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Orofacial disorders in children with HIV disease

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Pediatric HIV disease

Medical management of HIV infection among pediatric patients in the United States has improved dramatically during the past decade. Before the availability of more potent antiretroviral medications and prophylaxis to prevent opportunistic infections, most infected children died before the age of 5 years. Today, most children born with HIV disease (HIVD) will live into their third decade. Prolonged survival, however, depends on strict drug regimens and is associated with long stretches of immune suppression. To explore oral health care and oral diseases in this patient population, a general understanding of pediatric HIV is necessary.

In 2002, an estimated 800,000 children were born with HIV infection, and more than 600,000 children died from the ravages of HIVD. The epidemiology of pediatric HIVD is associated with three factors. (1) The prevalence of HIV among women in childbearing age greatly influences the incidence and prevalence of vertical HIV transmission. (2) Institution of antiretroviral medications during pregnancy can significantly reduce transmission of HIV to the fetus. (3) The availability and effective use of antiretroviral and prophylactic therapy changes the survival and overall health of children with HIVD. In developing countries almost half of all infected individuals are women of childbearing age. Little or no antiretroviral medications are available for these women, and the children usually do not have access to life-saving drugs later in life. Furthermore, breastfeeding, which may be the major source of nutrients for a child born in the developing world, is associated with transmission of HIV.

In developed countries the picture is very different. Testing pregnant women for HIV and institution of antiretroviral medications during

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pregnancy for HIV-infected women are becoming common practices [1]. Further reduction in maternal–child transmission is accomplished by elective cesarean delivery and avoidance of breastfeeding. Employing these methods may reduce the risk of mother-to-child transmission to less than 2%. In absolute numbers, this reduction translates into fewer than 500 children born with HIV infection; fewer than 100 deaths were reported in children under the age of 15 years in North America in 2002. Overall, through 2002 in the United States, a total of 9199 cases of AIDS were reported in children below the age of 13 years [2].

Classification system for pediatric HIV disease

The classification system for pediatric HIVD is different from that of adults. It is based on immune categories, which change according to the age of the child, and on different clinical categories (Table 1 and Box 1) [3].

In noninfected children the CD4 cell count is higher than in adults but declines over the first 6 years of life to approach adult levels by age 6 years. Although the absolute number of CD4 cells changes, the percentage of CD4 cells remains constant. A "CD4 percentage" is the percentage of total T-lymphocytes represented by CD4 cells. HIV-infected children should have a CD4 cell count/percentage performed every 3 months.

CD4 cell count and viral load have been shown to be significant markers of HIVD progression. These two parameters can fairly accurately predict progression to AIDS and the probability of dying for children at different ages [4] (Figs. 1 and 2). A 5-year-old child has a less than 5% chance of developing AIDS within 12 months if the CD4 cell percentage stays above 20%. If the CD4 cell percentage drops to 10%, the chance of developing AIDS within 12 months increases to 15%. Likewise, the likelihood of

Table 1
1994 Revised classification system for pediatric HIV disease based on CD4 cell count and percentage

	<12 months		1–5 years		6–12 years	
Immune category	CD4 cells/mm^3	%	CD4 cells/mm^3	%	CD4 cells/mm^3	%
Category 1: no suppression	>1500	25	>1000	>25	>500	>25
Category 2: moderate suppression	750–1499	15–24	500–999	15–24	200–499	15–24
Category 3: severe suppression	<750	<15	<500	<15	<200	<15

From Centers for Disease Control. 1994 Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR Mortal Wkly Rep 1994;43:1–10; with permission.

developing AIDS within the same time period changes from 3% to 6% to 17%, respectively, if the viral load increases from 10,000 to 100,000 to 1,000,000 HIV RNA copies. The mortality rate follows the same pattern. A change of CD4 cell percentage from 40% to 10% or a viral load increase from 10,000 to 1,000,000 increases the likelihood of dying 10 times.

Obviously these immunologic and virologic parameters are important markers for institution and change of therapy, need for follow-up, and development of clinical manifestations associated with immune suppression.

