

Periodontal Diseases of Children and Adolescents

Originating Group

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Epidemiologic studies indicate that gingivitis of varying severity is nearly universal in children and adolescents.¹⁻¹⁹ These studies also indicate that the prevalence of destructive forms of periodontal disease is lower in young individuals than in adults. Epidemiologic surveys in young individuals have been performed in many parts of the world and among individuals with a widely varied background. For the most part, these surveys indicated that loss of periodontal attachment and supporting bone is relatively uncommon in the young but that the incidence increases in adolescents aged 12 to 17 when compared to children aged 5 to 11.¹⁵⁻²² In general, in the United States, epidemiologic studies indicate that the prevalence of severe attachment loss on multiple teeth among children and young adults is approximately 0.2% to 0.5%.²³ Despite this low prevalence, children and adolescents should receive periodic periodontal evaluation as a component of routine dental visits.

On October 30-November 2, 1999, the American Academy of Periodontology assembled an International Workshop for a Classification of Periodontal Diseases and Conditions, which resulted in a new classification.²⁴ Periodontal diseases discussed here will reflect the new classification system. Clinically distinct periodontal infections that can affect young individuals include: 1) dental plaque-induced gingival diseases; 2) chronic periodontitis; 3) aggressive periodontitis; 4) periodontitis as a manifestation of systemic diseases; and 5) necrotizing periodontal diseases.

Dental plaque-induced gingival diseases

Gingivitis Associated with Dental Plaque Only and Gingival Diseases Modified by Systemic Factors Associated with the Endocrine System

Gingivitis characterized by the presence of gingival inflammation without detectable loss of bone or clinical attachment is common in children.^{1-19,25} Although the microbiology of this disease has not been completely characterized, increased subgingival levels of *Actinomyces* sp., *Capnocytophaga* sp., *Leptotrichia* sp., and *Selenomonas* sp. have been found in experimental gingivitis in

children when compared to gingivitis in adults. These species may therefore be important in its etiology and pathogenesis.^{26,27}

Normal and abnormal fluctuation in hormone levels, including changes in gonadotrophic hormone levels during the onset of puberty, can modify the gingival inflammatory response to dental plaque.^{28,29} Similarly, alterations in insulin levels in patients with diabetes can affect gingival health.^{28,29} In both situations, there is an increased inflammatory response to plaque.^{28,29} However, the gingival condition usually responds to thorough removal of bacterial deposits and improved daily oral hygiene.^{28,29}

Periodontitis

Aggressive Periodontitis, Chronic Periodontitis, and Periodontitis as a Manifestation of Systemic Diseases

Children and adolescents can have any of the several forms of periodontitis as described in the proceedings of the 1999 International Workshop for a Classification of Periodontal Diseases and Conditions (aggressive periodontitis, chronic periodontitis, and periodontitis as a manifestation of systemic diseases). However, chronic periodontitis is more common in adults, while aggressive periodontitis may be more common in children and adolescents.²⁴

The primary features of aggressive periodontitis include a history of rapid attachment and bone loss with familial aggregation. Secondary features include phagocyte abnormalities and a hyperresponsive macrophage phenotype.²⁴ Aggressive periodontitis can be localized or generalized. Localized aggressive periodontitis (LAgP) patients have interproximal attachment loss on at least two permanent first molars and incisors, with attachment loss on no more than two teeth other than first molars and incisors. Generalized aggressive periodontitis (GAgP) patients exhibit generalized interproximal attachment loss including at least three teeth that are not first molars and incisors. In young individuals, the onset of these diseases is often circumpubertal. Some investigators have found that the localized form appears to be self-limiting,³⁰ while others suggest that it is not.²⁰ Some patients initially diagnosed as having

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LAGP were found to have GAgP or to be periodontally healthy at a 6-year follow-up exam.^{31,32}

LAGP occurs in children and adolescents without clinical evidence of systemic disease and is characterized by the severe loss of alveolar bone around permanent teeth.³¹ Frequently, the disease is localized to the permanent first molars and incisors. However, some retrospective data obtained from LAGP patients suggest that bone loss around the primary teeth can be an early finding in the disease.³³ Linkage studies of the Brandywine population (a segregated group of people in Maryland that represents a relatively closed gene pool) have found a gene conferring increased risk for LAGP on chromosome 4.³⁴ Subsequent linkage studies of African American and Caucasian families did not confirm linkage to this locus, suggesting that there may be genetic and/or etiologic heterogeneity for aggressive periodontitis.³⁵⁻³⁷ Reported estimates of the prevalence of LAGP in geographically diverse adolescent populations range from 0.1% to 15%.^{23,33-35,37-42} Most reports suggest a low prevalence (0.2%), which is markedly greater in African American populations (2.5%).

Many reports suggest that patients with LAGP generally form very little supragingival dental plaque or calculus.^{31,43} In contrast, other investigators find plaque and calculus at levels similar to other periodontal diseases.^{44,45} Bacteria of probable etiologic importance include highly virulent strains of *Actinobacillus actinomycetemcomitans* in combination with Bacteroides-like species.⁴⁶⁻⁴⁹ In some populations, *Eubacterium* sp. have been associated with the presence of LAGP.^{50,51} To date, however, no single species is found in all cases of LAGP.⁵²

A variety of functional defects have been reported in neutrophils from patients with LAGP.⁵³⁻⁵⁵ These include anomalies of chemotaxis,⁵⁶⁻⁵⁸ phagocytosis,^{59,60} bactericidal activity,⁶¹ superoxide production,⁶²⁻⁶⁶ FcγIIIb (CD16) expression,⁶⁷ leukotriene B₄ generation,^{68,69} and Ca²⁺-channel and second messenger activation.⁷⁰⁻⁷⁵ The defect in chemotaxis is thought to be an intrinsic defect by some investigators⁵⁶⁻⁵⁸ and an induced defect by others.⁷⁶ The influence of these functional defects on the susceptibility of individuals to LAGP is unknown, but it is possible that they play a role in the clinical course of disease in some patients. Indeed, in some cases exhibiting phagocyte abnormalities, neutrophil defects may still be present after treatment.⁷⁷ Molecular markers of LAGP can include an abnormally low number of chemoattractant receptors⁷⁸⁻⁸¹ and an abnormally low amount of another cell surface glycoprotein designated GP-110.^{82,83} Adherence receptors on neutrophils and monocytes, such as LFA-1 and Mac-1, are normal in LAGP patients.^{82,83}

