

Leukocyte Adhesion Deficiency. An autosomal recessive condition in which the glycoprotein adhesion molecules on leukocytes are reduced. Oral features include

severe gingival inflammation and severe alveolar bone loss, which leads to early exfoliation of teeth.

Histiocytosis X. May be the result of the proliferation and dissemination of pathologic Langerhans cells.

Chediak-Higashi Syndrome. A rare autosomal recessive disease in which leukocyte defects are associated with impaired function of cytoplasmic microtubules or microtubule assembly in PMNs.

Leukemias. A group of conditions characterized by progressive uncontrolled proliferation of white blood cells.

Acrodynia. A rare disease thought to be caused by an unusual sensitivity or idiosyncrasy to mercury.

Juvenile Diabetes. A relative or absolute decrease in insulin secretion, availability, or responsiveness, possibly caused by a genetic defect, autoimmunity, or viral infections.

AIDS. An unusual gingivitis resembling an atypical form of acute necrotizing ulcerative gingivitis has been reported, although no reports exist of prepubertal AIDS patients with alveolar bone loss. Any of these diseases may manifest as periodontitis, thus patient evaluation to obtain a differential diagnosis may include complete blood cell count, leukocyte differential and cell morphology, serum alkaline phosphatase, examination for palmar and plantar hyperkeratosis, biopsy, and fasting blood glucose levels (Watanabe, 1990). The diagnosis of PP is made following confirmation that patients are not afflicted with one of the aforementioned systemic diseases.

Watanabe et al. (1991) also analyzed neutrophil chemotaxis and surface CD11b expression by neutrophils (PMNs) in localized prepubertal periodontitis patients and healthy controls. Results of this investigation indicated that there was no statistically significant correlation between neutrophil chemotaxis and surface CD11b expression between localized prepubertal periodontitis and pediatric control subjects. Data from this study, however, indicated that neutrophil chemotaxis was significantly depressed in children relative to that of the healthy adult control group. It is possible that decreased neutrophil chemotaxis in children, in combination with the presence of suspected pathogens, may precipitate periodontitis. The authors suggest that the diagnosis of localized PP cannot be made by clinical appearance and/or the patients' dental history of premature exfoliation of the primary teeth.

A genetic basis for some types of disorders may exist. Waldrop et al. (1987) described a family with deficiencies of MAC-1 (the iC3b receptor of human myeloid cells), lymphocyte function antigen-1 (LFA-1) and p 150, 95. These glycoproteins are normally found on granulocyte, monocyte, and/or lymphocyte surfaces and function in adhesion-dependent immune cell function that contribute to endothelial migration and subsequent infiltration of PMNs and monocytes into extravascular inflammatory sites. Individuals deficient in these glycoproteins manifest necrotic, nonpurulent infections, and delayed wound healing. Perio-

dontal findings include rapid bone loss, fiery-red inflammation, recession, bleeding, and other signs of generalized destruction. This emphasizes the importance of normal leukocyte function in maintaining the periodontium against pathogenic microorganisms. In affected individuals, the degree of host immunocompromise reflects the extent of the so-called "glycoprotein-based" leukocyte adhesion defect (LAD).

Treatment

Treatment for prepubertal periodontitis has ranged from local treatment (curettage) and/or systemic antibiotics to the extraction of involved teeth (Watanabe, 1990). Localized PP may be responsive to treatment by curettage and antibiotics, whereas generalized PP may be refractory to antibiotic therapy. Granulocyte infusion may improve the periodontal condition temporarily (Page et al., 1983A). To date, however, treatment of patients with PP has generally been unsuccessful. Generalized PP patients show early loss of primary and adult dentition (Waldrop et al., 1987).

RAPIDLY PROGRESSIVE PERIODONTITIS

DEFINITION

Rapidly Progressive Periodontitis (RPP): Most of the teeth are affected; the extent of clinical signs of inflammation may be less than expected; the age of onset is usually in the early 20s through the mid 30s.

