Perinatal HIV infection
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Human immunodeficiency virus (HIV) infection causes a broad spectrum of disease and a varied clinical course. Acquired Immunodeficiency Syndrome (AIDS) represents the most severe end of the clinical spectrum. HIV is human RNA retrovirus, HIV type -1 and less commonly, HIV -2.

The established modes of HIV transmission are (1) Sexual contact (homosexual and heterosexual), (2) Percutaneous (from needles or other sharp instruments) or mucousmembrane exposure to contaminated blood or other body fluids with high titers of HIV (3) Vertical (Mother to infant) transmission before or around the time of birth and (4) Breast feeding.

Causes of AIDS in children have accounted for 2% of all reported cases in the United States. Of the 16,236 AIDS cases reported in Canada upto December 1998, 75% of AIDS cases were amongst women1. The proportion of AIDS cases amongst women of child bearing age has steadily increase in the western countries; from 6.2% of the AIDS cases before 1990 to 13.6% in 1998. It is estimated that across Africa over 5,00,000.00 women are living with HIV2. Almost all of the infected women are of child bearing age. More than 90% of infected children in the United States acquired their infection from their mothers. As of December 1998; across Canada, 942 babies have been identified as born to HIV infected women, 325 have been confirmed as infected and 107 have died of AIDS3. So, Perinatal HIV infection not only threatens the under developing countries, it also becomes a major health hazard in developed countries also.

The exact timing of transmission from an infected mother to her infant is uncertain, but evidence suggests that about 30% of transmission occurs before birth and 70% occurs around the time of delivery. Available evidence suggest that two third of the infections occurring before delivery are due to transmission of virus within the last 14 days before delivery. In several prospective studies and a meta-analysis, mode of delivery has been found to affect the transmission rate4. The European Mode of Delivery Study was a randomized controlled trial comparing the transmission rates for elective caesarean section versus vaginal delivery. The transmission rates for delivery vaginally, by emergency caesarean and elective caesarean section were 10.2%, 8.8% and 2.4%, respectively (P=0.009)5. The lowest rate, 2.1%, was in mothers on Zidovudine delivering by cesarean section. In vaginal deliveries a first born twin is a greatest risk of HIV infection than a second born twin. In a prospective observational study of 522 deliveries, it was found that the duration of rupture of membranes was a major factor in the risk of perinatal transmission of HIV6. If the membranes were ruptured for more than 4h compared with less than 4h, the odds ratio was 1.82 and P=0.02. Prolonged rupture of membrane even in the presence of antiretroviral therapy is associated with an increased risk of transmission and must be considered with evaluating the mode of delivery and transmission. Post partum transmission occurs through breast feeding. World wide, as estimated 1/3rd to half of mother to child transmission of HIV may be through breast feeding. Human immunodeficiency virus genomes have been detected in cellular and cell free fractions of human milk.

To prevent vertical transmission of HIV, it is

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essential to identify the maternal infection. Even the most thorough history and physical examination will identify only fewer than half of HIV positive women. Therefore, routinely offering HIV testing to all pregnant women is now recommended. In a randomized controlled trial, therapy with the antiviral agent, ZIDOVUDINE, in three phases (during pregnancy, during labour and delivery and to the newborn) reduced the proportion of HIV-infected infants from 25% to 8%. In practice, ZIDOVUDINE therapy have been effective, with a reduction of vertical transmission rates to 5% of less.

Studies are continuing to determine the efficacy of ZIDOVUDINE. Although the median age of onset of symptoms is estimated to be (12 -18) months for untreated perinatally infected infants, increasing number of children are being now identified who have remained asymptomatic for more than 5 years. Infants born to HIV infected women have transplacentally acquired antibody and therefore, become seropositive from the time of birth. This transplacentally acquired antibody complicates the diagnosis of infection.

The American Academy of Pediatric (APP) recommends the following HIV serologic testing.

1. HIV nucleic acid detection by PCR (Polymerase chain of reaction) at DNA extracted from peripheral blood mononuclear cells is the preferred test for diagnosis of HIV infection in newborn and results can be available within 24 hours of obtaining a blood sample. About 30% of infants with HIV infection will have a positive DNA PCR results; from samples obtaining before 48 hours of age. About 93% of infected infants have detectable HIV DNA by 2 weeks of age and almost all by a month of age. DNA PCR is more sensitive on a single assay than is virus culture. A single DNA PCR assay has a sensitivity of 95% and specificity of 97%. Infants born to HIV infected women should be tested by HIV DNA PCR during the first 48 hours of life. Because of possible contamination with maternal blood, umbilical cord blood should not be used for this determination. A 2nd test should be performed at (1 -2) months of age; a third test at (3 -6) month of age. Any time an infant test positive, testing is repeated on a 2nd blood samples as soon as possible to confirm the diagnosis. An infant is infected if 2 separate samples are positive. Infection can be excluded when 2 HIV DNA PCR assay performed at or beyond 1 month of age are negative.

