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IMMUNIZATION OF CHILDREN INFECTED WITH
HUMAN IMMUNODEFICIENCY VIRUS

USA-1

by

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Expanded Programme on Immunization



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1. INTRODUCTION

The pandemic of acquired immune deficiency syndrome (AIDS) and infections with the human immunodeficiency virus (HIV) is a global health problem of extraordinary scope and urgency. First recognized in the United States in 1981, AIDS has now been reported in many countries throughout the world. Since cases have been reported in infants and young children questions as to the appropriateness of providing immunizations to HIV infected infants, particularly with live virus vaccines, have been raised.

This document reviews the epidemiology, clinical characteristics and pathophysiology of HIV infection in infants so that risks involved in EPI activities in developing countries with endemic and epidemic AIDS can be assessed.

2. EPIDEMIOLOGY

The AIDS epidemic in the United States continues to unfold and has been well described (1). The first cases occurred as early as 1978 but the disease was not characterized clinically until 1981. As of 1 December 1986, 28 246 cases had been reported to the Centers for Disease Control. The disease is due to infection with a retrovirus which has now been called human immunodeficiency virus (HIV). AIDS does not follow all cases of HIV infection and 25 to 100 HIV-infected persons exist for each case of clinical AIDS.

Approximately 66% of the AIDS cases in adults in the US have occurred in homosexual or bisexual men; 17% in IV drug users; 8% in homosexual drug abusers; 1% in hemophiliacs; 2% in transfusion recipients; 3% in heterosexual partners of AIDS patients and 3% could not be classified as having any known predisposing factor.

Between 1 June 1981 and 1 December 1986, 403 children with AIDS have been reported in the US. No seroprevalence studies in children have been done in the US and the number of asymptomatic infected children is unknown. Fifty percent of the above children developed disease during the first year of life.

Two risk factors have been identified in U.S. children with AIDS: 1) birth to a mother who has AIDS or is in a high risk group for AIDS (79% of cases) and 2) receipt of blood or clotting factors (2). Vertical transmission of AIDS from HIV-infected mother to her child is the most common source of infection in pediatric cases. The risk of perinatal transmission from an infected mother to her infant is not known exactly but in small studies has ranged from 0 (0/3) to 65% (13/20) (3-5). While not providing final answers, these studies do establish the point that HIV transmission from mother to child occurs and that AIDS can develop in a high fraction of children so infected.

Therefore, the prevalence of HIV infection in women of child bearing age largely establishes the level of risk to infants in any given country. In the U.S. seroprevalence in young women is low because the main reservoir of HIV infection remains male homosexuals.

The situation is quite different in Africa where the predominant mode of spread of HIV is heterosexual transmission (6). Currently 80% of AIDS cases in Africa are believed to come from Central and East Africa, 6% from Southern Africa and 14% from the rest of the continent (7). HIV seroprevalence among healthy adult populations studied in specific (usually urban) areas of Central and East Africa have generally ranged from less than 1% to 15% and higher. Seropositivity is particularly high in prostitutes and persons attending STD clinics (8).

In Kinshasa 1-2 percent of healthy infants greater than 9 months of age as well as children from 2 to 14 years old are seropositive for HIV. Five to eight percent of adolescents and adults are infected with the highest age and sex specific seroprevalence in women from 15 to 29 years of age (9). Seropositivity and cases are distributed equally among men and women in clear distinction to the male predominance in U.S. cases. Transmission from HIV-infected women to their offspring is occurring and increasing numbers of infected infants are being born, a portion of whom will receive EPI antigens.

3. HIV INFECTION IN INFANTS

The median time between birth and onset of symptoms in infants of high risk parents is 4 months. Children who develop AIDS are frequently brought to medical attention because they fail to thrive. Recurrent thrush, chronic pneumonitis, hepatosplenomegaly, persistent diarrhea and severe bacterial infections are common. Of the first 107 U.S. cases two-thirds had Pneumocystis carinii pneumonitis, 5% had Kaposi's sarcoma and a quarter had some other opportunistic infection (10). There is no evidence that AIDS is transmitted among infants as a result of casual contact associated with day to day living (11,12).

4. IMMUNOLOGIC ABNORMALITIES ASSOCIATED WITH HIV INFECTION

HIV preferentially infects and destroys a pivotal cell in host immune defenses (13). This cell, called the T4 cell, is responsible for triggering maturation of T lymphocytes from precursor forms to functionally distinct cells and serving a so called helper function which enables destruction of infected cells as well as enhancing B cell response to produce antibody. A decrease in T4 cells has a profound negative effect on the entire immune response; B cells are unable to produce adequate quantities of antibody not only to the AIDS virus but to any infection; clonal expansion of cytotoxic killer cells is inhibited and macrophage activation is suppressed. The clinical expression of this situation has been well described as AIDS patients are susceptible to a particular cancer, including Kaposi's sarcoma, and a wide variety of infectious agents.