GAgP, often considered to be a disease of adolescents and young adults, can begin at any age and often affects the entire dentition.^{84,85} Individuals with GAgP exhibit marked periodontal inflammation and have heavy accumulations of plaque and calculus.⁸⁴ In the United States, the reported prevalence of GAgP in adolescents (14 to 17 years of age) is 0.13%.²³ Subgingival sites from affected teeth harbor high percentages of non-motile, facultatively anaerobic, Gram-negative rods including *Porphyromonas gingivalis*.^{86,87} In one report, the levels of *P. gingivalis* and *Treponema denticola* were significantly higher in

GAgP and LAGP patients compared to matched controls, with GAgP patients having the highest levels.⁸⁸ Neutrophils from patients with GAgP frequently exhibit suppressed chemotaxis as observed in LAGP^{77,87} with a concomitant reduction in GP-110. This suggests a relationship between the two variants of aggressive periodontitis.^{82,83}

Alterations in immunologic factors such as immunoglobulins are known to be present in aggressive periodontitis. Immunoglobulins appear to be influenced by both genetic and environmental factors and have important protective disease-limiting effects in aggressive periodontitis patients.⁸⁹⁻⁹³ Human IgG antibody molecules (immunoglobulin G) are categorized into four subclasses designated as IgG1-4. Most of the antibody reactive with *A. actinomycetemcomitans* is specific for high molecular weight lipopolysaccharide and is of the IgG2 subclass. This antibody response appears to be protective, as early-onset periodontitis patients having high concentrations of antibody reactive with *A. actinomycetemcomitans* lipopolysaccharide have significantly less attachment loss (a measure of disease severity) than patients who lack this antibody.^{89,90}

Overall levels of IgG2 in serum are under genetic control.⁹¹ These levels have also been shown to be affected by periodontal diagnosis (LAGP patients have very high levels), race (African Americans have higher levels than Caucasians), and smoking (smokers have lower levels of IgG2, with notable exceptions in some patient groups).^{91,92,94,95} These factors also influence specific antibody responses to *A. actinomycetemcomitans*.^{91-93,95} Thus, the protective antibody response afforded by IgG2, as well as the clinical manifestations of aggressive periodontitis, is modified by patients' genetic background as well as environmental factors such as smoking and bacterial infection.^{89,91-93,95,96}

Successful treatment of aggressive periodontitis depends on early diagnosis, directing therapy against the infecting microorganisms and providing an environment for healing that is free of infection.⁹⁷ While there is some disagreement among individual studies regarding treatment of LAGP, most authors recommend a combination of surgical or non-surgical root debridement in conjunction with antimicrobial (antibiotic) therapy.^{47,98} These findings are supported by other work in which meticulous and repeated mechanical therapy with antibiotics proved to be sufficient to arrest most cases of LAGP.⁹⁹ However, surgical treatment may be effective in eliminating *A. actinomycetemcomitans* without the use of antibiotics.¹⁰⁰ In a study of 25 deep periodontal lesions (probing depths 5 to 11 mm) in young LAGP patients, scaling and root planing alone were ineffective for the elimination of *A. actinomycetemcomitans*, while surgical therapy was effective.¹⁰⁰ It is not known, however, if *A. actinomycetemcomitans* is the only organism involved in disease pathogenesis.

The majority of reports suggest that the use of antibiotics is usually beneficial in the treatment of LAGP. Two reports described using antibiotics exclusively.^{97,101} In both reports, LAGP patients attained significant clinical attachment gain when assessed after 12 months with tetracycline therapy alone. Most reports in the past 10 years, however, have recommended combination therapy using antibiotics and surgical or

non-surgical root debridement as the optimal treatment for LAgP.^{98,102-116} The most successful antibiotics reported are the tetracyclines, sometimes prescribed sequentially with metronidazole.^{103,117,118} Metronidazole in combination with amoxicillin has also been utilized, especially where tetracycline-resistant *A. actinomycetemcomitans* are present.¹¹¹ A single randomized control study in which oral penicillin was used reported that therapy was successful with or without the antibiotic.¹¹⁹

While the use of antibiotics in conjunction with surgical or non-surgical root debridement appears to be quite effective for the treatment of LAgP, GAgP does not always respond well to conventional mechanical therapy or to antibiotics commonly used to treat periodontitis.^{30,118,120} Alternative antibiotics may be required, based upon the character of the pathogenic flora. In GAgP patients who have failed to respond to standard periodontal therapy, laboratory tests of plaque samples may identify periodontal pathogens that are resistant to antibiotics typically used to treat periodontitis.¹⁰³ It has been suggested that follow-up tests after additional antibiotic or other therapy is provided may be helpful in confirming elimination of targeted pathogenic organisms.¹⁰³

