Sudanese Journal of Paediatrics 1986;5:10-18.

Invited Review Article

AIDS AND THE PAEDIATRICIAN IN AFRICA

J. Graham Watson
Children's Department Newcastle General Hospital, Newcastle Upon Tyne, United Kingdom.

In Europe and the USA paediatric AIDS & Human Immunodeficiency Virus (HIV) infection predominately affect children under the age of 2 years. These children form only about 1.5% of the local infected population. In Central Africa the situation is different; a much greater proportion of certain groups is infected; in one African capital 10% of children aged between 6 months and 2 years have antibody and have been infected. In Bangui 3% of healthy children and 12% of children with malnutrition have HIV antibody[1]. Other groups show a significant incidence of antibody positivity, e.g 10% of antenatal patients in Zambia, 2-12% of the urban adult population in Zambia, Ruanda, Uganda, Zaire[2] and the Central African Republic, and the age distribution reflects the predominately sexually transmitted nature of this disease. Sexually active persons are most at risk with between 50% & 80% of prostitutes in several African studies being virus antibody positive[3]. Rural populations are less affected. In the western world homosexuality and drug abuse play an important role in the creation of an antibody positive population but globally the conventional sexual route is probably more important. It seems likely that AIDS will become more common than poliomyelitis.

Infection appears to be life-long and clinical signs may appear at any time. Seroconversion occurs 3 to 6 weeks after infection and in adults there is then a latent period, the length of which is not known but can exceed 5 years. The most reliable data have been generated from recipients of infected blood but seems a similar pattern in all other HIV positive individuals. In adults immune complex diseases, thrombocytopenia, failure to thrive,

lymphadenopathy and infections which may be characteristic of immunosuppression are common problems. Two symptoms such as these plus two laboratory results suggestive of AIDS are called 'AIDS-related complex' (ARC). Clinical signs and symptoms frequently progress to AIDS with death in 2-3 years but the whole process may arrest at any time. The latent period may be much prolonged until an activating agent e.g. pregnancy occurs with a rapid deterioration thereafter. No doubt many activating agents remain to be identified, but venereal disease, parasite infections and malnutrition seem likely candidates[4].

In the west, most infected infants come from family groups which include parents in high risk categories such as prostitution, intravenous drug abuse or blood product treatment. There may be a maternal history of blood transfusion and quite possibly a previous child in that family suffered from AIDS although may not have been so identified at the time. Infection occurs primarily from three sources. Infants and neonates acquire the infection from their mothers by the transplacental, intrapartum or breast milk routes and HIV may or may not remain latent. Blood or blood products may infect children of any age and adolescents who may also aquire HIV by the sexual route. The age distribution of cases in childhood is bimodal, reflecting the major routes-perinatal and sexual. Blood sucking insects could transfer infection and there is some evidence to implicate bed bugs[5]. 'Blood brother' and some tribal scarring ceremonies will carry a certain risk. there is no evidence of casual spread.

Infection with HIV presents in several ways. In-utero infection is common if mother is infected[6]. Virus has been isolated from a fetus of 15 weeks gestation and evidence of intrauterine infection includes intrauterine growth retardation, low birth weight and cerebral atrophy delectable by prenatal cerebral ultrasound scan. Infection may also present postnatally, the infant having acquired HIV from mother or from infected blood. Congenital infection usually presents within the first 6 months with hepatosplenomegaly, thrush, pyrexia and failure to thrive. Cerebral atrophy both acute or chronic and failure to make developmenatal progress may occur or present as a single isolated finding[7]. The risks to the

infant of a positive mother cannot be over-emphasised. Two-thirds of such infants will become HIV antibody positive and half of these develop AIDS within 2 years. This aggressive course is due to a number of factors; the antibody transferred from mother is not protective against HIV; the infant's own immunity is relatively immature and thus more readily compromised; there is much T cell activation as a result of normal responses to foreign antigens[8] and the newborn has more T4 cells than adults. In a similar manner HIV acquired by infants from blood transfusions results in much more rapid progress to disease (mean 14 months) than when adults become infected by this route (mean 31 months)[2].

As an acute infection HIV most usually presents with an EB virus (EBV) like illness which may be easily confused with malaria.

Diagnosis is difficult even for an astute clinician unless there is a recognised event e.g. blood transfusion. Between 6 and 50+ days after infection adults may suffer fever, sweating, sore throat, headache, arthralgia, myalgia and nausea or present with an acute febrile encephalopathy. Such an acute onset would seem rare in children.

HIV infection results in immunodeficiency and so sequalae of this are frequently the initial presentation. The nature of these illnesses is the same in Africa as in Europe but the distribution is somewhat different. Pneumocystis carinii penumonia (PCP) is less common in African (14% of presentations) compared in Europeans (50%) and lymphoid pneumonitis (LP) due to EBV infection is both more common and is a good indication of HIV infection. The comparative features of LP and PCP are well described[9]. Oral candidiasis, cryptococcal menigitis CMV choreo-retinitis, persistent cryptosporidiosis and mucocutaneous herps simplex infections and enteropathic AIDS ("Slim" disease) are all common representation of HIV infection in Africa. Any infection unusual in its course or the causative organism may be a presentation. IgG2 deficiency leads to infections due to pnuemococci and haemophilus influenzae.

