Oral Diseases (2004) 10, 13–18

http://www.blackwellmunksgaard.com

HIV Disease

Oro-facial manifestations in paediatric HIV: a comparative study of institutionalized and hospital outpatients

S Naidoo, U Chikte

Department of Community Dentistry, School for Oral Health Sciences, Faculty of Health Sciences, University of Stellenbosch, Tygerberg, South Africa

The aim of the study was to compare dental caries status and the number and type of oral mucosal lesions in HIV positive children from a hospital outpatient department and an institutionalized setting. Oral examinations were performed using presumptive diagnostic criteria. The Fisher's Exact and the Mann–Whitney tests were used for statistical comparison of the two study groups. A total of 169 children were examined of whom 42% were institutionalized and 58% hospital outpatients. One institutionalized child presented with Noma. Twenty-one percent of the institutionalized population presented with molluscum contagiosum, while none of the hospital outpatients presented with this condition. Significantly more intraoral mucosal lesions were observed in the hospital compared with the institutionalized group. The most frequently encountered oral lesion was candidiasis. Pseudomembranous candidiasis was the most common type. Twice as many intraoral ulcers were recorded in the institutionalized group. Thirty-nine percent of the hospitalized patients had multiple lesions compared with 28% in the institutionalized group. Almost three quarters of both populations were caries-free. The mean DMFT was considerably higher in the hospital population. For both the permanent and primary teeth, the decayed component (D/d) made up the major part of the DMFT/dmft, followed by the missing (M/m) component. No fillings were recorded in either the primary or permanent teeth for both groups.Oral lesions are common in HIV populations and were seen in both the hospital and institutionalized groups, at high prevalence levels (63 and 45%). HIV infected children should be considered high risk for caries because of the use of chronic medications, and to receive appropriate care in terms of both treatment and services.

Oral Diseases (2004) **10**, 13–18

Correspondence: Prof. Sudeshni Naidoo, Department of Community Dentistry, School for Oral Health Sciences, Faculty of Health Sciences, University of Stellenbosch, Private Bag X1, Tygerberg 7505, South Africa. Tel: 021 937 3148, Fax: 021 931 2287, E-mail: snaidoo@sun.ac.za
Received 19 September 2002; revised 16 April 2003 and 7 July 2003; accepted 13 August 2003

Keywords: oral manifestations; paediatric; HIV

Introduction

The world has never seen a comparably complex public health hazard as that which it is currently experiencing in dealing with the effects of the AIDS epidemic on children. The impact of AIDS on children is not limited to their increasing rates of infection, but also to the fact that in 10 years time, over 40 million children are expected to be orphaned as a result of AIDS. Many children have to leave school and become heads of households or join the ranks of street children. HIV is posing a life-long threat to children: over 500 000 children were born with HIV because their mothers were infected and did not have access to prevention methods; every minute, five young people between 10–24 years become infected with HIV (UNAIDS, 2002). It is estimated that the total number of children orphaned by AIDS and living at the end of 2001 was 14 million, 11 million of which live in sub-Saharan Africa.

To date, UNAIDS (2002) estimates that over 40 million people are living with HIV/AIDS, with more than 95% in developing countries, including 28.5 million in sub-Saharan Africa. HIV/AIDS is now the number one overall cause of death in Africa, and has moved up to fourth place among all causes of death worldwide. In 2001, 19.9% of adult South Africans were infected up from 12.9%. With an estimated total of 4.2 million infected, South Africa is said to have more people living with HIV than any other country (UNAIDS, 2002). South Africa and its neighbouring countries, will see a doubling of infant mortality in the next few years from the effects of the AIDS epidemic (Department of Health, 2001).

Vertically acquired HIV infection (transmission from mother to offspring during gestation or parturition or as a result of breast feeding) accounts for 85% of all reported pediatric cases worldwide. In some areas of South Africa, one in three pregnant women is HIV-positive (Department of Health, 2001). Child-bearing

women who are infected via the heterosexual route of transmission constitute the main source of pediatric HIV infections (Quinn *et al*, 1986; Piot *et al*, 1987). Evidence suggests that around 30% of infants born to HIV-infected mothers in most African countries will also be infected (Dunn *et al*, 1992). Vertical (mother-to-child) transmission can occur in several ways: maternal bodily fluids during labour and delivery (Friedland and Klein, 1987); breast feeding (Thirty, Sprecher-Goldberger and Jonnckheer, 1985) and by crossing the placenta early in gestation (Lapointe *et al*, 1985; Lewis and Giorgi, 1990). The determinants of transmission are multifactorial and is dependent on maternal viral load, viral phenotype, obstetric factors and maternal immune response (Scarlatti, 1996).