Chronic periodontitis is most prevalent in adults, but can occur in children and adolescents. It can be localized (less than 30% of the dentition affected) or generalized (greater than 30% of the dentition affected) and is characterized by a slow to moderate rate of progression that may include periods of rapid destruction. Furthermore, the severity of disease can be mild (1 to 2 mm clinical attachment loss), moderate (3 to 4 mm clinical attachment loss), or severe (≥ 5 mm clinical attachment loss). Children and young adults with this form of disease were previously studied along with patients having LAgP and GAgP. Therefore, published data are lacking for this group. In patients with one of several systemic diseases that predispose to highly destructive disease of the primary teeth, the diagnosis is periodontitis as a manifestation of systemic disease. As with adults, periodontitis associated with systemic diseases occurs in children and adolescents. Such diseases include Papillon-Lefèvre syndrome,¹²¹⁻¹²⁵ cyclic neutropenia,¹²⁶⁻¹³⁰ agranulocytosis,^{131,132} Down syndrome,¹³³⁻¹³⁵ hypophosphatasia,¹³⁶ and leukocyte adherence deficiency.^{137,138} It is probable that defects in neutrophil and immune cell function associated with these diseases play an important role in increased susceptibility to periodontitis and other infections. In Down's syndrome, for example, the amount of periodontal destruction has been shown to be positively correlated with the severity of the neutrophil chemotaxis defect.¹³⁵ In some cases, specific genes have been associated with these diseases. Examples include the cathepsin C gene and Papillon-Lefèvre syndrome¹³⁹⁻¹⁴¹ and the tissue non-specific alkaline phosphatase gene and hypophosphatasia.¹³⁶

The consensus report of the 1999 Workshop specifically excluded diabetes-associated periodontitis as a specific form of periodontitis associated with systemic disease. Participants concluded that diabetes is a significant modifier of all forms of periodontitis. In a survey of 263 type 1 diabetics, 11 to 18 years of age, 10% were found to have overt periodontitis often

localized to first molars and incisors, although periodontitis was also found in a generalized pattern.¹⁴² Affected subgingival sites harbored *A. actinomycetemcomitans* and *Capnocytophaga* sp.¹⁴³

Periodontitis as a manifestation of systemic disease in children is a rare disease that often begins between the time of eruption of the primary teeth up to the age of 4 or 5.^{144,145} The disease occurs in localized and generalized forms. In the localized form, affected sites exhibit rapid bone loss and minimal gingival inflammation.¹⁴⁴ In the generalized form, there is rapid bone loss around nearly all teeth and marked gingival inflammation. Neutrophils from some children with a clinical diagnosis of periodontitis as a manifestation of systemic disease have abnormalities in a cell surface glycoprotein (LFA-1, leukocyte functional antigen-1, also known as CD11, and Mac-1). The neutrophils in these patients having LAD (leukocyte adhesion deficiency) are likely to have a decreased ability to move from the circulation to sites of inflammation and infection.¹³⁷ Affected sites harbor elevated percentages of putative periodontal pathogens such as *A. actinomycetemcomitans*, *Prevotella intermedia*, *Eikenella corrodens*, and *Capnocytophaga sputigena*.^{146,147}

Treatment of periodontitis as a manifestation of systemic disease in children is similar to the treatment of localized and generalized aggressive periodontitis in the permanent dentition and has been reported to include surgical or non-surgical mechanical debridement and antimicrobial therapy.^{124,127-130,132,134,142,144} Localized lesions have been treated successfully with this approach,^{144,145} but the degree of predictable success in managing generalized periodontitis is low when systemic diseases are contributing factors.^{144,145} In many cases, the affected teeth had to be extracted.^{138,144,145}

Necrotizing periodontal diseases

Necrotizing periodontal diseases (NPD) occur with varying but low frequency (less than 1%) in North American and European children. It is seen with greater frequency (2% to 5%) in certain populations of children and adolescents from developing areas of Africa, Asia, and South America.¹⁴⁸⁻¹⁵⁰ The two most significant findings used in the diagnosis of NPD are the presence of interproximal necrosis and ulceration and the rapid onset of gingival pain. Patients with NPD can often be febrile. Necrotizing ulcerative gingivitis/periodontitis sites harbor high levels of spirochetes and *P. intermedia*,¹⁵¹ and invasion of the tissues by spirochetes has been shown to occur.¹⁵² Factors that predispose children to NPD include viral infections (including HIV), malnutrition, emotional stress, lack of sleep, and a variety of systemic diseases.^{148-150,153} Treatment involves mechanical debridement, oral hygiene instruction, and careful follow-up.¹⁵⁴⁻¹⁵⁶ Debridement with ultrasonics has been shown to be particularly effective and results in a rapid decrease in symptoms.¹⁵⁷ If the patient is febrile, antibiotics may be an important adjunct to therapy. Metronidazole and penicillin have been suggested as drugs of choice.^{151,158}

Summary

Children and adolescents are subject to several periodontal diseases. Although there is a much lower prevalence of destructive periodontal diseases in children than in adults, children can develop severe forms of periodontitis.²³ In some cases, this destructive disease is a manifestation of a known underlying systemic disease. In other young patients, the underlying cause for increased susceptibility and early onset of disease is unknown. These diseases are often familial, suggesting a genetic predisposition for aggressive disease. Current modalities for managing periodontal diseases of children and adolescents may include antibiotic therapy in combination with non-surgical and/or surgical therapy. Since early diagnosis ensures the greatest chance for successful treatment,⁹⁷ it is important that children receive a periodontal examination as part of their routine dental visits.