Although many clinical features are common to both adults and children, some are more typical and more pronounced among the pediatric population. Failure to thrive, which is associated with an abnormal growth rate, may affect as many as 50% of HIV-infected children. Other conditions more commonly found among children are lymphoid interstitial pneumonia (LIP), invasive and recurrent bacterial infections, and parotitis. The most common malignancies in children are non-Hodgkin's lymphoma and leiomyosarcoma, whereas Kaposi's sarcoma, the most common neoplasm developing among HIV-infected adults, is rare in children.

Orofacial manifestations

As with HIV-infected adults, the likelihood of developing oral manifestations depends on several factors. Presentation of orofacial disorders in patients with HIVD is strongly associated with immune suppression. In developing countries, and even in certain parts of the United States, reduced access to care may change patterns of oral disease. Patients with weakened immune systems show prevalence and incidence rates of orofacial manifestations different from those of individuals with a stronger immune system. Also, medications and nutrition may influence type and patterns of oral disease. One study trying to elucidate nonphysiologic factors in the development of oral disease found a strong association between oral manifestations in children and socioeconomic and cultural conditions, family structure and income, access to information concerning AIDS, and adherence to therapy [5].

Classification of oral lesions in pediatric HIV disease

Classification of orofacial lesions in HIV-infected children has been based on the likelihood of a lesion's being associated with HIVD (Box 2) [6].

This type of classification depends on good epidemiologic studies but is probably geographic site–specific, because the frequency of specific lesions differs from region to region and from country to country. Furthermore, children with access to more potent antiretroviral medications and prophylaxis for opportunistic infections will probably show epidemiologic

Box 1. 1994 Revised classification system for pediatric HIV disease based on clinical manifestations

Category N: Not symptomatic
No signs or symptoms as a result of HIV infection or only one of the conditions listed in category A

Category A: Mildly symptomatic
Children with two or more of the following conditions but none of the conditions listed in Category B or Category C
Lymphadenopathy ($\geq$ 0.5 cm at more than two sites or bilateral at one site)
Hepatomegaly
Splenomegaly
Dermatitis
Parotitis
Recurrent or persistent upper respiratory infection, sinusitis, or otitis media

Category B: Moderately symptomatic
Children who have symptomatic conditions, other than those listed in for Category A or Category C, that are attributed to HIV infection
Anemia (8 g/dL), neutropenia (<1000 cells/mm^3), or thrombocytopenia (<100,000 cells/mm^3) persisting for 30 days or longer
Bacterial meningitis, pneumonia, or sepsis (single episode)
Candidiasis, oropharyngeal persisting for more than 2 months in children older than 6 months
Cardiomyopathy
Cytomegalovirus infection with onset before age 1 month
Diarrhea, recurrent or chronic
Hepatitis
Herpes simplex virus (HSV) stomatitis, recurrent (ie, >two episodes within 1 year)
HSV bronchitis, pneumonitis, or esophagitis with onset before the age 1 month
Herpes zoster infection involving at least two distinct periods or more than one dermatome
Leiomyosarcoma
Lymphoid interstitial pneumonia (LIP) or pulmonary lymphoid hyperplasia complex
Nephropathy
Nocardiosis

Fever lasting less than 1 month
Toxoplasmosis with onset before age 1 month
Varicella, disseminated

Category C: Severely symptomatic
Children who have any condition listed in the 1987 surveillance case definition for AIDS with the exception of LIP.

patterns different from those of their counterparts without access to adequate and appropriate medical care. Oral lesions among HIV-infected adults have been strongly associated with changes in the immune system during different eras of antiretroviral therapy, and it is highly likely that the same phenomenon will be observed among pediatric populations [7,8].