Children with symptomatic HIV infection have the same immunologic abnormalities that have been described in adults. These include polyclonal hypergammaglobulinemia, reversed helper/suppressor T-cell ratios and impaired T-lymphocyte response (10). Humoral immunity to tetanus toxoid and pneumococcal vaccine is also impaired (14). Detailed immunologic studies have not been done in infants with asymptomatic HIV infection. In general, asymptomatic adults have normal immunologic function, an observation which suggests that asymptomatic infected infants could respond normally to the usual EPI antigens. A small prospective study showed that 2 of 7 asymptotically infected children had evidence of immunologic abnormalities (15).

5. CONCERNS ABOUT IMMUNIZATION OF HIV INFECTED CHILDREN

There are several pressing questions concerning HIV infection and immunization programmes. The most important of these are as follows:

a. What is the risk of transmitting HIV from HIV-infected infants to vaccinators?

HIV can be spread parenterally which introduces the possibility of needle stick transmission from an HIV-infected infant to a health worker, a well described problem with hepatitis B. Fortunately there are good data showing that HIV is far less infectious than hepatitis B. One possible explanation for the lower infectivity of HIV is that the number of viral particles in blood with HIV infection is far lower (10^4 /ml) than that noted in hepatitis B carriers (10^{13} /ml).

U.S. data show that the risk of transmission of HIV through needle stick is very low, perhaps twenty times lower than in the case of HBV, in the order of one per 100 accidents. Two cases of needle stick transmission of HIV have been well documented. Both these accidents involved deep injection with highly contaminated needles of a large calibre (16,23). Over 900 other health workers with needle exposure from AIDS patients have been followed over a period of more than 12 months and have not seroconverted (16). Furthermore, the types of injections given during immunization sessions do not as a rule cause bleeding. Thus the risk of transmission of HIV to vaccinators is extremely low and there is no reason to curtail or restrict immunizations to be provided to confirmed or suspected HIV carriers on that basis.

b. What is the risk of HIV infection to other infants being immunized?

Needle sharing is a well described mode of spread of HIV among IV drug users. Since HIV is not spread by casual contact the risk to other infants in immunization clinics would be parenteral transmission of HIV from an infected to an uninfected child via a contaminated needle. No instances of immunization-related spread of HIV have been reported and if proper sterilization of needles and syringes is done and vaccines are administered correctly the risk of transmission of HIV is zero.

Additional evidence on the lack of association between immunization and HIV infection has recently been described from Zaire where HIV-infection in infants and children was not associated with immunization (9).

Because of logistic and financial constraints the practice of multiple immunizations with a single needle and syringe (or with multiple needles and a single syringe) still occurs in immunization programmes. These practices must be stopped and the "each child - one sterile needle - one sterile syringe" rule meticulously followed.

c. Will infants with symptomatic and asymptomatic HIV infection respond to EPI antigens?

There is evidence that infants with asymptomatic HIV infection will respond to EPI antigens although more information needs to be obtained on this point.

Halsey has studied measles seroconversion rates in infants born of HIV-positive mothers and showed that they were no different than those noted in infants born of mothers who were seronegative (17). He was able to identify

four infants who were HIV positive by Western blot testing. Two were susceptible to measles and both seroconverted after immunization. No adverse effects were noted in any of the children. Krasinski measured measles antibody titers in 10 children with HIV infection who had received measles vaccine (18). Four of the ten children had been immunized at 18 months and had not seroconverted. These data suggest a poor immune response to measles vaccine.

There is little question that infants with clinical AIDS have all of the immunologic abnormalities of adults with AIDS and in one study have been shown to respond poorly if at all to killed antigens (14).

Most of the data are fragmentary and a systematic study of the responsiveness of symptomatic and asymptomatic HIV-infected infants to EPI antigens needs to be done.

d. Are any EPI antigens dangerous to infants with symptomatic and asymptomatic HIV infection?

Many children infected perinatally with HIV have received routine immunization with OPV and Measles-Mumps-Rubella vaccine before their illness was recognized. Vaccine histories were tabulated for 74 in the US who were children subsequently found to have AIDS, AIDS related illness, or asymptomatic HIV infection. Seventy (95%) had received at least one dose of OPV and 21 (28%) had received Measles-Mumps-Rubella (MMR) vaccine. Eleven, eight and one had received one, two or three doses of OPV respectively and six had received MMR after the onset of symptoms of AIDS. There were no reports of paralytic poliomyelitis or atypical measles in this group. The population is small but the results suggest no evidence for a high incidence of side effects (19).

