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Preventive Strategies for Pediatric AIDS

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The International community set for itself the seemingly possible goal of 'Health for All by 2000.' However, in the last decade and a half the onset of HIV/AIDS as a global pandemic has offset the plans of health care providers. The absence of any effective vaccine, and the rather bleak prospect of finding one in the near future has forced countries to have a fresh look on their priorities in the health sector, and redefine public health principles.

The infection mainly is prevalent among the productive age groups, but a significant factor that has been emerging in the recent years has been that of the infection being passed on to the infants through an infected mother has also affected the gains in infant mortality. This is increasingly being seen in developing countries.

This poses the challenge of pediatric AIDS. The absence of a cure however, to a large extent is offset by the knowledge that AIDS or the HIV infection is largely preventable. HIV infection among babies and children is being recorded since the year 1983. Of all the pediatric AIDS cases reported thus far, it is estimated that 90% of the cases are from Sub-Saharan Africa where it poses to be a major source of worry for AIDS workers. Though the spread of the infection in India was considerably later than that in Africa, it has now reached almost to all parts of the country.

Pediatric HIV infection is preventable and public health measures have to be tuned to stem the spread of the infection to new-borns. Once acquired, HIV infection is lifelong and in most cases is fatal. Pediatric AIDS on the other hand is fatal. However, early diagnosis of Pediatric AIDS helps in providing the available therapy and in further prevention in transmission of the infection.

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HIV Transmission

In pediatric AIDS, the common modes of HIV transmission are :

1. through blood or blood products.

2 by vertical transmission from an infected mother to her child.

3. in addition to the above, in adolescent children the transmission could occur due to the sexual contact and injecting drug use.

There are certain situations like in the case of thalassemic and hemophiliac children, transmission by transfusion on infected blood or blood products could occur due to the frequent transfusion that they have to undertake. In areas of the North-east, cases of injecting drug use have also been reported, but in small number.

Vertical transmission constitutes the major mode of transmission of pediatric

AIDS. With increase of seropositivity among pregnant women, there is a concurrent rise in number of HIV infected infants, who at the time of birth are clinically and immunologically normal. Several prospective studies conducted in Europe and Africa reveal that 15-30% of children born to HIV infected mothers become infected with the virus. Preliminary reports from Thailand indicate that the rate of vertical transmission is between 27-41%. Of these infected children, 80% will develop clinical diseases within the first two years of their life.

Breast feeding also constitutes some amount of risk for transmission of the virus to infants after they have been born. In some cases, it has been reported that women who were infected after delivery have subsequently transmitted the infection to their babies, presumably through breast feeding.

Diagnosis of Pediatric HIV Infection

Diagnosis of pediatric HIV infection is difficult as the known testing methods rely on detection of antibodies. At birth, the infants also inherit antibodies from their mother which live in their bodies for several months, thus making it difficult to distinguish the child's antibodies from those of the mother. This is further compounded if the mother is also breast feeding.

Diagnosis of HIV infection among newborns for the first 15 months is difficult because of the presence of maternal antibodies. Specific diagnosis of the virus culture is possible, but is time consuming and expensive. Another method is to use another type of viral assay called Polymerase Chain Reaction (PCR) which enables one to detect an extremely sensitive, specific and fast turned around time (2-3 days). While this test is promising, it is very costly for developing countries to afford.

Dr. James Brenner of the Rush Presbyterin – St. Lukes Medical Center, Chicago, U.S.A. has investigated the ability of a new kit called the HIV DNA Amplicor PCR assay, which is soon to be marketed and would be able to detect HIV infection among infants within the first six months. His investigations revealed that HIV infected children could be identified using this kit within the first six months and mostly within the first two months, after birth. He also observed that the kit is particularly useful and requires only 2 litres blood.

Other laboratory tests for determining immunological functioning are :

1. Elevation of serum IgG level with a 1.8 gm/dl at one year or over 2.3 mg/dl at two years.
2. Reversal T-helper/a suppressor ratio (T4/T8) and less often marked in children.
3. Cutaneous delayed hyper sensitivity test is delayed or absent.