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References

1. Marshall-Day CD, Shourie KL. A roentgenographic survey of periodontal disease in India. *J Am Dent Assoc* 1949; 39:572-88.
2. Ramfjord SP. The periodontal status of boys 11 to 17 years old in Bombay, India. *J Periodontol* 1961;32: 237-48.
3. Basu MK, Dutta AN. Report of "Prevalence of periodontal disease in the adult population in Calcutta," by Ramfjord's technique. *J All India Dent Assoc* 1963; 35:187-201.
4. McHugh WD, McEwen JD, Hitchin AD. Dental disease and related factors in 13-year-old children in Dundee. *Br Dent J* 1964;117:246-53.
5. Sheiham A. The prevalence and severity of periodontal disease in Surrey school children. *Dent Pract Dent Rec* 1969;19:232-8.
6. Russell AL. The prevalence of periodontal disease in different populations during the circumpubertal period. *J Periodontol* 1971;42:508-12.
7. Kelly JE, Sanchez MJ. Periodontal disease and oral hygiene among children. United States. *Vital Health Stat* 1 1972;11(117):1-28.
8. Lennon MA, Davies RM. Prevalence and distribution of alveolar bone loss in a population of 15-year-old schoolchildren. *J Clin Periodontol* 1974;1:175-182.
9. Hull PS, Hilliam DG, Beal JF. A radiographic study of the prevalence of chronic periodontitis in 14-year old English schoolchildren. *J Clin Periodontol* 1975;2:203-10.
10. Davies PHJ, Downer MC, Lennon MA. Periodontal bone loss in English secondary schoolchildren. A longitudinal radiological study. *J Clin Periodontol* 1978;5:278-84.
11. Blankenstein R, Murray JJ, Lind OP. Prevalence of chronic periodontitis in 13-15-year-old children. A radiographic study. *J Clin Periodontol* 1978;5:285-92.
12. Latcham NL, Powell RN, Jago JD, Seymour GJ, Aitken JF. A radiographic study of chronic periodontitis in 15-year-old Queensland children. *J Clin Periodontol* 1983;10:37-45.
13. Gjermo P, Bellini HT, Santos VP, Martens JG, Ferracyoli JR. Prevalence of bone loss in a group of Brazilian teenagers assessed in bitewing radiographs. *J Clin Periodontol* 1984;11:104-13.
14. Hansen BF, Gjermo P, Bergwitz-Larsen KR. Periodontal bone loss in 15-year-old Norwegians. *J Clin Periodontol* 1984;11:125-31.
15. Wolfe MD, Carlos JP. Periodontal disease in adolescents: Epidemiologic findings in Navajo Indians. *Community Dent Oral Epidemiol* 1987;15:33-40.
16. Wei SJY, Yang S, Barmes DE. Needs and implementation of preventive dentistry in China. *Community Dent Oral Epidemiol* 1986;14:19-23.
17. Durward CS, Wright FA. The dental health of Indo-Chinese and Australian-born adolescents. *Austr Dent J* 1989;34(3):233-9.
18. Miyazaki H, Hanada N, Andoh MI, et al. Periodontal disease prevalence in different age groups in Japan as assessed according to the CPITN. *Community Dent Oral Epidemiol* 1989;17:71-4.
19. Pilot T, Barmes DE, Leclercq MH, McCombie BJ, Sardo IJ. Periodontal conditions in adolescents, 15-19 years of age: An overview of CPITN data in the WHO Global Oral Data Bank. *Community Dent Oral Epidemiol* 1987;15: 336-8.
20. Brown LJ, Albandar JM, Brunelle JA, Loe H. Early onset periodontitis: Progression of attachment loss during 6 years. *J Periodontol* 1996;67:968-75.
21. Oliver RC, Brown LJ, Loe H. Periodontal diseases in the United States population. *J Periodontol* 1998;69:269-78.
22. Perry DA, Newman MG. Occurrence of periodontitis in an urban adolescent population. *J Periodontol* 1990;61:185-8.
23. Loe H, Brown LJ. Early onset periodontitis in the United States of America. *J Periodontol* 1991;62:608-16.
24. Armitage G. Development of a classification system for periodontal diseases and conditions. *Ann Periodontol* 1999;4:1-6.
25. Arnlaugsson S, Magnusson TE. Prevalence of gingivitis in 6-year-olds in Reykjavik, Iceland. *Acta Odontol Scand* 1996;54:247-50.
26. Moore W, Holdeman L, Smibert R, et al. Bacteriology of experimental gingivitis in children. *Infect Immun* 1984; 46:1-6.
27. Slots J, Moenbo D, Langebaek J, Frandsen A. Microbiota of gingivitis in man. *Scand J Dent* 1978;86:174-81.
28. Nakagawa S, Fujii H, Machida Y, Okuda K. A longitudinal study from prepuberty to puberty of gingivitis. Correlation between the occurrence of *Prevotella intermedia* and sex hormones. *J Clin Periodontol* 1994;21:658-65.