Major systemic findings in paediatric HIV infection include: chronic pneumonitis, recurrent bacterial infections including otitis media, persistent oral candidiasis, chronic diarrhoea, lymphadenopathy, hepatosplenomegaly and failure to thrive (Rubinstein, 1990). Certain clinical findings are typical in the paediatric age group, such as salivary gland enlargement, pyogenic bacterial infections, developmental delay and dysmorphic craniofacial features (Rubinstein, 1990) Although various clinical aspects of paediatric HIV infection have been documented in African countries very few report on the oral manifestations (Emodi and Okafor, 1998).

Infection with HIV results in profound immunosuppression, rendering the host susceptible to the development of a variety of opportunistic infections and neoplasms. The oral cavity is particularly susceptible to infection since it habours numerous microorganisms that thrive in conditions of immunosuppression and cause characteristic fungal, viral, bacterial and neoplastic lesions. Oral lesions are frequently among the first symptoms of HIV-infected children (Klein *et al*, 1984; Schiodt and Pindborg, 1987; Moniaci *et al*, 1990; Howell *et al*, 1996; Nicolatou *et al*, 1999; Ramos-Gomez *et al*, 2000; Magalhães *et al*, 2001).

Early detection of HIV-related oral lesions can be used to diagnose HIV infection, elucidate progression of the disease, predict immune status, and provide timely therapeutic intervention (Moniaci *et al*, 1993; Ikeda and Maeda, 1994; Barasch *et al*, 2000).

Rogers *et al*, (1987) and Rubinstein (1990) have reported that roughly half of the infected infants become clinically symptomatic in the first year of life. In children individual signs and symptoms are often non-specific and may be seen in a variety of pediatric disorders. Although many of the immune system abnormalities are similar in pediatric and adult HIV infection, important differences exist. Unlike adults, vertically infected children have an immature immune system and, consequently, a shorter incubation period with a more rapid and fulminant disease process (Rosenberg and Fauci, 1994).

Oral manifestations of HIV in adults is relatively well described in the literature but comparative data for paediatric HIV is limited. There are no published papers on the oral and dental manifestations of HIV in children in Africa, and a few from North America. To address this issue, oral manifestations of HIV in a South African paediatric population were investigated. Most of the positively diagnosed HIV infected patients are found in institutions or as hospital outpatients. The aim of the study was to assess caries status and the number and type of oral mucosal lesions in HIV positive children from a hospital outpatient department and an institutionalized setting.

Materials and methods

The study was designed as a cross sectional, descriptive investigation conducted from January 2000–June 2001. Ethical clearance for the study was obtained from the research committee, University of Stellenbosch and authorization was secured from the institutions where the study was carried out. Informed consent was attained from patient's parents, guardians or caregivers before oral examinations were performed. Patients were provided with treatment and/or referred where appropriate.

The sample population was drawn from (i) HIV infected paediatric patients referred to Infectious Diseases Family Clinic at the Tygerberg Academic Hospital Complex and (ii) from three institutions caring for children who were diagnosed with HIV. On the days of the examinations, all patients who attended the outpatient clinic and those who were resident in the institutions were included in the study. None of the patients were on anti-retroviral therapy. This was a convenient sample as it is difficult to determine the HIV status of children in a general population because of ethical reasons. In terms of the previous Population Registration Act in South Africa, people were classified according to population/ethnic groups as Black (African), Coloured, Indian and White. This sample comprised only of the former two.

The majority of the children in this sample were born into extreme poverty with its concomitant factors such as malnutrition, tuberculosis, ill health. Most of the institutionalized were orphaned or abandoned, and were well cared for relative to the hospital outpatients. The hospital outpatient population were cared for by a family member, mainly grandmothers or aunts and came from the deprived areas around the Cape Peninsula. The fact that this sample comprised only African and Coloured is an indication of the burden of disease that these groups bear in terms of the HIV pandemic in South Africa.