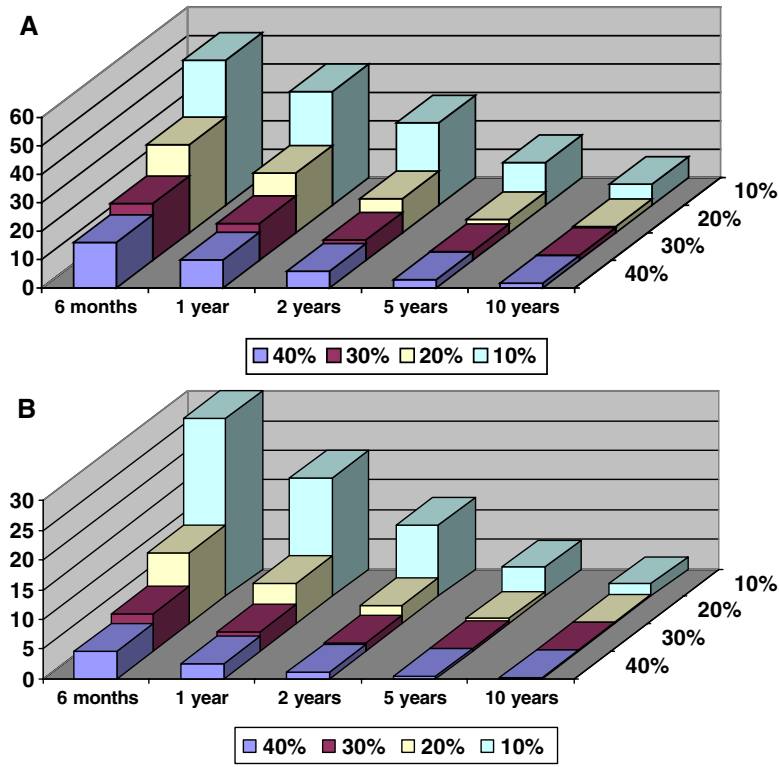

Fig. 1. (*A*) Likelihood for developing AIDS within 12 months by CD4 cell percentage and age. (*B*) Likelihood of death within 12 months by CD4 cell percentage and age. (*From* Dunn D. HIV Paediatric Prognostic Markers Collaborative Study Group. Short-term risk of disease progression in HIV-infected children receiving no antiretroviral therapy or zidovudine monotherapy: estimates according to CD4 percent, viral load, and age. Lancet 2003;362: 1605–11; with permission.)

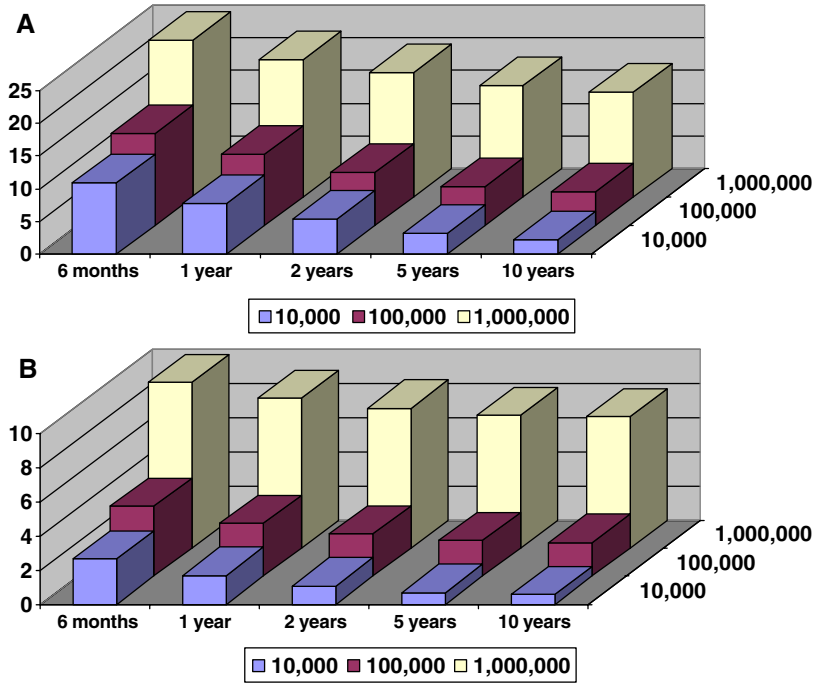

Fig. 2. (*A*) Likelihood for developing AIDS within 12 months by viral load (HIV RNS copy) and age. (*B*) Likelihood of dying within 12 months by viral load (HIV RNA copy) and age. (*From* Dunn D. HIV Paediatric Prognostic Markers Collaborative Study Group. Short-term risk of disease progression in HIV-infected children receiving no antiretroviral therapy or zidovudine monotherapy: estimates according to CD4 percent, viral load, and age. Lancet 2003;362:1605–11; with permission.)