Features according to Page et al. (1983A) are:

1. Age of onset is between puberty and about age 35.
2. Lesions are generalized, affecting most of the teeth, without any consistent pattern of distribution.
3. Some, but not all, patients may have had juvenile periodontitis previously.
4. There is evidence of severe and rapid bone destruction, after which the destructive process may cease spontaneously or greatly slow down.
5. During the active phase, the gingival tissue is acutely inflamed with marginal proliferation; during the arrested phase, the tissues may appear free of inflammation.
6. The amounts of microbial deposits are highly variable.
7. Approximately 83% of the patients have functional defects in neutrophils or monocytes.
8. The disease sometimes, but not always, has systemic manifestations including weight loss, mental depression, and general malaise.
9. Some individuals are remarkably responsive to treatment by S/RP or open/closed curettage with adjunctive antibiotic therapy.

Chen et al. (1991) investigated immune responses of 36 young adults with rapidly progressive periodontitis to *Porphyromonas gingivalis* (Pg). This study demonstrated that one-third of the RPP patients did produce IgG reactive to Pg but with low avidity (strength of binding). The remaining two-thirds had lower IgG and avidity than control sub-

jects. The change in titer and avidity occurring after treatment may have been due to a decreased bacterial load which has been shown to result in the selection of clones of B lymphocytes that produce antibodies of higher avidity, or the reduced load may allow maturation of the immune system. Results showing that the sero-positive group had more bone loss may be the result of longer presence of the disease, or a faster rate of disease progression which allowed production of higher titers of low avidity antibody.

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Section 3. Acute Periodontal Conditions: Periodontal Abscess

DEFINITION

Periodontal Abscess: Localized purulent inflammation in the periodontal tissues; also called lateral abscess.

CLINICAL FEATURES

The acute periodontal abscess may have symptoms such as throbbing radiating pain, exquisite tenderness of the gingiva to palpation, sensitivity of the tooth to percussion, tooth mobility, and lymphadenitis. It appears as an ovoid elevation of the gingiva. The gingiva is generally edematous and red, with a smooth shiny surface. The shape and consistency of the elevated area may vary from dome-like and relatively firm to pointed and soft. Purulent exudate can usually be expressed from the gingival margin by gentle digital pressure (Glickman, 1979).

RADIOGRAPHIC APPEARANCE

The typical radiographic appearance of the periodontal abscess is that of a discrete radiolucency along the lateral aspect of the root. Many variables may alter this such as: 1) stage of the lesion; 2) extent of bone destruction and morphology of the bone; and 3) the location of the abscess (i.e., abscesses on the facial or lingual surface are obscured by radiopacity of the root). The radiograph alone is not sufficient for the diagnosis (Glickman, 1979).

DIAGNOSIS

Continuity of the lesion with the gingival margin is clinical evidence of the presence of a periodontal abscess. The abscess is not necessarily located on the same surface of the root as the pocket but may follow a tortuous course from the depth of the pocket (Glickman, 1979).

Differential Diagnosis. Table 1 shows the usual characteristics of periapical and periodontal abscesses.

TABLE 1. PERIODONTAL VERSUS PERIAPICAL ABSCESS*

Periapical	Periodontal
non-vital tooth	vital tooth
caries	no caries
no pocket	pocket
apical radiolucency	lateral radiolucency
none or minimal mobility	mobility
sensitive to percussion	sensitive to percussion (acute)
draining sinus usually located in apical area	draining sinus usually located at lateral aspect of root

*Adapted from Glickman, 1979.

ETIOLOGY

Newman and Sims (1979) performed microbiological culturing of periodontal abscesses in 9 patients. An exudate sample was taken at the gingival margin after light digital pressure to the external abscess wall. An apical sample was taken from the apical portion of the periodontal pocket. All samples were taken using a barbed broach under flow of anaerobic gas within a cannula. Microbiota recovered from the respective abscess sites were predominantly Gram-negative (66.2%) and anaerobic (65.6%). In the exudate, 49.5% of the predominant cultivable microbiota were Gram-negative anaerobic rods including *Bacteroides melaninogenicus* subspecies, *Fusobacterium* species, and vibrio-corroders. The apical sites contained more Gram-positive organisms (40% versus 27.6%); however, the apical sites were still predominated by Gram-negative (60%) and anaerobic (64.3%) bacteria. *Capnocytophaga* species were isolated in all exudate samples.