Examinations were performed by two calibrated examiners. The classification for presumptive diagnostic criteria for oral mucosal lesions were based on the report from the EC-Clearinghouse on Oral Problems related to HIV infections and WHO Collaborating Centre on Oral Manifestations of the Immunodeficiency Virus (1993) and for caries status the Basic WHO Oral Health Surveys (World Health Organization, 1997). Oral examinations consisted of palpation and inspection of the mouth and facial structures, using a mouth mirror, periodontal probe, gauze and head light. Data was

collected over a period of 18 months (Jan 2000–June 2001). Photographs were taken in some cases. This paper will report on the extra-oral manifestations, lymphadenopathy, salivary gland pathology, oral mucosal lesions and caries status.

The Fisher's Exact test was used for comparing the prevalences between the two groups. The Mann–Whitney test was used to compare the number of oral lesions and DMFT components between the two groups. A significance level of 5% was used.

Results

A total of 169 patients were examined of whom 42% were institutionalized and 58% hospital outpatients. A profile of the demography of the study population is shown in Table 1. Overall the gender ratio was reasonably balanced with slightly more males than females. More African children were examined than any other classified group. The mean age of the institutionalized patients was slightly higher than that of the hospital outpatients.

One institutionalized 4-year-old African child presented with Noma. This case which is the first reported case of NOMA associated with an HIV positive individual in South Africa has been reported on previously (Naidoo and Chikte, 2000).

A total of 21% of the institutionalized population presented with molluscum contagiosum, while none of the hospital outpatients presented with this condition ($P < 0.01$).

Extra-oral (submental, submandibular and cervical) lymphadenopathy was observed in both hospital outpatient and institutionalized groups (Table 2). Submandibular lymphadenopathy occurred most frequently in both groups accounting for about a third of the lymph *node* enlargements. Cervical lymphadenopathy was the second most frequently encountered swelling (18%). Almost half the institutionalized population were diagnosed with parotid enlargement compared with <10% in the hospital and this was statistically significant. In most cases the enlargement of the parotid gland was unilateral.

Significantly more intra-oral mucosal lesions were observed in the hospital compared with the institutionalized group (Table 3). The most frequently encountered oral lesion was candidiasis, with 63 and 45% observed in the hospital and institutionalized groups respectively. Pseudomembranous candidiasis was the most common type. One case of hairy leukoplakia was observed and this was in the hospital group. Twice as many intraoral ulcers were recorded in the institutionalized group.

An analysis was carried out on the number of lesions seen in a mouth (Table 4). About two thirds of the

Table 1 Demography

Sample	*Hospital outpatients*	*Institutional*
Size		
$n = 169$	98	71
Age		
Mean	3.72 (s.d. 3.17)	4.04 (s.d. 2.55)
Median	3.17	3.97
Range	1 month–10 years	4 months–11 years
Gender		
Male (%)	55	54
Female (%)	45	46
Ethnicity		
African (%)	55	85
Coloured (%)	45	15

Table 2 Lymphadenopathy and parotid gland swellings

Site	*Yes (%)*	*Submental (%)*	*Submandibular (%)*	*Cervical (%)*	*Parotid (%) (unilateral)*	*Parotid (%) (bilateral)*
Hospital outpatients ($n = 97$)	49	11	34	18	7	1
Institutionalized ($n = 71$)	45	4	32	18	39	11
Fisher's exact test *P*-value	1.00	0.24	0.87	0.84	<0.01	<0.01

Table 3 Intraoral mucosal lesions

Site	*Oral lesions (%)*	*Cd (%)*	*Ps (%)*	*Ec (%)*	*AC (%)*	*HL (%)*	*Ulcers (%) (all types)*
Hospital outpatients ($n = 97$)	63	63	50	29	10	1	6
Institutionalized ($n = 71$)	45	45	24	18	10	0	14
Fisher's exact test *P*-value	0.02	0.02	<0.01	0.46	1.00	1.00	0.11

Cd, candidiasis; Ps, pseudomembranous candidiasis; Ec, erythematous candidiasis; AC, angular chelitis; HL, hairy leukoplakia.