29. De Pommereau V, Dargent-Par C, Robert JJ, Brion M. Periodontal status in insulin-dependent diabetic adolescents. *J Clin Periodontol* 1992;19:628-32.
30. Gunsolley JC, Califano JV, Koertge TE, Burmeister JA, Cooper LC, Schenkein HA. Longitudinal assessment of early onset periodontitis. *J Periodontol* 1995;66:321-8.
31. Baer PN. The case for periodontosis as a clinical entity. *J Periodontol* 1971;42:516-20.
32. Albandar JM, Brown LJ, Genco RJ, Loe H. Clinical classification of periodontitis in adolescents and young adults. *J Periodontol* 1997;68:545-55.
33. Sjödin B, Matsson L, Unell L, Egelberg J. Marginal bone loss in the primary dentition of patients with juvenile periodontitis. *J Clin Periodontol* 1993;20:32-6.
34. Boughman JA, Halloran SL, Roulston D, et al. An autosomal dominant form of juvenile periodontitis: Its localization to chromosome 4 and linkage to dentinogenesis imperfecta and Gc. *J Craniofac Genet Dev Biol* 1986;6:341-50.
35. Marazita ML, Burmeister JA, Gunsolley JC, Koertge TE, Lake K, Schenkein HA. Evidence for autosomal dominant inheritance and race-specific heterogeneity in early onset periodontitis. *J Periodontol* 1994;65:623-30.
36. Hart TC, Kornman KS. Genetic factors in the pathogenesis of periodontitis. *Periodontol 2000* 1997;14:202-15.
37. Hart TC, Marazita ML, McCanna KM, Schenkein HA, Diehl SR. Reevaluation of the chromosome 4q candidate region for early onset periodontitis. *Hum Genet* 1993;91:416-22.
38. Saxén L. Juvenile periodontitis. *J Clin Periodontol* 1980;7:1-19.
39. Saxén L. Prevalence of juvenile periodontitis in Finland. *J Clin Periodontol* 1980;7:177-86.
40. Kronauer E, Borsa G, Lang NP. Prevalence of incipient juvenile periodontitis at age 16 years in Switzerland. *J Clin Periodontol* 1986;13:103-8.
41. Harley AF, Floyd PD. Prevalence of juvenile periodontitis in schoolchildren in Lagos, Nigeria. *Community Dent Oral Epidemiol* 1988;16:299-301.
42. Neely AL. Prevalence of juvenile periodontitis in a circum-pubertal population. *J Clin Periodontol* 1992;19:367-72.
43. Butler J. A familial pattern of juvenile periodontitis (periodontosis) *J Periodontol* 1969;40:115-8.
44. Albandar JM, Brown LJ, Brunelle JA, Loe H. Gingival state and dental calculus in early-onset periodontitis. *J Periodontol* 1996;67:953-9.
45. Burmeister JA, Best AM, Palcanis KG, Caine FA, Ranney RR. Localized juvenile periodontitis and generalized severe periodontitis: Clinical findings. *J Clin Periodontol* 1984;11:181-92.
46. Haraszthy V, Hariharan G, Tinoco E, et al. Evidence for the role of highly leukotoxic *Actinobacillus actinomycetemcomitans* in the pathogenesis of localized and other forms of early-onset periodontitis *J Periodontol* 2000;71:912-22.
47. Kornman KS, Robertson PB. Clinical and microbiological evaluation of therapy for juvenile periodontitis. *J Periodontol* 1985;56:443-6.
48. Genco RJ, Zambon JJ, Christersson LA. The origin of periodontal infections. *Adv Dent Res* 1988;2:245-59.
49. Zambon JJ. *Actinobacillus actinomycetemcomitans* in human periodontal disease. *J Clin Periodontol* 1985;12:1-20.
50. Moore WEC, Holdeman LV, Cato EP, et al. Comparative bacteriology of juvenile periodontitis. *Infect Immun* 1985;48:507-19.
51. Han N, Xiao X, Zhang L, et al. Bacteriological study of juvenile periodontitis in China. *J Periodont Res* 1991;26:409-14.
52. Moore W, Moore L. The bacteria of periodontal diseases. *Periodontol 2000* 1994;5:66-77.
53. Daniel MA, Van Dyke TE. Alterations in phagocyte function and periodontal infection. *J Periodontol* 1996; 67:1070-5.
54. Dennison DK, Van Dyke TE. The acute inflammatory response and the role of phagocytic cells in periodontal health and disease. *Periodontol 2000* 1997;14:54-78.
55. Van Dyke TE, Lester MA, Shapira L. The role of host response in periodontal disease progression: Implications for future treatment strategies. *J Periodontol* 1993;64:792-806.
56. Genco RJ, Van Dyke TE, Levine MJ, Nelson RD, Wilson ME. Molecular factors influencing neutrophil defects in periodontal disease. *J Dent Res* 1986;65:1379-91.
57. Van Dyke TE, Levine MJ, Genco RJ. Neutrophil function and oral disease. *J Oral Pathol* 1985;14:95-120.
58. Van Dyke TE, Hoop GA. Neutrophil function and oral disease. *Crit Rev Oral Biol Med* 1990;1:117-33.
59. Van Dyke TE, Zinney W, Winkel K, Taufig A, Offenbacher S, Arnold RR. Neutrophil function in localized juvenile periodontitis: Phagocytosis, superoxide production and specific granule release. *J Periodontol* 1986;57:703-8.
60. Cogen RB, Roseman JM, Al-Joburi W, et al. Host factors in juvenile periodontitis *J Dent Res* 1986;65:394-9.
61. Kalmar JR, Arnold RR, Van Dyke TE. Direct interaction of *Actinobacillus actinomycetemcomitans* with normal and defective (LJP) neutrophils. *J Periodont Res* 1987;22:179-81.
62. Åsman B, Bergström K, Wijkander P, Lockowandt B. Influence of plasma components on luminol-enhanced chemiluminescence from peripheral granulocytes in juvenile periodontitis. *J Clin Periodontol* 1986;13:850-5.
63. Åsman B, Bergström K, Wijkander P, Lockowandt B. Peripheral PMN cell activity in relation to treatment of juvenile periodontitis. *Scand J Dent Res* 1988;96:418-20.
64. Zafropoulos GG, Flores-de-Jacoby L, Czerch W, Kolb G, Markitzu A, Havemann K. Neutrophil function in patients with localized juvenile periodontitis and rapidly progressive periodontitis. *J Biol Buccale* 1988;16:151-6.
65. Zafropoulos GG, Flores-de-Jacoby L, Plate VM, Eckle I, Kolb G. Polymorphonuclear neutrophil chemiluminescence in periodontal disease. *J Clin Periodontol* 1991;18:634-9.
66. Shapira L, Borinski R, Sela MN, Soskolne A. Superoxide formation and chemiluminescence of peripheral polymorphonuclear leukocytes in rapidly progressive periodontitis patients. *J Clin Periodontol* 1991;18:44-8.