Epidemiology

Several cross-sectional oral examination studies of HIV-infected children have been published. A study from 1990 evaluating 47 perinatally infected children (22 boys and 25 girls, 3 months–6.5 years of age) revealed a prevalence of 26.7% for oral candidiasis, and one case of parotid enlargement [9]. An Italian study of 69 children found a similar prevalence of oral candidiasis (28.9%) [10]. Even among hospitalized children with AIDS, a 35% prevalence of oral candidiasis was observed among 40 patients [11].

Another study reported an overall 17% prevalence rate of oral candidiasis, a 7% prevalence of oral ulcers, and one child with bilateral parotid enlargement among 28 HIV-infected children [12]. An intrastudy comparison between asymptomatic children and children with more severe immune suppression revealed that the rate of oral lesions was more than five times higher in children at more advanced stages of disease than in asymptomatic children. All of the children had contracted HIV from their

Box 2. Classification of orofacial lesions associated with pediatric HIV infection

Group 1: Lesions commonly associated with pediatric HIV infection
Oral candidiasis
HSV infection
Linear gingival erythema
Parotid gland enlargement
Recurrent oral ulcerations without microbial origin

Group 2: Lesions less commonly associated with pediatric HIV infection
Bacterial infection of oral tissue
Necrotizing gingival/periodontal disease
Necrotizing stomatitis
Seborrheic dermatitis
Cytomegalovirus infection
Varicella zoster virus infection
Human papillomavirus infection
Molluscum contagiosum
Xerostomia

Group 3: Lesions strongly associated with HIV infection but rare in children
Kaposi's sarcoma
Non-Hodgkin's lymphoma
Oral hairy leukoplakia
Tuberculosis-related ulcers

mothers and were taking antiretroviral medications at the time of examination.

A retrospective study of 91 perinatally exposed HIV-infected children in the United States attempted to determine risk factors for the development of oral lesions [13]. One hundred eighty-five HIV-negative children born to HIV-infected mothers served as a control group. Oropharyngeal candidiasis was found in 67% of HIV-infected children, and in 8% of the HIV-negative children. Parotid gland enlargement had a prevalence of 4% among the HIV-infected group, but no such pathology was found among the HIV-negative group. Three percent of the HIV-infected cohort had evidence of HSV infection, whereas no HSV infections were found among the HIV-negative children. Children with oropharyngeal candidiasis were four times as likely to have a low CD4 cell count and nine times as likely to have an AIDS diagnosis. Furthermore, presence of oral lesions was significantly associated with failure to thrive.

In one of only a few prospective cohort studies of 99 HIV-infected children in the United States, 72% presented with oral candidiasis, 47% had parotid enlargement, and 24% had evidence of HSV infection [14]. Presence of oral candidiasis was a marker for a more rapid progression to death (relative hazard, 14.2; 95% confidence interval [CI], 4.8–41.8). In contrast, parotid gland enlargement was associated with a much slower disease progression (relative hazard, 0.38; 95% CI, 0.16–0.88). It is suspected that parotid gland enlargement may be caused by the infiltration of CD8 cells, which are cytotoxic to HIV-infected cells and have the ability to destroy the virus, possibly explaining the slower progression in children with such pathology.

Another longitudinal study of 73 children, all of whom were receiving antiretroviral therapy, was conducted over a period of 4 years (1994–1998) [15]. The most common oral conditions were oral dryness and oral candidiasis with a point prevalence of 36% and 33%, respectively. Cervical lymphadenopathy was present in 51% of all children. Other less common orofacial manifestations were oral ulcers (3.4%–7.6%), mucositis (0–19.6%), parotid enlargement (0.9–6.8%), and oral hairy leukoplakia (0–1.0%). Prior oral manifestations, such as xerostomia and oral candidiasis, predicted the presence of manifestations at subsequent examinations.