Table 4 Number of oral lesions in a mouth

Number of lesions	*0*	*1*	*2*	*3*	*4*	*5*
Site						
Hospital outpatients (97)	34 (36%)	25 (26%)	17 (17%)	8 (8%)	4 (4%)	9 (9%)
Institutionalized (71)	34 (48%)	17 (23%)	13 (18%)	4 (6%)	1 (1%)	2 (3%)
Mann–Whitney *P*-value			0.04			

Table 5 Mean DMFT, mean dmft and % caries-free

	DMFT (s.d.)	*D (s.d.)*	*M (s.d.)*	*F*	*Caries-free*
Hospital ($n = 98$)	1.26 (3.46)	1.05 (2.86)	0.20 (1.0)	0	79%
Institution ($n = 71$)	0.17 (0.81)	0.15 (0.74)	0.01 (0.12)	0	96%
Mann–Whitney *P*-value	< 0.01	< 0.01	0.08	1.00	< 0.01 (Fisher)
	dmft	*d*	*m*	*f*	*Caries-free*
Hospital ($n = 98$)	1.91 (4.29)	1.31 (3.38)	0.56 (2.84)	0	74%
Institution ($n = 71$)	1.21 (2.66)	1.09 (2.40)	0.11 (0.72)	0	75%
Mann–Whitney *P*-value	0.67	0.89	0.76	1.00	1.00 (Fisher)

hospitalized patients had oral lesions compared with about half of the institutionalized patients. Nearly a quarter of the patients from both groups had at least one oral lesion. Almost four times as many hospital patients had four lesions and three times as many had five lesions compared with the institutionalized group.

Almost three quarters of both populations were caries-free (Table 5). The mean DMFT was considerably higher in the hospital population. The mean dmft was greater in the hospitalized group but did not differ significantly. For both the permanent and primary teeth, the decayed component (D/d) made up the major part of the DMFT/dmft, followed by the missing (M/m) component. No fillings were recorded in either the primary or permanent teeth for both groups.

Discussion

All the patients were infected from vertical transmission mother-to-child during birth, except for two from the hospital group who were infected through a contaminated blood transfusion. Data obtained from studies on vertical transmission imply that both intrauterine and intrapartum transmission occurs. The expression of HIV-related symptomatic disease as early and late HIV infection may reflect the differences in timing of transmission: infants with an *in utero* infection have a rapid onset of clinical disease and infants with intrapartum or postpartum infection have a slower onset of clinical disease. In this study we were unable to establish the timing of the vertical transmission.

It is difficult to conduct HIV population-based studies because of ethical problems for HIV testing for research purposes. Comparison of results with other studies is also difficult because of differences in the diagnostic methods employed (Gray and Carter, 1997). Further difficulties arise in comparing oral mucosal lesions with other studies due to a dearth of literature on oral mucosal lesions within the general paediatric population.

Enlargement of the cervical lymph nodes in children with HIV infection is usually a part of generalized lymphadenopathy. Lymphadenopathy is often accompanied by salivary gland enlargement. In a study by Chan *et al* (1994), cervical lymphadenopathy was the most prevalent orofacial manifestation (54.5%) in HIV-infected children in their study. A report from the Italian register of pediatric HIV infection, documented that lymphadenopathy was a non-specific clinical sign in 91% of the long-term survivors, and 58% of the short term survivors, indicating that the presence of lymphadenopathy was a positive predictor of survival in HIV-infected children (De Martino, 1989). In this study lymphadenopathy was the second most common finding after candidiasis for the hospital outpatients, but it was most common in institutionalized population together with candidiasis (45%).

Parotid gland enlargement has been recognized as a distinct feature of HIV infection in children since the first descriptions of the disease. This manifestation has been reported in 10–30% of children with symptomatic HIV infection (Pawha *et al*, 1987). In this study, the prevalence of parotid gland enlargement in the institutionalized population was much higher (50%) than has been previously reported and six times more than the hospital outpatients (8%). The presence of parotitis is a predictor of positive prognosis and long term survival in HIV-infected children (Tovo *et al*, 1992). Typically, the parotid glands are diffusely swollen and firm without evidence of inflammation or tenderness. The swelling is chronic with unilateral or bilateral involvement, occasionally accompanied by xerostomia. It is often associated with lymphoid interstitial pneumonitis (LIP) and diffuse lymphadenopathy, which probably represents a lymphoproliferative stage of HIV infection in children.