67. Nemoto E, Nakamura M, Shoji S, Horiuchi H. Circulating promyelocytes and low levels of CD16 expression on polymorphonuclear leukocytes accompany early onset periodontitis. *Infect Immun* 1997;65:3906-12.
68. Offenbacher S, Scott SS, Odle BM, Wilson-Burrows C, Van Dyke TE. Depressed leukotriene B4 chemotactic response of neutrophils from localized juvenile periodontitis patients. *J Periodontol* 1987;58:602-6.
69. Van Dyke TE, Offenbacher S, Kalmar J, Arnold RR. Neutrophil defects and host parasite interactions in the pathogenesis of localized juvenile periodontitis. *Adv Dent Res* 1988; 2:354-8.
70. Agarwal S, Reynolds MA, Duckett LD, Suzuki JB. Altered free cytosolic calcium changes and neutrophil chemotaxis in patients with juvenile periodontitis. *Adv Dent Res* 1989;24:149-54.
71. Daniel MA, McDonald G, Offenbacher S, Van Dyke TE. Defective chemotaxis and calcium response in localized juvenile periodontitis neutrophils. *J Periodontol* 1993;64: 617-21.
72. Hurttia HM, Pelto LM, Leino L. Evidence of an association between functional abnormalities and defective diacylglycerol kinase activity in peripheral blood neutrophils from patients with localized juvenile periodontitis. *J Periodont Res* 1997;32:401-7.
73. Kurihara H, Murayama Y, Warbington ML, Champagne C, Van Dyke TE. Depressed protein kinase C (PKC) activity of neutrophils in localized juvenile periodontitis. *Infect Immun* 1993;61:3137-42.
74. Leino L, Hurrta H, Peltonen E. Diacylglycerol in peripheral blood neutrophils from patients with localized juvenile periodontitis. *J Periodont Res* 1994;29:334-8.
75. Tyagi SR, Uhlinger DJ, Lambeth JD, Champagne C, Van Dyke TE. Altered diacylglycerol level and metabolism in localized juvenile periodontitis neutrophils. *Infect Immun* 1992;60:2481-7.
76. Agarwal S, Suzuki J. Altered neutrophil function in localized juvenile periodontitis: Intrinsic cellular defect or effect of immune mediators? *J Periodont Res* 1991; 26:276-8.
77. Van Dyke TE, Levine MJ, Genco RJ. Periodontal diseases and neutrophil abnormalities. In: Genco RJ, Mergenhagen SE, eds. *Host-Parasite Interactions in Periodontal Diseases*. Washington, DC: American Society for Microbiology; 1982:235-45.
78. Van Dyke T. The role of neutrophils in host defense to periodontal infections. In: Hamada S, Holt S, McGhee J, eds. *Periodontal Disease: Pathogens and Host Immune Responses*. Tokyo: Quintessence Publishing Co; 1991:251-61.
79. Van Dyke T, Levine M, Tabak L, Genco R. Reduced chemotactic peptide binding in juvenile periodontitis: A model for neutrophil function. *Biochem Biophys Res Commun* 1981;100:1278-84.
80. Van Dyke T, Levine M, Tabak L, Genco R. Juvenile periodontitis as a model for neutrophil function: Reduced binding of complement chemotactic fragment, C5a. *J Dent Res* 1983;62:870-2.
81. Van Dyke T, Schweinebraten M, Cianciola U, Offenbacher S, Genco R. Neutrophil chemotaxis in families with localized juvenile periodontitis. *J Periodont Res* 1985;20:503-14.
82. Van Dyke TE, Wilson-Burrows C, Offenbacher S, Hensen P. Association of an abnormality of neutrophil chemotaxis in human periodontal disease with a cell surface protein. *Infect Immun* 1987;55:2262-7.
83. Van Dyke TE, Warbington M, Gardner M, Offenbacher S. Neutrophil surface protein markers as indicators of defective chemotaxis in LJP. *J Periodontol* 1990;61:180-4.
84. Page RC, Altman LC, Ebersole JL, et al. Rapidly progressive periodontitis: A distinct clinical condition. *J Periodontol* 1983;54:197-209.
85. Spektor MD, Vandesteen GE, Page RC. Clinical studies of one family manifesting rapidly progressive, juvenile and prepubertal periodontitis. *J Periodontol* 1985;56:93-101.
86. Slots J. Importance of black-pigmented *Bacteroides* in human periodontal disease. In: Genco RJ, Mergenhagen SE, eds. *Host-Parasite Interactions in Periodontal Diseases*. Washington, DC: American Society for Microbiology; 1982:27-45.
87. Wilson ME, Zambon JJ, Suzuki JB, Genco RJ. Generalized juvenile periodontitis, defective neutrophil chemotaxis and *Bacteroides gingivalis* in a 13-year-old female. *J Periodontol* 1985;56:457-63.
88. Albandar JM, Brown LJ, Le H. Putative periodontal pathogens in subgingival plaque of young adults with and without early-onset periodontitis. *J Periodontol* 1997;68: 973-81.
89. Califano JV, Gunsolley JC, Nakashima K, Schenkein HA, Wilson ME, Tew JG. Influence of anti-*Actinobacillus actinomycetemcomitans* Y4 (serotype b) lipopolysaccharide on severity of generalized early-onset periodontitis. *Infect Immun* 1996;64:3908-10.
90. Califano JV, Pace BE, Gunsolley JC, Schenkein HA, Lally ET, Tew JG. Antibody reactive with *Actinobacillus actinomycetemcomitans* leukotoxin in early-onset periodontitis patients. *Oral Microbiol Immunol* 1997;12:20-6.
91. Marazita ML, Lu H, Cooper ME, et al. Genetic segregation analyses of serum IgG2 levels. *Am J Hum Genet* 1996; 58:1042-9.
92. Quinn SM, Zhang JB, Gunsolley JC, Schenkein JG, Schenkein HA, Tew JG. Influence of smoking and race on immunoglobulin G subclass concentrations in early-onset periodontitis patients. *Infect Immun* 1996;64:2500-5.
93. Tangada SD, Califano JV, Nakashima K, et al. The effect of smoking on serum IgG2 reactive with *Actinobacillus actinomycetemcomitans* in early-onset periodontitis patients. *J Periodontol* 1997;68:842-50.
94. Lu H, Wang M, Gunsolley JC, Schenkein HA, Tew JG. Serum immunoglobulin G subclass concentrations in periodontally healthy and diseased individuals. *Infect Immun* 1994;62:1677-82.
95. Quinn SM, Zhang JB, Gunsolley JC, Schenkein HA, Tew JG. The influence of smoking and race on adult periodontitis and serum IgG2 levels. *J Periodontol* 1998;69:171-7.