A 2-year observational study of 104 HIV-infected children treated at an inner city medical center reported significantly more oral lesions among an infected cohort than in an HIV-negative control group [16]. Oral lesions were found in 76% of the HIV-infected group of children but in only 36% in the control group. Among the HIV-positive group, the most common oral lesion was oral candidiasis (28%), followed by linear gingival erythema (22%). Development of oral candidiasis was significantly associated with a low CD4 cell count.

An interesting prospective study comparing the frequency of oral soft tissue lesions in a cohort of 38 children taking either highly active antiretroviral therapy or only reverse transcriptase inhibitors did not reveal any difference in lesion patterns based on the antiretroviral therapy [17]. The prevalence rates for different lesions were 32% for linear gingival erythema, 24% for oral candidiasis, 35% for parotitis, 3% for herpes labialis, and 3% for herpetic gingivitis. There was a statistical difference in the absolute CD4 cell count and CD4 cell percentage between children with oral lesions and the children without oral disease. Patients with oral lesions had both lower absolute counts and lower percentages. There was no significant difference in viral load between the group with lesions and the group without lesions.

To assess the relative morbidity associated with oral lesions in a pediatric population, 26 HIV-infected children were followed for a mean duration of 28.8 months [18]. Hospitalization of a child for various reasons was necessary on 28 separate occasions. Twenty-five percent of all hospital admissions were the result of oral complaints. The oral lesions were documented as oral candidiasis with esophageal extension, oral candidiasis

with associated candidemia, major aphthous ulceration, and HSV-associated stomatitis. The duration of hospitalization for these lesions was 22 days, as compared with 343 days for the other 21 hospital admissions. The estimated hospital cost to care for the children with oral lesions was approximately $15,000.

Since the institution of more effective antiretroviral therapy in the mid-1990s, several studies have been published on the prevalence of orofacial manifestations from different countries in the world.

The mucocutaneous manifestations in a group of 85 HIV-infected children were evaluated in Rome, Italy [19]. Almost all of the children with AIDS (93%) developed oral candidiasis, whereas 56% of all children in the study developed this condition. Many of the children also developed dysphagia, which is thought to be related to esophageal candidiasis.

A study of 173 children from Romania revealed a prevalence rate of oral lesions of 55% [20]. This cohort of children ranged from 6 to 12 years of age and consisted of 88 boys and 85 girls. Only 30% of the children received any antiretroviral therapy. The primary mode of HIV transmission (in 88%) was by contaminated needles, blood, or blood products. The most common orofacial manifestations were oral candidiasis (29%), oral ulcers (15%), and salivary gland disease (9%). Other observed conditions included necrotizing ulcerative gingivitis and periodontitis (5%), linear gingival erythema (4%), labial molluscum contagiosum (3%), oral warts (2%), oral hairy leukoplakia (2%), and herpes zoster virus infection (1%). No immunologic or virologic parameters were reported.

An evaluation of 51 children in Brazil attending a pediatric AIDS outpatient clinic revealed a prevalence rate of 21.6% for pseudomembranous candidiasis, 5.9% for erythematous candidiasis, 19.6% for salivary gland disease, and one case each of linear gingival erythema and oral hairy leukoplakia. Children with oral lesions had more deteriorated immune systems than the children who were lesion free [21].

Another report from Brazil studied 38 perinatally HIV-infected children [22]. Numerous oral conditions were found, with candidiasis being the most common (65.8%) among all the children. The frequency of parotid enlargement was 18.4%; two patients had HSV infections; one patient presented with a recurrent oral ulcer; one child had oral hairy leukoplakia; and one patient had an oral condyloma acuminatum. The patient with the papilloma infection shared a toothbrush with her mother and brother, who both had oral papilloma virus infections.