Candidiasis has been documented in various studies as the most frequently occurring oral manifestation in HIV-infected children, with a prevalence ranging from 20–76% (Chan *et al*, 1994). Recurrent candidiasis, which is persistent for long periods of time and often resistant to conventional antifungal therapy, is a frequent oral manifestation of pediatric HIV/AIDS (Samarayanake, 1993). In this study, the prevalence of candidiasis was high in both groups, although it was higher (63%) in hospital out patients. Oral thrush is also a finding in healthy infants in the first 6 months of life. However, in the immunocompetent child, candidal lesions are often mild, readily amenable to treatment, or regress spontaneously and are rarely seen beyond infancy in the absence of predisposing factors. The clinical presentation was variable. Lesions were often characteristic of the pseudomembraneous and erythematous types and often affected large areas of the oral mucosa. This was similar to what was reported by Ketchem *et al*, 1990.

Oral hairy leukoplakia (OHL) is rarely manifested in children with perinatally acquired HIV infection (Greenspan *et al*, 1988). It varies between 1–3% (Flaitz *et al*, 2001; Magalhães *et al*, 2001; Santos *et al*, 2001). In this study one individual presented with OHL. It is however, a common finding in adults and has been

documented as a predictor of progression of HIV infection to CDC-defined AIDS (Greenspan and Greenspan, 1992). Studies have shown that OHL is associated with intraepithelial proliferation of EBV and that multiple strains for the virus are often present in OHL tissues (De Souza *et al*, 1989).

Flaitz *et al* (2001) report a prevalence of 15% of oral ulcers in HIV infected Romanian children. In this study, the prevalence of ulcers in institutionalized patients (14%) was more than double that of hospital outpatients. Most of the oral ulcerations were of the herpetic variety (6%).

Previous studies suggest that poverty is an important risk indicator for noma in sub-Saharan Africa. Chronic malnutrition and environmental factors increase exposure to viral, bacterial and fungal infections. With increasing prevalence of HIV infection especially among children in Africa, there appears to be a re-emergence of noma (Barrios *et al*, 1995; Costini *et al*, 1995; Chidzonga, 1996; Nath and Jovic, 1998). An aggressive form of periodontal disease in HIV infected patients has been described and some of clinical features resemble noma (Winkler and Murray, 1987; Williams *et al*, 1990).

Noma is a challenging, but preventable condition for health care providers. Its occurrence in South Africa is an indication of the failure of the health services to contain both the rising scourges of HIV with the concomitant immunosuppression and malnutrition. There is an urgent need for both professional and public education in the early detection and prevention of noma; for training and services of health care workers in immediate care and for referral for treatment of sequelae. Surveillance at sentinel sites in areas where high prevalence of HIV is also recommended.

The differences in prevalence of molluscum contagiosum in hospital outpatients and institutionalized populations was anticipated because of the contagiousness of this condition and the ability of the virus to spread rapidly in populations living in close proximity to each other.

Madigan *et al* (1996) found that although HIV positive children did not have more caries than their siblings, more nursing bottle caries and white spot lesions were found. It has been speculated that HIV positive children display a different decay pattern, which may be related to decreased salivary flow (Courderc *et al*, 1987) and the use of viscous, sugary nutrient supplements (Madigan *et al*, 1996). Caries prevalence in disadvantaged South African urban populations is high. Direct comparison with published South African national oral health data is problematic because of differences in age groups. However, much of the caries was untreated. It appears that hospital outpatients had higher levels of caries because of unfavourable dental behaviour (dietary, brushing and toothpaste usage) and greater exposure to sugar-based medicines.

Conclusions

Oral lesions are common in HIV populations and were seen in both groups, at high prevalence levels. In this study the prevalence of oral mucosal lesions was higher in hospital outpatients than in institutionalized group. The number of lesions per child was also greater in hospital outpatients than the institutionalized. HIV infected children should be considered high risk for caries, because of reduced salivary flow and use of chronic medications, and to receive appropriate care in terms of both treatment and services.

Acknowledgements

The authors would like to thank the Department of Community Dentistry, Tygerberg Hospital Family Clinic especially Dr Mark Cotton and Anita, Guguletu and Chapel Street City of Cape Town Clinics (Jacqui Ross), Cotlands Baby Care Sanctuary (Jackie Schoeman), Nazareth House–Cape Town and Johannesburg especially Sister Breda, data capturer Chrismara Guttler, Nomonde Gwebushe and Dr Carl Lombard for the computing and statistical comparisons, Biostatistics Unit of the MRC, Tygergberg.