96. Schenkein HA, Gunsolley JC, Koertge TE, Schenkein JG, Tew JG. Smoking and its effects on early-onset periodontitis. *J Am Dent Assoc* 1995;126:1107-13.
97. Novak MJ, Stamatelakys C, Adair SM. Resolution of early lesions of juvenile periodontitis with tetracycline therapy alone: Long-term observations of 4 cases. *J Periodontol* 1991;62:628-33. Erratum 1992;63:148.
98. Mandell RL, Socranksy SS. Microbiological and clinical effects of surgery plus doxycycline on juvenile periodontitis. *J Periodontol* 1988;59:373-9.
99. Gjermo P. Chemotherapy in juvenile periodontitis. *J Clin Periodontol* 1986;13:982-6.
100. Christersson LA, Slots J, Rosling BG, Genco RJ. Microbiological and clinical effects of surgical treatment of localized juvenile periodontitis. *J Clin Periodontol* 1985;12:465-76.
101. Christersson LA, Zambon JJ. Suppression of *Actinobacillus actinomycetemcomitans* in localized juvenile periodontitis with systemic tetracycline. *J Clin Periodontol* 1993;20:395-401.
102. Seymour RA, Heasman PA. Pharmacological control of periodontal disease. II. Antimicrobial agents. *J Dent* 1995;23:5-14.
103. van Winkelhoff AJ, Rams TE, Slots J. Systemic antibiotic therapy in periodontics. *Periodontol 2000* 1996;10:45-78.
104. Palmer RM, Watts TL, Wilson RE. A double-blind trial of tetracycline in the management of early onset periodontitis. *J Clin Periodontol* 1996;23:670-4.
105. Saxén L, Asikainen S. Metronidazole in the treatment of localized juvenile periodontitis. *J Clin Periodontol* 1993;20:166-71.
106. Mandell RL, Tripodi LS, Savitt E, Goodson JM, Socranksy SS. The effect of treatment on *Actinobacillus actinomycetemcomitans* in localized juvenile periodontitis. *J Periodontol* 1986;57:94-9.
107. Zambon JJ, Christersson LA, Genco RJ. Diagnosis and treatment of localized juvenile periodontitis. *J Am Dent Assoc* 1986;113:295-9.
108. Sterrett JD. Atypical localized juvenile periodontitis. A case report and review of current treatment considerations. *J Periodontol* 1986;57:486-91.
109. Levine RA. Localized juvenile periodontitis: Historical background and therapy. *Compendium Continuing Educ Dent* 1986;7:552-6.
110. Krill DB, Fry HR. Treatment of localized juvenile periodontitis (periodontosis). A review. *J Periodontol* 1987;58:1-8.
111. van Winkelhoff AJ, Rodenburg JP, Goene RJ, Abbas F, Winkel EG, de Graaff J. Metronidazole plus amoxicillin in the treatment of *Actinobacillus actinomycetemcomitans*-associated periodontitis. *J Clin Periodontol* 1989;16:128-31.
112. Saxon L, Asikainen SKA, Kaneroo A, Kari K, Jousimies-Somer H. The long-term efficacy of systemic doxycycline medication in the treatment of localized juvenile periodontitis. *Arch Oral Biol* 1990;35(suppl):227S-9S.
113. Muller HP, Lange DE, Muller RF. A 2-year study of adjunctive minocycline-HCl in *Actinobacillus actinomycetemcomitans*-associated periodontitis. *J Periodontol* 1993;64:509-19.
114. Donly KJ, Ashkenazi M. Juvenile periodontitis: A review of pathogenesis, diagnosis, and treatment. *J Clin Pediatr Dent* 1992;16:73-8.
115. Gordon JM, Walker CB. Current status of systemic antibiotic usage in destructive periodontal disease. *J Periodontol* 1993;64:760-71.
116. Wisner-Lynch A, Giannobile WV. Current concepts in juvenile periodontitis. *Curr Opin Periodontol* 1993;28-42.
117. Aitken S, Birek P, Kulkarni G, Lee W, McCulloch C. Serial doxycycline and metronidazole in prevention of recurrent periodontitis in high risk patients. *J Periodontol* 1992;63:87-92.
118. van Winkelhoff AJ, de Graaff J. Microbiology in the management of destructive periodontal disease. *J Clin Periodontol* 1991;18:406-10.
119. Kunihira DM, Caine FA, Palcanis KG, Best AM, Ranney RR. A clinical trial of phenoxymethyl penicillin for adjunctive treatment of juvenile periodontitis. *J Periodontol* 1985;56:352-8.
120. Asikainen S, Jousimies-Somer H, Kanervo A, Saxén L. The immediate efficacy of adjunctive doxycycline treatment of localized juvenile periodontitis. *Arch Oral Biol* 1990;35(suppl):231S-4S.
121. Hart TC, Stabholz A, Meyle J, et al. Genetic studies of syndromes with severe periodontitis and palmoplantar hyperkeratosis. *J Periodont Res* 1997;32:81-9.
122. Gorlin RJ, Sedano H, Anderson V. The syndrome palmar-plantar hyperkeratosis and premature periodontal destruction of teeth. A clinical and genetic analysis of the Papillon-Lefèvre syndrome. *J Pediatr* 1964;65:895-908.
123. Schroeder HE, Segar RA, Keller HU, Rateitschak-Plüss EM. Behavior of neutrophilic granulocytes in a case of Papillon-Lefèvre syndrome. *J Clin Periodontol* 1983;10:618-35.
124. Rateitschak-Plüss EM, Schroeder HE. History of periodontitis in a child with Papillon-Lefèvre syndrome. A case report. *J Periodontol* 1984;55:35-46.
125. Tinanoff N, Tanzer JM, Kornman KS, Maderazo EG. Treatment of the periodontal component of Papillon-Lefèvre syndrome. *J Clin Periodontol* 1986;13:6-10.
126. Andrews RG, Benjamin S, Shore N, Canter S. Chronic benign neutropenia of childhood with associated oral manifestations. *Oral Surg Oral Med Oral Pathol* 1965;20:719-25.
127. Deasy MJ, Vogel RI, Macedo-Sobrinho B, Gertzman G, Simon B. Familial benign chronic neutropenia associated with periodontal disease. A case report. *J Periodontol* 1980;51:206-10.
128. Baehini PC, Payot T, Tsai CC, Cimasoni G. Periodontal status associated with chronic neutropenia. *J Clin Periodontol* 1983;10:222-30.