Glickman (1979) gives 5 scenarios for abscess formation: 1) extension of the pocket into supporting periodontal tissues along lateral aspect of the root; 2) lateral extension from the inner surface of the pocket into connective tissue of the pocket wall; 3) in the tortuous (complex) pocket, an abscess may form in the deep end (cul-de-sac); 4) incomplete removal of calculus results in shrinkage of the gingival wall and occlusion of the pocket orifice; and, 5) an abscess may form in the absence of periodontitis following trauma to tooth (fractured root) or perforation of the lateral wall of the root during endodontic therapy.

TREATMENT

Grant et al. (1988) describe 3 methods for treating periodontal abscesses: 1) curettage via the sulcus; 2) flap surgery; and, 3) incision and drainage. Treatment may be dictated by availability of time at emergent presentation. Management under these conditions should be reevaluated post-treatment for subsequent therapeutic needs. Antibiotics may be indicated pending patient manifestations and should be supported by culture and sensitivity where practical and indicated.

PROGNOSIS

Nabers et al. (1964) suggest that the acute inflammation present in a periodontal abscess provides excellent potential for regeneration of bone, periodontal ligament, and cementum. They conclude that the prognosis of teeth with extensive osseous pocketing depends not only on the morphology of the lesion but on chronology as well.

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Section 4. Necrotizing Ulcerative Periodontitis

DEFINITIONS

Necrotizing Ulcerative Periodontitis (NUP): Severe and rapidly progressive disease that has a distinctive erythema of the free gingiva, attached gingiva, and alveolar mucosa; extensive soft tissue necrosis; severe loss of periodontal attachment; deep pocket formation is not evident. Previously termed necrotizing ulcerative gingivitis (ANUG).

Acute: 1) Sharp, severe. 2) Denoting the swift onset and course of a disease.

CLINICAL FEATURES

Barnes et al. (1973) state that the diagnosis can be based on clinical findings alone. The authors examined 218 patients and found pain to be the most consistent symptom while bleeding and interdental cratering were the most consistent objective signs. Pseudo-membrane formation and fetor oris were also common. Fever, lymphadenopathy, and malaise are rare and are considered a secondary finding associated with dehydration.

In an army population (active duty and dependents), Barnes et al. (1973) reported an incidence of less than 1% while Pindborg (1951) found an incidence of 6.9%.

Kristoffersen and Lie (1983) suggested a condition which they termed chronic necrotizing gingivitis. However, the concept of "chronic ANUG" is contradictory and recurrent ANUG was considered more appropriate (Johnson and Engel, 1986).

ETIOLOGY

In a classic description of the ANUG lesion, Listgarten (1965) described four distinct zones. The surface bacterial zone consisted of a wide variety of microorganisms including spirochetes and fusiforms. The neutrophil-rich zone was comprised of leukocytes (mainly PMNs) migrating from the underlying connective tissue and adjacent epithelium. Spirochetes were also observed in this layer and were occasionally located within mononuclear leukocytes, suggesting phagocytosis. The necrotic zone was characterized by cellular and connective tissue debris, with the predominant morphotype being spirochetes of varying sizes. The zone of spirochetal infiltration exhibited spirochetes within vital connective tissue, infiltrating to depths of 250 μ m beneath the surface of the lesion. The invading spirochetes were predominantly of the medium and large varieties and were

also observed within the intercellular spaces of the adjacent epithelium.

In a more recent light and transmission electron microscopic (TEM) study, Courtois et al. (1983) examined papillae from 8 ANUG patients. They also observed 4 layers as previously reported, but noted blending of the neutrophil-rich and necrotic zones. Bacterial invasion (primarily spirochetes) was present to depths of 155 to 400 μm within the connective tissue. Unlike Listgarten, they noted that plasma cells and lymphocytes were the predominant inflammatory infiltrate.