Aggressive Kaposi's sarcoma occurs and must be differentiated from the more common slowly evolving endemic Kaposi's sarcoma. Tumours have also been reported[10], drug allergies are particularly common in patients with HIV as is the return of childhood allergies or eczema. Blood transfusions given to HIV positive patients should be irradiated to 1.5Gy to prevent an incompatible graft being established by the donated lymphocytes.

Although live immunisations should not be given to an immunosuppressed child, many HIV positive children must have received oral polymyelitis vaccine (OPV) without coming to harm. Inactivated poliomyelitis vaccine if available should be given to HIV antibody positive children. If unavailable, OPV would be appropriate but not for those with clinical AIDS or ARC. The same holds true for measles immunisation where inactivated vaccine would again be preferable. There is no data however showing that live vaccine is harmful to HIV positive children. BCG should not be given to HIV positive individuals of any age and pertussis immunisation however should not be given to antibody positive children. HIV is neurotropic and the risks of encephalopathy probably outweigh the benefits of immunisation.

HIV infects lymphocytes bearing the CD4 glycoprotein and gains access to cells by this receptor. CD4 is present on helper/inducer T lymphocytes (T4 in the previous nomenclature), macrophages, and neural cells. The virus can enter all these cells with profound effects on the brain and the immune system. Certain laboratory results suggest AIDS. The lymphocyte count is reduced though less so than in adults and there is a particular and specific reduction in CD4 lymphocytes and some minor increase in CD8 (T8 suppressor/cytotoxic) lymphocytes. This results in a profoundly low 4/8 ratio. Cell mediated immunity and delayed hypersensitivity become greatly impaired with greatly reduced levels of interleukin-2, γ interferon and macrophage activating factor. There is early polyclonal hyperimmunoglobulinemia with progressive humoral antibody deficiency[11]. Responses to new antigens become

grossly impaired and despite the hypergammaglobulinaemia IgG2 levels are particularily reduced. The combination of hypergammaglobulinemia with severely depressed CD4 lymphocyte markers is not seen in severe combined immunodeficiency and there should be little practical difficulty, given laboratory facilities, of differentiating between the major immunodeficiencies of infancy and childhood and AIDS. There is no evidence that HIV is an opportunist pathogen in primary immunodeficiency. These problems have been well discussed [12, 13, 14].

Specific identification of HIV or HIV antibody is important but not essential to make the diagnosis and 80% of those clinically suspected of having AIDS have been found to be HIV positive when sophisticated laboratory tests became available. The most common antibody test detects HIV IgG antibody by immunofluor escence. IgM immunoflourescence is not reliable and so cord specific IgM results may be misleading. ELISA is more sensitive and useful in epidemiological studies in Africa because of the problem of non-specific reactivity with immunoflourescence. ELISA does not wholly overcome this problem. Malaria, parasite infections and cross reactions with minor components derived from the HIV culture cells give non-specific and HLA specific reactions. More of a problem in adults, it is unlikely to cause diagnostic difficulty in infants or young children. Western blotting in which antibody to HIV genome specific DNA is identified is the most sophisticated test and may be necessary if diagnostic doubt remains. This investigation may also be misused and its reliability is dependant on the quality of laboratory performing the assay[4].

There is no specific treatment for AIDS. HIV antibody is not protective and infusions of high titre antibody (300mg/kg, biweekly) do not usualy reverse the basic disease but will improve the humoral immunodeficiency for a time [15]. Some antiviral agents show promise but only in the short term. Mediator therapy (interleukin, interferon) has proved disappointing. Infective complications can be

treated with appropriate drugs although the incidence of side-effects and allergic reactions is comparatively high. Prophylactic Septrin and acyclovir may be useful. As with adults half the children who develop clinical AIDS are dead in 2 years and three quarters are dead in 3 years. Infants have a more rapid course.

Preventing AIDS may however be more successful. Fifty percent of HIV positive mothers develop AIDS during their second pregnancy so women at risk should be advised to avoid pregnancy until more is known about how pregnancy precipitates clinical AIDS. Given the rapidity of advances in knowledge of AIDS this is not impractical advice. Although the methodology of not becoming pregnant is easy, overcoming paternal prejudices may prove more difficult. Once pregnant there is little which will effect the outcome. Two-thirds of infants will become infected and caesarean section does not prevent infection. However one-third of infants born to HIV positive mothers do not acquire HIV and it would seem reasonable to minimise their exposure to virus. The infant is put at little additional risk by antibody positive breast milk compared to the risks of receiving formula. Nevertheless breast milk can transmit HIV infection[16] and so in an ideal world milk from a positive mother should be avoided by a HIV negative infant. However it is not usually possible to know which infants are HIV positive so breast feeding should be allowed.