The latest report from Brazil evaluated oral manifestations in children with AIDS in an ambulatory care setting [23]. All 30 children were treated with antiretroviral medications but not with protease inhibitors. The most common orofacial manifestation was cervical lymphadenopathy (40%), followed by gingivitis (33%), candidiasis (23%), parotid gland enlargement (13%), and ulcerations (3%). No lesion was found in children with CD4 cell counts above 1000 cells/mm^3. Eleven lesions were observed in children with

a CD4 cell count of 500 to 999 cells/mm^3, whereas 23 lesions were associated with severe immune suppression with CD4 cell counts below 500 cells/mm^3.

Two studies from Thailand evaluated orofacial manifestations in 85 HIV-infected children [24,25]. All of the children were from the same region in Thailand and presented with a remarkably similar frequency of lesions, 22/45 (49%) and 23/40 (58%), respectively. Oral candidiasis was present in 35.5% of children in one study and 45% in the other study. Also the findings of oral hairy leukoplakia, a lesion not commonly found in children, were similar in magnitude: 3/45 (7%) and 6/40 (15%), respectively. Oral ulcerations were noted in 7% and 5% of the children, respectively.

A larger study involving 91 HIV-infected Thai children (46 boys and 45 girls ranging from 2 to 11 years of age) revealed a prevalence of 51.6% of mucocutaneous lesions [26]. Oral candidiasis was present in 36.3% of the children. There was a marked increase in lesions among the more immune-suppressed children.

In one of few studies from Africa, 59% of 63 documented HIV-infected children presented with lymphadenopathy, and 19% presented with oral candidiasis [27].

Treatment modalities for oral lesions

Oral candidiasis should be treated with topical antifungal medications when the patient's CD4 cell percentage is above 15%. Clotrimazole, 10-mg oral troches, dissolved in the mouth 3 to 5 times per day are preferred as initial therapy. For bottle-fed infants, a vaginal tablet of 100,000 U/mL can be placed within the nipple. Nystatin mouth rinses, 1- to 5-mL suspension, also can be used but may be less efficacious than clotrimazole troches. Topical antifungal medications typically contain dextrose, which may be cariogenic with prolonged use, especially in children with reduced salivary flow. In patients with a CD4 cell percentage below 15%, systemic antifungal medications should be considered. Fluconazole, 2 to 5 mg/kg, and ketoconazole, 4 to 6 mg/kg, are well tolerated. Hepatotoxicity has been associated with both of these medications, and resistance may develop when these medications are used for prolonged periods of time. Antifungal therapy should continue 2 to 3 days after disappearance of clinical signs.

Necrotizing periodontal conditions are treated with aggressive plaque removal, scaling, and root planing. Antibiotic mouthrinses can be used together with oral antibiotics, such as metronidazole (15–35 mg/kg, every 8 hours), amoxicillin with clavulanate potassium (40 mg/kg, every 8 hours), or clindamycin (20–30 mg/kg, every 6 hours).

Treatment for herpesvirus infections is usually indicated only when the child has profound immune suppression. Acyclovir, 200- to 400-mg tablets every 6 hours, can be used. For varicella zoster infections a higher dose is needed. Valcyclovir, a prodrug to acyclovir, is also effective but may be

associated with hemolytic uremic syndrome in severely immune suppressed individuals. This drug should be prescribed for children only in consultation with the patient's physician.

Parotid enlargement cannot be treated effectively. Antibiotics and even glucocorticosteroids have been used with mixed success.

Children with decreased salivary flow can be treated conservatively by stimulating stimulation by chewing of sugar-free gum or sucking on sugar-free candies. Artificial saliva and oral lubricants may alleviate some of the symptoms of oral dryness and may, to some degree, improve oral functions. Several over-the-counter products, such as Biotene mouthrinse, toothpaste, and chewing gum (Laclede, Laclede, Inc., Dominguez, California), Oral Balance oral lubricant (Laclede), and Salivart aerosolized artificial salivary spray (Gebauer, Gebauer Co., Cleveland, Ohio), are available. Medications such as pilocarpine or cevimeline can also be considered but only in collaboration with the patient's physician [28].