Loesche et al. (1982) studied 8 ANUG patients using darkfield microscopy and anaerobic culturing. They reported *P. intermedia*, *Fusobacterium*, and *Treponema* species in each of the plaque samples examined. Of the total cultivable flora, *P. intermedia* represented 24.0%, and *Treponema* species and large spirochetes comprised 30% and 10%, respectively. These results were interpreted to indicate a pathogenic role for *P. intermedia*. Chung et al. (1983) also implicated *P. intermedia* and spirochetes in the etiology of ANUG by reporting high antibody titers to intermediate-sized spirochetes in these patients.

Sabiston (1986) suggests that the correlation between features of ANUG and virus infections (notably cytomegalovirus) point to a viral etiology for ANUG.

Cogen et al. (1983) reported that leukocyte function in ANUG patients showed depressed chemotaxis and phagocytosis. The authors also observed that peripheral blood lymphocytes from ANUG patients exhibited reduced proliferation when stimulated with concanavalin-A mitogen.

MacCarthy and Claffey (1991) evaluated 13 patients (18 to 27 years of age) with a history of ANUG and non-surgical treatment. All 13 patients smoked and 6 had recurring episodes of ANUG. The sites affected by ANUG appeared to have a greater loss of attachment than non-ANUG control sites (2.2 mm and 0.8 mm, respectively). This study associates ANUG with attachment loss, but does not account for the severity of the lesions or the potential for attachment loss as a result of treatment.

PREDISPOSING FACTORS

Stress. This is probably the main factor contributing to the development of ANUG. Pindborg (1951) indicated that psychological stress accompanying transfers of enlisted men in military service may cause a sudden increase in the incidence of ANUG. In a subsequent military study, Goldhaber and Giddon (1964) reported that there was a higher incidence of ANUG in personnel just entering the army or going on leave (i.e., occasions they associated with higher levels of psychological stress). Shannon et al. (1969) observed that patients with ANUG had a higher level of 17 hydroxycorticosteroids (17-OHS) than controls. Maupin and Bell (1975) reported that ANUG patients had significantly higher levels of 17-OHS during the course of the disease than at post-disease evaluations.

Smoking. Pindborg (1951) noted that 98% of the ANUG patients studied were smokers. The effect of smoking appears to be more complex than a mere reflection of patient stress. Clarke et al. (1981) have demonstrated that intra-arterial infusion of epinephrine and nicotine in rabbits resulted in reduced gingival blood flow rates in spite of increased systemic perfusion pressure.

Pre-Existing Inflammation. Schluger (1943) claimed that a low standard of oral hygiene is the most important factor contributing to ANUG, considering it a disease of filth. Pindborg (1951) noted that 90% of ANUG cases begin as simple marginal gingivitis.

HIV-Positive Patients. Smith et al. (1987) reported a high incidence of ANUG in patients at risk of contracting acquired immune deficiency syndrome (AIDS). They also related that these male homosexuals had reduced numbers of the helper/inducer T cell subset (T4+) and an abnormal ratio of helper/inducer T cells to suppressor/cytotoxic T cells (T4:T8) ratio. This association between AIDS and ANUG could be of clinical and scientific interest to the dentist when treating ANUG patients.

TREATMENT

Schluger (1949) describes a simplified treatment of thorough, deep curettage followed by frequent rinses with diluted hydrogen peroxide, primarily as a lavage. Fitch et al. (1963) reported that immediate ultrasonic debridement proved to be highly effective in treating ANUG with rapid relief of symptoms. Goldhaber and Giddon (1964) augmented these local measures with antibiotics (principally penicillin) when treating advanced cases of the disease. Loesche et al. (1982) reported prompt resolution of clinical symptoms following metronidazole treatment. Elimination of the residual soft tissue craters via gingivoplasty is believed to be important to minimize recurrence of the disease (Schluger, 1949; Goldhaber and Giddon, 1964).

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Section 5. Periodontal Cysts

DEFINITIONS

Periodontal Cyst: A small cyst of the periodontal ligament found most often in the mandibular canine and premolar areas; associated with a vital tooth and postulated to originate from the rests of Malassez, the rests of the dental lamina, or a supernumerary tooth bud.