Post-natal blood transfusion and ultimately sexual experience are the most likely ways in which the virus will be acquired. There is little evidence that intra-family spread occurs except by the sexual route although secretions do contain HIV.

With the incidence of antibody in central Africa all blood should be regarded as infected and the risk of infection increases with the number of blood donors encountered by a patient. Whole blood blood containing cellular components and plasma carry the

greatest risks. Immunoglobulin, albumin, plasma protein fraction and blood products such as hepatitis B vaccine are free of HIV. Testing each blood donation will require sophisticated techniques if much blood is not to be discarded because of false positive results obtained by immunofluoresence. Testing will be necessary, but who will do it and how will it be organised? Meantime, the use of family donors, as few as possible, and using mother for infants needing blood will be helpful, but clearly the less the exposure to blood or factor concentrates the better. These should only be given when there is a very real need. Heating factor concentrates to 56°C for 30 minutes should render them safe (as regards HIV).

Clinic health workers should be carefully instructed to follow precautions. The virus is more delicate than many give it credit. It is heat sensitive and destroyed by hypochlorite, aldehydes, lipid solvents and by drying. Spills of blood should be routinely cleaned with bleach and running water. Needless must be disposed of securely and should never be re-sheathed. One third of accidents with blood HIV positive patients have occurred when re-sheathing a needle. Nevertheless the virus density in whole blood is very much less than that of e.g. hepatitis B and the risk of infection after a needle-stick injury must be put in perspective. It is extremely low (3 seroconversions after 900+ needle-sticks with HIV positive contamination.

A child with AIDS or HIV antibody positivity should attend school or nursery school if he is well because, unless he has open wounds, or suffers e.g. nosebleeds he poses no threat to other children or staff. In that other children may be a source of nosocomial infection, they pose a greater threat to the child with AIDS than the unfortunate child does to his uninfected peers. If encephalopathic or retarded however, the antibody positive child may pose a greater risk because of biting, excess salivation and uninhibited behaviour. Shared cutlery, crockery and toilet arrangements pose no

dangers and mouthing objects e.g. toys is not considered a risk. Swimming and body contact sports should be allowed. Ear piercing, tattooing and traditional scarification carry a risk. Children who receive repeated blood transfusions e.g. with haemophilia, sickle cell disease or thalassaemia may well be antibody positive. They should be treated no differently to their colleagues. The only real likely risks to arise from HIV positive children are in the event of bleeding either from trauma or menstruation. Soiled materials should be placed in plactic bags and burned, and contaminated surfaces cleaned with bleach.

REFERENCES

1. Lesbordes JL, Chassignol S, Manaud F et al, Malnutrition and HIV infection in children in the Central African Republic. Lancet 1986; 2:337-338.
2. Melbye M. The natural history of human T lymphotrophic virus-III infection: the cause of AIDS. BMJ 1986;292:5-12.
3. Kreiss JK, Keoch D, Plummer FA et al. AIDS virus infection in Nairobi prostitutes: spread of the epidemic to East Africa. N Engl J Med 1986; 314;414-418.
4. Biggar RJ. The AIDS problem in Africa. Lancet 1986;1:79-83.
5. Lyons SF, Jupp PG and Schoub BD. Survival of HIV in the common bedbug. Lancet 1986;2:45
6. Scott GB, Fischi MD, Klimas N et al. Mothers of infants with the Acquired Immunodeficiency Syndrome JAMA 1985;253:363-366.
7. Carne CA and Adler MW, Neurological manifestations of HIV infection. BMJ 1986;293:462-463.
8. Wachter H, Fuchs D, Hausen A et al .Are conditions linked with T-cell stimulation necessary for progressive HTLV-III infection? Lancet 1986;1:97.
9. Rubinstein A, Moreki R, Silverman B et al. Pulmonary disease in children with acquired immune deficiency syndrome and AIDS related complex, J Paediatr 1986;108:498-503.
0. Ninane J, Moulin D, Latinne D et al AIDS in two African children-one with fibrosarcoma of the

11. Bernstein LJ, Ochs HD, Wedgewood RJ and Rubinstein A. Defective humoral immunity in paediatric acquired immune deficiency syndrome. J Paediatr 1985;107:352-357.
12. Ammann AJ, Kaminsky L, Gowan M and Levy JA, Antibodies to AIDS - associated retrovirus distinguish between paediatric primary and acuired immunodeficiency diseases. JAMA 1985;253:3116-3118.
13. Ammann AJ. The acquired immunodeficiency syndrome in infants and children. Ann Int Med 1985;103: 734-737.
14. Jones P and Watson JG AIDS in Recent Advances in Paediatrics .Ed. Meadow R , 1986 Churchil Livingston: London.
15. Rubinstein A, Sicklick M, Bernstein L et al. Treatment of AIDS with intravenous gammaglobulin (abst). Paediatr Res 1984;18:264A.
16. Ziegler JB, Cooper DA, Johnson RD and Gold J. Postnatal transmission of AIDS-associated retrovirus from mother to infant. Lancet 1985;1:896-898.