In asymptomatic cases, detection in infants is only possible by doing a serological test of detective HIV antibodies. The ELISA or rapid test using agglutination methods could be employed as a screening test. This has to however be followed by a western blot, and immuno-fluorescent technique. Since maternal antibodies could be present up to the first fifteen months, the confirmatory test would have to be conducted after this period. Various methods to distinguish between

the material antibodies from those of the fetus like estimation of the IgA and anti-HIV antibody IgM anti-HIV antibody or differentiating western blot of new born are being tried, but are in experimental stages.

Prevention of AIDS : Pediatric Perspective

The mode of transmission of HIV infection in children below 13 years of age is just the reverse of the adult HIV infection. In 75% of the infected children, infection is transmitted perinatally from infected mothers, and in remaining cases repeated blood transfusion due to some primary illness like Hemophilia or Thallassemia are responsible for infection.

Perinatal transfusion can occur within utero, during delivery and post-natally through breast milk.

Chance of HIV infection in babies born of HIV infected mother is 25-30%.

Increased risks are observed with maternal history of AIDS, injecting drug abuses, sexual intercourse with high risk males etc.

Children born to mothers, and their partners who have high risk behaviour are more at risk of acquiring the infection.

Preventive Strategies

1. All blood or blood products being used for pediatric patients must be tested for HIV.

2 (a). Infected mothers wanting to have a child must weigh all the consequences before having a child, preferably with the help of a trained counsellor.

2 (b). HIV infected mothers have maximal chance of transmitting the infection to the foetus during the time of delivery, as there is presence of the virus in good number in vaginal secretion and blood. To minimise this the following strategies have been generally undertaken:

(i) Caesarean section in case of known HIV positive mothers before the 36 weeks of pregnancy so that uterine contraction has not started and chance of transmitting the infection is minimal.

(ii) To minimise the handling of the foetus during delivery.

(iii) To shorten the period of labour by various means.

2 (c). HIV may be transmitted postnatally through breast milk and it is therefore recommended that infected mothers should not continue to breast feed the child. Nevertheless W.H.O. advocates for the developing countries that breast feeding should be continued by the infected mothers in view of the fact that the child may potentially fall prey to many infectious diseases like diarrhea, respiratory diseases etc. in the absence of breast feeding, as also the nutritional and economic status are poor in these countries.

Prevention

The best way of avoiding HIV infection in infants is with the infected mother opting not to have children biologically. However, since this is not feasible, hence enforceable counselling of such infected individuals and their spouses is recommended. Dr. Stephane Blanche of the Hospital Necker, France gave comprehensive review of the subject in the Xth International Conference on AIDS.

He first stated there are multiple ways that the virus can be transmitted from

mother to child, but the materno-foetal blood exchange during delivery is the most probable route.

There are several instances which suggest that the majority of HIV transmission occurs towards the end of pregnancy. According to Dr. Blanche infection of foetus before 20 weeks of gestation is rare, with transmission occurring at delivery in majority of the cases. The literature quotes the different maternal factors which influence the transmission like maternal viral load and CD_4 cell count of the infected mother.

For the prevention of materno-foetal transmission of HIV, several reports appeared in the Xth International Conference on AIDS and STD. The noted amongst those was a report by Dr. J. Lange, Chief of Clinical Research and Drug Development at GPA. In his report he gave an interim analysis of a phase III randomised placento control trial to evaluate the efficacy, safety and tolerance to zidovudine in preventing materno-foetal HIV transmission. He reported significantly high reduction of transmission risk amongst women who received zidovudine. In a multi-centric trial, 477 women were enrolled in the study. The interim results have shown a significant decline in materno-foetal transmission of HIV infection. It has approved the validity of zidovudine in reducing the materno-foetal transmission. Unfortunately, the cost and logistical issues will probably prevent this type of intervention in developing countries. It was announced in the conference that U.S. Food and Drug Administration (FDA) has approved zidovudine for use as therapy to prevent transmission of virus from HIV infected pregnant women to their babies.

Dr. Blanche further reviewed on the possible protection afforded by caesarean section. However, contradictory results have been published about this. He has also dealt with the possibility of discouraging breast feeding. There is also a potential risk from artificial feeding in developing countries.