2. Virus isolation by culture is expensive and requires upto 28 days for results.
3. Detection of the P24 antigen is specific but less sensitive than DNA PCR.
4. Enzyme immune assays are used most widely as the initial test for serum HIV antibody.
5. Another is finding of high viral load by RNA PCR, it does not decline during the first year of life unless antiretroviral therapy is initiated.

Because all babies will be HIV antibody positive due to a passive transfer of antibodies from their mother, the diagnosis of HIV infection must be confirmed by testing for viral antigen (p24), HIV DNA sequences using polymerase chain reaction (PCR) or HIV culture. Selected laboratories for a region perform these tests. Viral load testing dose use PCR testing; however, this is not the standard diagnostic test for HIV. A larger volume of blood is required for viral load testing than for the diagnostic test using HIV DNA PCR testing. It is hypothesized that infants who are infected peripartum do not have a measurable viremia until a few days after birth and that most infections occur peripartum. Therefore, the sensitivity of available diagnostic tests for perinatal HIV infection in the first 48 h of life is less than 50%. However, because there is increasing evidence that supports early combination antiretroviral therapy, identification of infection as early as possible in recommended. Cord blood should not be used to test the infant's HIV status because of the risk of contamination with the mother's blood.

Antiretroviral Therapy
The only antiretroviral agent that has been licensed for use in pregnancy is zidovudine. However, antiretroviral therapy is such a
rapidly evolving area that an expert should be consulted for appropriate therapy for an HIV-positive pregnant woman.

Antiretroviral therapy for an HIV-infected woman should be chosen to offer the best therapy for the woman's health while weighing the benefits and risks of the drugs for the fetus\textsuperscript{13}. The major benefit to the fetus is the reduction of HIV transmission and the major risk is potential drug toxicity. The literature on the toxicity of antiretroviral agents in pregnancy is sparse. The most experience is with the use of zidovudine and so far, no long term adverse effects have been observed\textsuperscript{14}.

There are no clinical features that distinguish infected from non-infected infants at birth. HIV-exposed infants should receive prophylaxis for HIV from birth. Treatment with ZIDOVUDINE in the three periods-prenatal, intrapartum and neonatal is recommended, but there is potential benefit even if given in one or two periods. In situations, where maternal HIV therapy has been sub-optimal, HIV management of the infant must be individualized so the opinion of an expert should be sought. Usually, the infant is premature the dose may need to be modified. One of the most common side effects of ZIDOVUDINE prophylaxis is anemia; therefore, hemoglobin should be checked at birth and at one month of age. Doctors should encourage giving hepatitis B vaccine to all infants of HIV-infected women and if the mother is a hepatitis B virus carrier, then in addition, the infant should be given hepatitis B immune globulin. It is recommended that an HIV-positive mother not breastfeed because of potential HIV transmission through breast milk\textsuperscript{15}.

With current therapy that dramatically reduce the rate of mother-to-child transmission\textsuperscript{11}, almost all infants followed should serorevert, that is, lose maternal HIV antibodies and become negative by all HIV tests. One goal of care is to determine, as efficiently and safely as possible, which infants are not infected. In an infected infant, the viral load increases rapidly over the first few weeks of life and by 14 days of age, the sensitivity of the DNA PCR reaches 93\%\textsuperscript{16}. It has been shown that two sequential samples tested for HIV by either PCR or culture have a negative predictive value of more than 90\%\textsuperscript{17}. The sensitivity and specificity of virological test in detecting HIV-1 in exposed infants whose mothers where taking zidovudine is similar to that of tests in untreated mother-infant pairs. The sensitivities of DNA PCR, RNA PCR and cell culture are 81.9\%, 99.6\% and 85.3\%, respectively, and specificities are 97.6\%, respectively\textsuperscript{18}. Therefore, if an infant has all negative HIV tests by PCR or culture on two specimens, one at one month and another at two to four months of age, that infant is very likely not infected. To confirm and document that an infant is not infected, he or she should be followed to at least 18 months of age, at which time he or she should have no physical findings to suggest HIV and an HIV antibody test that has become negative. Pneumocystis carinii pneumonia (PCP) occurs most frequently in infants with HIV infection between two and eight months of age, and there is a high mortality rate associated with PCP. Prophylaxis with trimethoprim/sulphamethoxazole (TMP/SMX) is recommended for all infants until their HIV status is determined\textsuperscript{19}. If the infant is known not to be infected, TMP/SMX should be stopped. For infants who have been confirmed to be infected, TMP/SMX should be used as previously recommended\textsuperscript{20}. Referral to a pediatric HIV program should be offered because the multidisciplinary teams in such programs have the resources to deal with the complexity of medical and psychosocial issues that face many of these families. Even after tests show that an infant is not infected, that child should still be followed annually because of the psychosocial issues that may affect the health of a child living in a family with other members infected with HIV. Some of the long-term issues for an affected child are disclosure of the sibling and death of a parent or sibling.
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