Gingival Cyst: Found within the gingiva, most commonly in the mandibular canine-premolar region. Believed to be derived from epithelial rests of the dental lamina.

HISTOLOGIC AND CLINICAL FEATURES OF THE GINGIVAL CYST

Moskow and Bloom (1983) investigated the embryogenesis of the gingival cyst (GC) in humans. They reported cystic degeneration of the dental lamina as early as 10 weeks in utero and rapid cystic proliferation and growth in 15 to 20 week embryos during the bell stage of tooth development. Distinct GCs were lined with a thin squamous epithelium and filled with keratin. Nxumalo and Shear (1992) described GCs of adults as having a cystic lining consisting of 1 to 3 epithelial cell layers resembling reduced enamel epithelium or a thicker nonkeratinized stratified squamous epithelium with pyknotic nuclei. Clinically, the GC of adults is a painless, well-circumscribed, fluctuant soft tissue swelling < 1 cm in diameter. It commonly occurs between the fifth and sixth decades in the mandibular (73%) canine-premolar area. Superficial bone resorption can occur (Shear, 1983). Nxumalo and Shear (1992) support the junctional epithelium as the tissue of origin because

of the frequent occurrence of lining epithelium resembling reduced enamel epithelium and the continuity of the cyst with the junctional epithelium. Similarities between the GC and the lateral periodontal cyst (LPC) suggest that they are both of developmental origin and both are derived from the reduced enamel epithelium.

HISTOLOGIC AND CLINICAL FEATURES OF THE LATERAL PERIODONTAL CYST

Cohen et al. (1984) reported light microscopic observations on 37 lateral periodontal cysts (LPCs). LPCs were more prevalent in the fifth to seventh decade with no sex or race predilection. They are generally asymptomatic, although there is some degree of buccal or lingual plate expansion. The majority occur in the mandibular canine-premolar region and are associated with vital teeth. Detection is by routine radiographic examination. Radiographically, they present as a well-defined, solitary radiolucency associated with the lateral aspect of a tooth root and are round or tear drop in shape. Treatment is by enucleation with no anticipated recurrence. Histologically, the LPC is a cavity supported by fibrous connective tissue with little surrounding inflammation. The epithelium often has areas of focal thickening (plaques) which may be interspersed with glycogen-rich clear-cells.

The LPC has a similar appearance to the GC of the adult and it is believed that the LPC and the GC of the adult develop from the dental lamina (Wysocki et al., 1980). The only difference between the lesions is that the LPC occurs within bone while the GC of the adult occurs within the gingiva. The term LPC should be reserved for those intraosseous cysts with this histologic description and not for all cysts located lateral to the root. Wysocki et al. (1980) reported on 39 examples of the LPC and 10 cases of the GC of the adult and similarly concluded that the dental lamina was the tissue of origin because of the association of both these cysts with the glycogen-rich clear-cell rests of the dental lamina.

LATERAL PERIODONTAL CYST AND PERIODONTAL DEFECTS

Filipowicz and Page (1982) suggested the possibility that proliferation of epithelial elements other than crevicular epithelium could be implicated in isolated periodontal defects. They outlined 4 possible explanations of isolated periodontal defects: 1) an LPC in the marginal periodontium could enlarge until it communicates with the crevicular epithelium; 2) crevicular epithelium could migrate apically until it communicates with an existing LPC; 3) apical migration of the crevicular epithelium could communicate with remnants of Hertwig's root sheath epithelium and initiate proliferation; or 4) pulpal injury causing tissue damage in accessory pulpal canals in the coronal portion of the root could communicate with the periodontium.

Spouge et al. (1986) examined the association between

the reduced enamel epithelium (REE) and the junctional epithelium (JE) and the rests of Malassez (ROM) in the pig. The ROM were present in the deeper portions of the periodontal ligament below the alveolar bony crest. The ROM formed spiral strands of epithelial cells running around the long axis of the tooth. Near the CEJ, the loops diverged away from the tooth surface and the strands became thinner and more scarce. However, the strands remained continuous and eventually joined with either the JE or the REE. The ROM have a proliferative potential and could form an area of entry for apical JE migration through the connective tissue.

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