Only two adverse effects following immunization have been documented among HIV infected persons:

- A 19 year old asymptomatic army recruit received multiple immunizations during basic training including primary immunization with smallpox vaccine. Two and one half weeks later he developed cryptococcal meningitis and a diagnosis of AIDS was made. While being treated for the meningitis he developed generalized vaccinia. He was treated with vaccinia immune globulin and recovered from his generalized vaccinia (20).

- A 29 year old man with known AIDS and Kaposi's sarcoma traveled to Mexico for medical treatment of his AIDS. In February 1984 he was given a dose of BCG. In June 1984 the site of the BCG inoculation ulcerated and drained. He developed axillary adenopathy on the side of the ulceration and persistent fever. He was treated with isoniazid and ethambutol and promptly recovered. Two blood cultures taken when therapy was started grew Mycobacterium bovis (21).

There have been no reported cases of vaccine-associated poliomyelitis in HIV-infected vaccine recipients or contacts nor have there been reports of severe adverse effects following MMR administration in U.S. areas where pediatric AIDS cases are occurring.

Concerns have been expressed on theoretical grounds that antigenic stimulation by immunization with inactivated vaccines might lead to a deterioration of the clinical status of HIV infected children, but this effect has not been documented (24).

In summary, except for the case of disseminated M. bovis infection cited above there are no data that suggest that routine immunization would be hazardous to infants with symptomatic or asymptomatic infection with HIV.

More data need to be obtained on this crucial point, particularly on the safety of BCG immunization in infected infants. It must also be remembered that all these observations have been made in the United States where the great majority of AIDS case have occurred in adults, an age group not likely to receive many vaccines.

6. RECOMMENDATIONS

Table 1 summarizes recommendations on the use of EPI vaccines in HIV-infected infants in countries where a significant risk from the EPI target diseases persists. They are based on incomplete data. Each of the questions discussed above should be studied more formally.

While the risks of immunization are not known with certainty, potential risks may exist if HIV infected children are not immunized. HIV infected children are more likely to visit health facilities and it is known that health facilities play a significant role in the transmission of EPI diseases. Measles infection among patients with immune deficiency may be severe, protracted and fatal (24).

Table 1. Recommendations on the use of EPI antigens in HIV-infected individuals in countries where the EPI target diseases remain important causes of morbidity

	Vaccine	Asymptomatic	Clinical AIDS
Infants	BCG	yes	no
	DPT	yes	yes
	OPV	yes	yes
	IPV	yes	yes
	Measles	yes	yes
Women	Tetanus toxoid	yes	yes

a. Killed vaccines

There appears to be no risk to giving killed EPI antigens such as DPT or IPV vaccine to infants with HIV infection. Asymptomatic infected infants may respond to these antigens and even if response is blunted or absent there is little likelihood of harm being done. The usual EPI schedule emphasizes DPT at 6, 10 and 14 weeks. Since clinical AIDS occurs for the most part 4 to 6 months after birth there may be sufficient time to complete a primary immunization series at a time when antibody production is likely to occur.

b. Measles and OPV

In general live vaccines are not given to severely immunocompromized infants. However any recommendation not to give a particular antigen should be based on an appropriate weighing of the risks of the vaccine and the risks of acquiring the disease. For example, in virtually all developing countries the risk of infection from measles and poliovirus is currently 100% in unvaccinated children. Since more than one percent of all measles cases in developing countries die and the risks from measles vaccine in HIV-infected infants appear to be low, a strong case can be made for measles immunization in HIV-infected infants. Similarly, OPV appears to be a safe vaccine even when given to children with symptomatic HIV-infection and it should be used where the risk of poliomyelitis exists.

c. BCG

A firm recommendation pertaining to BCG is difficult to make at this time because so few HIV infected persons that have received BCG have been studied. There is one well documented case of progressive BCG infection after immunization in an AIDS patient and tuberculous infections are common among AIDS patients (22).

An argument for continuing BCG immunizations at birth in populations with both vertical transmission of HIV and a high prevalence of infection with Mycobacterium tuberculosis can be made on the grounds that soon after birth, infants will not have signs of immunodeficiency and may therefore respond to BCG like normal infants and this vaccine may give them some protection from tuberculosis, one of the diseases from which HIV infected children are more likely to suffer than others.

The situation for infants who have clinical AIDS is different. The likelihood that BCG would be effective is low and the possibility of dissemination would be expected to be high. Thus, any infant who is thought to have AIDS ought not receive BCG.

d. Administration of vaccines

To date there has been no evidence of HIV transmission by immunization. Nonetheless it is theoretically possible and the only means for guaranteeing that this will never occur is rigorous adherence to the principle of "each child - one sterile needle - one sterile syringe". Supervision and programme reviews should emphasize this point.

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