129. Prichard JF, Ferguson DM, Windmiller J, Hurt WC. Prepubertal periodontitis affecting the deciduous and permanent dentition in a patient with cyclic neutropenia. *J Periodontol* 1984;55:114-22.
130. Kirstilä V, Sewón L, Laine J. Periodontal disease in three siblings with familial neutropenia. *J Periodontol* 1993;64:566-70.
131. Davey KW, Konchak PA. Agranulocytosis. *Oral Surg Oral Med Oral Pathol* 1969;28:166-71.
132. Awbrey JJ, Hibbard ED. Congenital agranulocytosis. *Oral Surg Oral Med Oral Pathol* 1973;35:526-30.
133. Cohen MM, Winer RA, Schwartz S, Shklar G. Oral aspects of mongolism. I. Periodontal disease in mongolism. *Oral Surg Oral Med Oral Pathol* 1961;14:92-107.
134. Orner G. Periodontal disease among children with Down syndrome and their siblings. *J Dent Res* 1976;55:778-82.
135. Izumi Y, Sugiyama S, Shinozuki O, Yamazaki T, Ohyama T, Ishikawa I. Defective neutrophil chemotaxis in Down syndrome patients and its relationship to periodontal destruction. *J Periodontol* 1989;60:238-42.
136. Watanabe H, Goseki-Sone M, Iimura T, Oida S, Orimo H, Ishikawa I. Molecular diagnosis of hypophosphatasia with severe periodontitis. *J Periodontol* 1999;70:688-91.
137. Page RC, Beatty P, Waldrop TC. Molecular basis for the functional abnormality in neutrophils from patients with generalized prepubertal periodontitis. *J Periodont Res* 1987;22:182-3.
138. Waldrop TC, Anderson DC, Hallmon WW, Schmalstieg FC, Jacobs RL. Periodontal manifestations of the heritable Mac-1, LFA-1 syndrome —Clinical, histopathologic and molecular characteristics. *J Periodontol* 1987;58:400-16.
139. Hart TC, Hart PS, Bowden DW, et al. Mutations of the cathepsin C gene are responsible for Papillon-Lefèvre syndrome. *J Med Genet* 1999;36:881-7.
140. Hart TC, Hart PS, Michalec MD, et al. Localization of a gene for prepubertal periodontitis to chromosome 11q14 and identification of a cathepsin C gene mutation. *J Med Genet* 2000;37:95-101.
141. Hart TC, Shapira L. Papillon-Lefèvre syndrome. *Periodontol* 2000, 1994;6:88-100.
142. Cianciola LJ, Park BH, Bruck E, Mosovich L, Genco RJ. Prevalence of periodontal disease in insulin-dependent diabetes mellitus (juvenile diabetes). *J Am Dent Assoc* 1982;104:653-60.
143. Mashimo PA, Yamamoto Y, Slots J, Park BH, Genco RJ. The periodontal microflora of juvenile diabetics. Culture, immunofluorescence, and serum antibody studies. *J Periodontol* 1983;54:420-30.
144. Page RC, Bowen T, Altman L, et al. Prepubertal periodontitis. I. Definition of a clinical entity. *J Periodontol* 1983;54:257-71.
145. Watanabe K. Prepubertal periodontitis: A review of diagnostic criteria, pathogenesis, and differential diagnosis. *J Periodont Res* 1990;25:31-48.
146. Sweeney EA, Alcoforado GAP, Nyman S, Slots J. Prevalence and microbiology of localized prepubertal periodontitis. *Oral Microbiol Immunol* 1987;2:65-70.
147. Delaney DE, Kornman KS. Microbiology of subgingival plaque from children with localized prepubertal periodontitis. *Oral Microbiol Immunol* 1987;2:71-6.
148. Taiwo JO. Severity of necrotizing ulcerative gingivitis in Nigerian children. *Periodontal Clin Investig* 1995;17:24-7.
149. Smith BW, Dennison DK, Newland JR. Acquired HIV deficiency syndrome: Implications for the practicing dentist. *Va Dent J* 1987;63:38-42.
150. Contreras A, Falkler WA Jr., Enwonwu CO, et al. Human Herpes viridae in acute necrotizing ulcerative gingivitis in children in Nigeria. *Oral Microbiol Immunol* 1997;12:259-65.
151. Loesche WJ, Syed SA, Laughon BE, Stoll J. The bacteriology of acute necrotizing ulcerative gingivitis. *J Periodontol* 1982;53:223-30.
152. Listgarten M. Electron microscopic observations on the bacterial flora of acute necrotizing ulcerative gingivitis. *J Periodontol* 1965;36:328-39.
153. Horning G, Cohen M. Necrotizing ulcerative gingivitis, periodontitis, stomatitis: Clinical staging and predisposing factors. *J Periodontol* 1995;66:990-8.
154. Enwonwu CO. Epidemiological and biochemical studies of necrotizing ulcerative gingivitis and noma (cancrum oris) in Nigerian children. *Arch Oral Biol* 1972;17:1357-71.
155. Jimenez LM, Baer PN. Necrotizing ulcerative gingivitis in children: A 9-year clinical study. *J Periodontol* 1975;46:715-20.
156. Pindborg JJ, Bhat M, Devanath KR, Narayana HR, Ramachandra S. Occurrence of acute necrotizing gingivitis in South Indian children. *J Periodontol* 1966;37:14-9.
157. Fitch H, Bethant H, Alling C, Munns C. Acute necrotizing ulcerative gingivitis. *J Periodontol* 1963;34:422-6.
158. Johnson B, Engel D. Acute necrotizing ulcerative gingivitis. A review of diagnosis, etiology and treatment. *J Periodontol* 1986;57:141-50.

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