Treatment of oral ulcerations should be based on an accurate diagnosis [29,30]. Topical corticosteroid applications, such as fluocinonide 0.05% or clobetasol 0.05%, mixed with Orabase 1:1 are usually beneficial for localized aphthous ulcers. Dexamethasone elixir, swish and expectorate, can be used for more generalized and multiple lesions. Systemic glucocorticosteroids therapy is indicated for more severe cases. In refractory cases, low doses of colchicines may be beneficial to spare the patient from the adverse effects of long-term corticosteroid use [30].

Oral hairy leukoplakia can be treated with acyclovir, but because this lesion usually does not cause any discomfort or undergo any malignant transformation, treatment should be based on the patient's desire to have it eliminated.

Summary

The prevalence of orofacial manifestations differs among geographic regions and is strongly related to the level of medical care. Three different orofacial manifestations are commonly found in most studies of HIV-infected children—oral candidiasis, enlarged parotid glands, and lymphadenopathy. Oral dryness is also a common finding and may be directly associated with parotid dysfunction, other salivary gland disorders, or secondary to medications.

There is a significant association between the development of oral lesions and immune suppression. It is yet not clear how HIV viral load influences orofacial manifestations among children. Orofacial manifestations among children with HIV infection, however, serve as early markers for immune deterioration and disease progression. More studies are needed to elucidate this relationship. The revised classification system for pediatric HIVD clearly emphasizes the importance of immunologic and virologic markers as they relate to treatment, disease progression, and survival. The strength of

orofacial manifestations as clinical markers for disease progression needs to be appreciated and incorporated in future classification systems. Furthermore, the classification of oral lesions needs to be revisited to reflect not merely epidemiologic findings but rather the relationship between immunologic parameters and the development of orofacial disorders.

References

[1] Cooper ER, Charurat M, Mofenson L, et al. Combination antiretroviral strategies for the treatment of pregnant HIV-1 infected women and prevention of perinatal HIV-1 transmission. J Acquir Immune Defic Syndr Hum Retrovirol 2002;29:484–94.
[2] Centers for Disease Control. Table A5. AIDS cases and annual rate (per 100,000 population), by metropolitan area and age category, reported through December 2002–United States. HIV/AIDS surveillance report, vol. 14. Addendum. April 7, 2004. Atlanta (GS): Centers for Disease Control; 2004.
[3] Centers for Disease Control. 1994 Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR Morb Mortal Wkly Rep 1994;43:1–10.
[4] Dunn D. HIV Paediatric Prognostic Markers Collaborative Study Group. Short-term risk of disease progression in HIV-infected children receiving no antiretroviral therapy or zidovudine monotherapy: estimates according to CD4 percent, viral load, and age. Lancet 2003;362:1605–11.
[5] Grando LJ, Yurgel LS, Machado DC, et al. The association between oral manifestations and the socioeconomic and cultural characteristics of HIV-infected children in Brazil and in the United States. Pan Am J Public Health 2003;14:112–8.
[6] Ramos-Gomez FJ, Flaitz C, Catapano P, et al. Classification, diagnostic criteria, and treatment recommendations for orofacial manifestations in HIV-infected pediatric patients. J Clin Pediatr Dent 1999;23:85–95.
[7] Glick M, Muzyka BC, Lurie D, Salkin LM. Oral manifestations associated with HIV disease as markers for immune suppression and AIDS. Oral Surg Oral Med Oral Pathol 1994;77:344–9.
[8] Patton LL. Sensitivity, specificity, and predictive value of oral opportunistic infections in adults with HIV/AIDS as markers of immune suppression and viral burden. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;90:182–8.
[9] Ketchem L, Berkowitz RJ, McIlveen L, Forrester D, Rakusan T. Oral findings in HIV-seropositive children Pediatr Dent 1990;12:143–6.
[10] Moniaci D, Cavallari M, Greco D, et al. Oral lesions in children born to HIV-1 positive women. J Oral Pathol Med 1993;22:8–11.
[11] Valdez IH, Pizzo PA, Atkinson JC. Oral health of pediatric AIDS patients: a hospital-based study. J Dent Child 1994;61:114–8.
[12] Del Toro A, Berkowitz R, Meyerowitz C, Frenkel LM. Oral findings in asymptomatic (P-1) and symptomatic (P-2) HIV-infected children. Am Acad Paediatr Dent 1996;18:114–6.
[13] Ramos-Gomez FJ, Hilton JF, Canchola AJ, Greenspan D, Greenspan JS, Maldonado YA. Risk factors for HIV-related orofacial soft-tissue manifestations in children. Pediatr Dent 1996;18:121–6.
[14] Katz MH, Mastrucci MT, Leggott PJ, Westenhouse J, Greenspan JS, Scott GB. Prognostic significance of oral lesions in children with perinatally acquired human immunodeficiency virus infection. Am J Dis Child 1993;147:45–8.
[15] Kozinetz CA, Carter AB, Simon C, et al. Oral manifestations of pediatric vertical HIV infection. Aids Patient Care 2000;14:89–94.

