Perinatal HIV and Its Prevention: Progress Toward an HIV-free Generation

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KEYWORDS

- Mother-to-child transmission of HIV-1
- Epidemiology of perinatal HIV infections • Early infant diagnosis
- United States • Resource-limited settings

Since the first cases of infant HIV infection were described in the early 1980s, significant progress has been made in our understanding of risk factors for mother-to-child transmission (MTCT) of HIV as well as effective interventions to prevent transmission. MTCT of the human immunodeficiency virus type-1 (HIV-1) can occur during pregnancy particularly in the third trimester, during the intrapartum period, and for infants exposed to HIV, who are breastfed, throughout the period of lactation.[1] Before the availability of antiretroviral and obstetric interventions, about 1 in 4 infants born to women infected with HIV became infected. Among these infected infants, 50% to 60% of transmission occurred around the time of labor or delivery based on newborn infants exposed to HIV having negative cord blood or newborn polymerase chain reaction (PCR) tests that subsequently became positive within the first weeks of life.[2] Among HIV-infected breastfeeding populations, about 20% to 25% of infections occurred in utero based on positive PCRs at birth; 35% to 50% intrapartum; and another 25% to 35% of infants negative at birth and in the first 6 weeks became infected later, presumably as a result of transmission through breast milk.[1]

The authors have no conflicts of interest.

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Clin Perinatol 37 (2010) 699–719
doi:10.1016/j.clp.2010.09.002 **perinatology.theclinics.com**
0095-5108/10/$ – see front matter

Since the initial US Pediatric AIDS Clinical Trials Group Protocol (PACTG) 076 clinical trial results[3] were announced in 1994, which showed that giving pregnant women infected with HIV oral zidovudine from 14 weeks, intravenously at labor and delivery, and followed by 6 weeks of zidovudine prophylaxis to their newborns, could reduce transmission by two-thirds, significant progress has been made in resource-rich settings such as the United States and Europe, where combination antiretroviral drugs are routinely given during pregnancy and at labor, and where breast milk substitutes can be safely used and provided by government programs. Current transmission rates are estimated at less than 2% with the use of triple antiretroviral drugs during pregnancy.[4,5] International trials aimed at reducing transmission among women infected with HIV in resource-limited settings using simpler deliverable regimens have also been conducted and shown to be efficacious.[6–8] Recent studies[9–11] have focused on ways to make breastfeeding safer given the high risk of mortality from other causes among infants exposed to HIV who are not breastfed.

Despite this progress, researchers still have limited understanding of the exact mechanisms of transmission; including the maternal and infant host factors that either protect or increase the risk of transmission; whether mucosal exposure is the primary route of transmission during labor, or occurs by microtransfusions across the placenta during contractions; whether transmission through breast milk is primarily caused by cell-associated or cell-free virus; and how the virus is transported across the infant gastrointestinal mucosa.

This update focuses primarily on the epidemiology of MTCT of HIV-1 in the United States, briefly summarizes what is known about the timing and mechanisms of MTCT, and describes current efforts in the United States to eliminate new cases of mother-to-child HIV-1 transmission, including innovative national and state strategies. Updates on the epidemiology of the global MTCT epidemic, current prevention of mother-to-child transmission (PMTCT) strategies in international settings, as well as challenges, and future research directions in PMTCT of HIV are provided.

TIMING AND MECHANISMS OF TRANSMISSION

In Utero Infection

The placenta has proved an effective barrier to HIV transmission during pregnancy given that even before effective interventions only about 1 in 4 infants who were exposed to HIV became infected. Based on the timing of positivity, only about 20% to 25% of infections occurred in utero[1] and PCR analyses of aborted fetuses and early miscarriages indicated almost no transmission in the first trimester[12] or during the second trimester based on amniocentesis.[13] However, in the third trimester, the vascular integrity of the placenta begins to break down and statistical modeling data[14] suggest that most in utero transmissions probably occur in the last few weeks before delivery. It has been postulated that this may be caused by microtransfusions across the maternal-fetal placenta circulation during late pregnancy.[15,16] Intrauterine contractions during labor/delivery could also increase the risk of intrapartum transmission.

Intrapartum Infection

Other mechanisms that can contribute to intrapartum transmission are infant mucosal exposure to maternal blood and other HIV-infected secretions as the baby goes through the birth canal. The protective effect of scheduled cesarean delivery before labor onset with a 50% reduction in transmission risk[17–19] is potentially due to