Vaccine against HIV

In any communicable disease the normal practice is to develop a vaccine against the causative organism which is isolated and characterised. AIDS has no cure. Scientists all over the world are trying to develop a safe and effective vaccine for HIV. This would be an important advantage to present future prevention strategies.

As is already known, HIV infection has a long incubation period. In the natural history of HIV infection it is seen that after initial HIV infection, there is a viral burst in the body and there is a viraemia. It is soon followed by a period when there is a major decrease in the amount of virus, culturable from blood. For 8 to 10 years sometimes even more, the specific immune response to HIV plays an important role in which it delays the replication of virus thereby onset of symptoms also get delayed. The HIV specific immune response is 100 fold more active than a drug being currently used to treat HIV infection and late stage disease. For effective prevention of progression of HIV infection, proper understanding of the immune effect mechanism that controls the viral replication has to be known. During the primary infection, the virus target the mucosal surfaces. From the mucosal surfaces, the viral is disseminated to multiple organs like lymph nodes, brain

etc. The important reservoir of HIV in the body are CD_4 lymphocytes, monocytes and macrophages. During the period of clinical and viral latency, there is an attempt by the host to control viral replication. An effective mechanism to control the viral replication is the antibody response and cell mediated immunity.

Two general goals in the development of a vaccine for AIDS are :

1. To prevent infection by developing immunity in people who have not been infected by virus.
2. To augment immunity in people who are already infected and prevent disease progression. The ideal vaccine which would be prophylactic against HIV infection should have the following properties :

(a) conforms complete sterilising immunity; (b) 100% effective against all strains of HIV; (c) effective against all mode of transmission; (d) immunity is long lasting; (e) inexpensive to prepare; (f) simple to administer; (g) should not have side effects

For preparing such a vaccine, the three aspects of viral host relationship have to be understood :

(i) Mode of causation of disease by the virus

(ii) Viral diversity

(iii) Mode of inducing immune response at mucosal surface from where HIV is commonly transmitted.

Presently, viral diversity poses a major problem in vaccine development as reverse transcriptase makes DNA coding cause an error in one out of every 1000 neucledtides types leading to substantial diversity of HIV. This diversity poses major problem with respect to developing a vaccine that will offer protection against the variety of viral strains that would be five subtypes of HIV should also be taken into consideration while testing candidates for vaccine. However, countries such as Thailand have isolated two subtypes.

Despite considerable research, there is not yet any vaccine for any remedy of sexually transmitted disease excluding

TABLE. Approaches to HIV Vaccine

	Advantages	*Disadvantages*
Recombinant envelope	Envelope epitopes targets for neutralizing antibodies.	High variability
Killed virus	Includes additional epitopes	Concerns regarding safety; absence of envelope
Vaccine based	Induction of cellular immunity	Safe
Salmonella based	Induction of mucosal immunity	Safety, Stability.
Naked DNA	Cellular immunity	Little prior experience.

Source : JAMA (Supplement 1993)

Hepatitis 'B'. For an effective vaccine against HIV induction of immunity at mucosal surface is important, as in that 80% of the lymphoid tissue are in the mucosal surface.

There are three phases of vaccine trial - in phase I, small number of uninfected individuals are given vaccine to assess safety and tolerability, phase II studies have evaluated immune response and doses, finally phase III trial determines whether a vaccine actually prevents infection.

A variety of potential vaccines are in phase I and phase II of development. Most of these vaccines have been prepared by the recombinant DNA technology, and a majority of these have included envelops component of the virus.

There is a group of researchers who have been trying to develop attenuated virus vaccine. The various technical approaches to HIV vaccine are given in the table on the previous page.

Despite these claims, researchers in phase I and II trials are progressing but recently Dr. Bologenes, Director, The Centre for AIDS Research, Duke University of U.S.A. spoke at length about the present research controversies and related issue of medical ethics. The NIHID AIDS Research Advisory Committee recommended that the Institute continue, but not expand the current vaccine trials with two GP 120 sub unit vaccine further along with the development.

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