References

Barasch A, Safford NM, Catalanotto FA *et al* (2000). Oral soft tissue manifestations in HIV-positive vs. HIV negative children from an inner city population: A two-year observational study. *Paediatr Dent* **22:** 215–220.

Barrios TJ, Aria AA, Brahney C (1995). Cancrum oris in an HIV positive patient. *J Oral Maxillofacial Surg* **51:** 851–855.

Chan A, Milnes A, King SM *et al* (1994). The relationship of oral manifestations to parameters of immune function and CDC state in children born to HIV positive women. In: pediatric AIDS and HIV Infection. *Fetus to Adolescent* **15:** 101–107.

Chidzonga MM. (1996) Noma (cancrum oris) in human immunodeficiency virus/acquired immune deficiency syndrome patients: report of eight cases. *J Oral Maxillofac Surg* **54:** 1056–1060.

Costini B, Larroque G, Duboscq JC *et al* (1995). Noma or cancrum oris: Etiopathogenic and nasologic aspects. *Med Trop* **55:** 263.

Courderc L-J, D'Agay M-F, Danon F *et al* (1987). Sicca complex and infection with HIV. *Arch Intern Med* **147:** 898–901.

De Souza Y, Greenspan D, Felton JR *et al* (1989). Localization of Epstein-Barr virus DNA in the epithelial cells of oral hairy leukoplakia by in situ hybridization on tissue secretions (Letter). *N Engl J Med* **320:** 1559–1560.

Department of Health (2001) *2000 Antenatal Survey and Health News Service*, Pretoria.

Dunn DT, Newell ML, Ades AE *et al* (1992). Risk of human immunodeficiency virus type 1 transmission through breastfeeding. *Lancet* **340:** 585–588.

EC-Clearinghouse on Oral Problems related to HIV infections and WHO Collaborating Centre on Oral Manifestations of the Immunodeficiency Virus (1993). Classification and diagnostic criteria for oral lesions in HIV infection. *Oral Pathol Med* **22:** 289–291.

Emodi IJ, Okafor GO (1998). Clinical manifestations of HIV infection in children at Enugu, Nigeria. *J Trop Pediatr* **44:** 73–76.

Flaitz C, Wullbrandt B, Sexton J *et al* (2001). Prevalence of orodental findings in HIV-infected Romanian children. *Pediatr Dent* **23:** 44–50.

Friedland GH, Klein RS (1987). Transmission of the human immunodeficiency virus. *N Eng J Med* **317:** 1125–1135.

Gray IP, Carter JY (1997). An evaluation of clinical laboratory services in sub-Saharan Africa. Ex africa semper aliquid novi. *Clin Chim Acta* **267:** 103–128.

Greenspan JS, Greenspan D (1992). Significance of oral hairy leukoplakia (Review). *Oral Surg Oral Med Oral Pathol* **73:** 151–154.

Greenspan JS, Mastrucci MT, Leggott PJ *et al* (1988). Oral hairy leukoplakia in a child. *AIDS* **2:** 143–148.

Howell BR, Jandinski JJ, Palumbo P *et al* (1996). Oral soft tissue manifestations and CD4 lymphocyte counts in HIV-infected children. *Pediatr Dent* **18:** 117–120.

Ikeda M, Maeda N (1994). Survey of oral lesions of HIV/AIDS patients in Japan (Report 1). *Int Conf AIDS* **10:** 190–195.

Ketchem L, Berkowitz RJ, McIlveen L Forrester D, Rakusan T *et al* (1990). Oral findings in HIV seropositive children. *Pediatr Dent* **4:** 143–146.

Klein RS, Harris CA, Small CB, Moll B, Lesser M, Friedland GH *et al* (1984). Oral candidiasis in high risk patients as the initial manifestation of the acquired immunodeficiency syndrome. *N Engl J Med* **311:** 354–358.

Lapointe L, Michaud J, Pekovic D *et al* (1985). Transplacental transmission of HTLV-III virus. *N Engl J Med* **312:** 1325.

Lewis DE, Giorgi JV (1990). Immunology of HIV infection. *Int Rev Immunol* **7:** 1–13.