[16] Barasch A, Safford MM, Catalanotto FA, Fine DH, Katz RV. Oral soft tissue manifestations in HIV-positive vs. HIV-negative children from an inner city population: a two-year observational study. Am Acad Pediatr Dent 2000;22:215–20.
[17] Flanagan MA, Barasch A, Koenigsberg SR, Fine D, Houpt M. Prevalence of oral soft tissue lesions in HIV-infected minority children treated with highly active antiretroviral therapy. Am Acad Pediatr Dent 2000;22:287–91.
[18] Hauk M, Berkowitz RJ, Moss M, Meyerowitz C, Cassman B, Weinberg GA. Hospitalizations associated with oral lesions in perinatally HIV-infected children. Am Acad Pediatr Dent 1997;19:484–5.
[19] El Hachem M, Bernardi S, Pianosi G, et al. Mucocutaneous manifestations in children with HIV infection and AIDS. Pediatr Dermatol 1998;15:429–34.
[20] Flaitz C, Wullbrandt B, Sexton J, Bourdon T, Hicks J. Prevalence of orodental findings in HIV-infected Romanian children. Pediatr Dent 2001;23:44–50.
[21] Fonseca R, Cardoso AS, Pomarico I. Frequency of oral manifestations in children infected with human immunodeficiency virus. Quintessence International 2000;31:419–22.
[22] Magalhaes MG, Bueno DF, Serra E, Goncalves R. Oral manifestations of HIV positive children. J Clin Pediatr Dent 2001;25:103–6.
[23] Bosco VL, Birman EG. Oral manifestations in children with AIDS and in controls. Pesqui Odontol Bras 2002;16:7–11.
[24] Khongkunthian P, Grote M, Isaratanan W, Piyaworawong S, Reichart PA. Oral manifestations in 45 HIV-positive children from Northern Thailand. J Oral Pathol Med 2001;30:549–52.
[25] Pongsiriwet S, Iamaroon A, Kanjanavanti S, Pattanaporn K, Krisanaprakornkit S. Oral lesions and dental caries status in perinatally HIV-infected children in Northern Thailand. Int J Pediatr Dent 2003;13:180–5.
[26] Wananukul S, Thisyakorn U. Mucocutaneous manifestations of HIV infection in 91 children born to HIV-seropositive women. Pediatr Dermatol 1999;16:359–63.
[27] Emodi IJ, Okafor GO. Clinical manifestations of HIV infection in children at Enugu, Nigeria. J Trop Pediatr 1998;44:73–6.
[28] Cohen-Brown G, Ship JA. Diagnosis and treatment of salivary gland disorders. Quintessence International 2004;35:108–19.
[29] Kademani D, Glick M. Diagnosis, management and relevance to HIV disease progression. Quint Inter 1998;29:523–34.
[30] Glick M, Muzyka BC. Alternate treatment for major aphthous ulcerations in patients with AIDS. J Am Dent Assoc 1992;123:61–5.