Madigan A, Murray PA, Houpt M *et al* (1996). Caries experience and cariogenic markers in HIV-positive children and their siblings. *Pediatr Dent* **18:** 129–136.

Magalhães GM, Bueno DF, Serra E *et al* (2001). Oral manifestations of HIV positive children. *J Clin Pediatr Dent* **25:** 103–106.

Moniaci D, Greco D, Flecchia G *et al* (1990). Epidemiology, clinical features and prognostic value of HIV-1 related oral lesions. *J Oral Pathol Med* **19:** 477–481.

Moniaci D, Cavallari M, Greco D *et al* (1993). Oral lesions in children born to HIV-1 positive women. *J Oral Pathol Med* **22:** 8–11.

Naidoo S, Chikte UME (2000). Noma (Cancrum Oris): case report in a 4-year-old HIV positive South African child. *SADJ* **55:** 683–686.

Nath S, Jovic G (1998). Cancrum oris: management, incidence and implications of human immunodeficiency virus in Zambia. *Plastic Reconstr Surg* **102:** 350–357.

Nicolatou O, Theodoridou M, Mostrou G *et al* (1999). Oral lesions in children with perinatally acquired human immunodeficiency virus infection. *J Oral Pathol Med* **28:** 49–53.

Pawha S, Kaplan M, Fikrig S *et al* (1987). Spectrum of human T-cell lymphotropic virus type III infection in children: recognition of symptomatic, asymptomatic and seronegative patients. *JAMA* **125:** 2299–2305.

Piot O, Kreiss JK, Ndinya-Achola JO *et al* (1987). Heterosexual transmission of HIV. *AIDS* **55:** 199–206.

Quinn TC, Mann JM, Curran JW *et al* (1986). AIDS in Africa: an epidemiologic paradigm. *Science* **14:** 955–963.

Ramos-Gomez FJ, Petru A, Hilton JF *et al* (2000). Oral manifestations and dental status in paediatric HIV infection. *Int J Paed Dent* **10:** 3–11.

Rogers MF, Thomas PA, Starcher ET *et al* (1987). AIDS in children: report of the Centers for Disease Control National Surveillance, 1982–1985. *Pediatr* **5:** 1008–14.

Rosenberg ZF, Fauci AS (1994). Immunopathology and pathogenesis of HIV infection. In: Pizzo AP, Wilfert CM, eds. *Pediatric AIDS: The Challenge of HIV infection in Infants, Children and Adolescents*, 2nd edn. Williams and Wilkins: Baltimore, pp. 115–127.

Rubinstein A (1990). HIV infections in infants and children. In: Holmes KK, ed. *Sexually Transmitted Diseases*, 2nd edn. Mc Graw-Hill: New York, pp. 843–899.

Samarayanake LP (1993). Oral care of the HIV-infected patient. *Dental Update* **9:** 24–26.

Santos LC, Castro GF, de Souza IP (2001). Oral manifestations related to immunosuppression degree in HIV-positive children. *Braz Dent J* **12:** 135–138.

Scarlatti G (1996). Paediatric HIV infection. *Lancet* **348:** 863–868.

Schiodt M, Pindborg JJ (1987). AIDS and the oral cavity. Epidemiology and oral manifestations of HIV infection: a review. *Int J Oral Maxillofac Surg* **16:** 1–14.

Thirty L, Sprecher-Goldberger S, Jonnckheer T (1985). Isolation of AIDS virus from cell-free breast milk of three healthy virus carriers. *Lancet* **2:** 891–892.

Tovo PA, de Martino M, Gabjano C *et al* (1992). Prognostic factors and survival in children with perinatal HIV-1 infection. The Italian Register for HIV Infections in Children. *Lancet* **339:** 1249–53.

UNAIDS. (2002). *Report on the global HIV/AIDS epidemic 2002*. Joint United Nation Programme on AIDS: WHO, Geneva.

Williams CA, Winkler JR, Grassi M *et al* (1990). HIV associated periodontitis complicated by necrotising stomatitis. *Oral Surg* **69:** 351.

Winkler JR, Murray PA (1987). Periodontal disease: a potential intra-oral expression of AIDS may be rapidly progressive periodontitis. *Calif Dent Assoc* **15:** 20.

World Health Organization (1997). *Oral Health Surveys. Basic Methods*. 4th edn. WHO, Geneva.