Preventing perinatal and infant HIV infection

Somewhere in the world a child dies of AIDS every minute of every day. Nearly all of these infants became infected with the virus that causes AIDS from their mothers before, during, or shortly after birth. As global rates of new HIV infections soar, millions of vulnerable women and their newborn infants remain in the path of this typhoon of misery. Evidence-based methods for protecting infants from mother-to-child HIV transmission are described.

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Key points

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1. As national epidemics of HIV/AIDS continue to accelerate the rates of infection in women, increasing numbers of infants are becoming infected with HIV as a result of mother-to-child transmission (MTCT).
2. Preventing HIV infection in women of reproductive age is the most effective way to reduce the risk of HIV/AIDS to infants and young children.
3. Screening women for HIV infection during antenatal care is the foundation for targeting MTCT prevention strategies.
4. Antiretroviral treatment for infected mothers and/or neonatal antiretroviral chemoprophylaxis, along with elective caesarean section delivery and modifications in infant feeding practices can significantly protect infants and young children from the risk of MTCT HIV infection.

Since it was first recognised in 1981, AIDS (acquired immunodeficiency syndrome) has raged throughout the world killing more than 25 million people and becoming one of the most destructive global epidemics in recorded history. Despite widespread health education and prevention initiatives and recent improved access to treatment and care in many regions, last year the AIDS pandemic claimed over three million lives, including half a million children. During 2005, nearly five million people were newly infected with the human immunodeficiency virus (HIV), the cause of AIDS, including almost three-quarters of a million children (**TABLE 1**). At the beginning of this year, over 40 million people were living with HIV infection, including over 2.3 million children under the age of 15 years[1]. Each day more than 1800 children throughout the world become infected with HIV and another 1400 die as a result of AIDS[2]. Between 1982 and the end of March 2005, 1264 infants in the United Kingdom (UK) became infected with HIV as a consequence of mother-to-child transmission[3].

Almost half of the adults living with HIV and AIDS today are women. Over the past two years, the number of women and girls infected with HIV has increased in every region of the world, with rates rising particularly rapidly in Eastern Europe, Asia, and Latin America. In sub-Saharan Africa, women and girls already make up almost 60% of adults living with HIV[1].

As HIV infection rates increase in women, the risk of perinatal and infant HIV infection accelerate as a consequence of maternal infection. Viral transmission can occur during pregnancy, during birth when the newborn infant comes into contact with infected maternal birth fluids, shortly after birth or during the early months and years of life while being breastfed. Most children become infected during the peripartum period, i.e. during or shortly after delivery[2].

Preventing HIV infection in women

Any effective strategy aimed at preventing MTCT must first focus on preventing young women from becoming infected with HIV. Throughout the world, they are often more vulnerable than men to exposure and infection because of their socio-economic status and various biological influences, sexual practices and epidemiological factors[4-6]. Developing and implementing strategies to empower women (**TABLE 2**) can reduce their vulnerability to HIV infection and position them to make a more substantial (and perhaps, defining) contribution to global efforts to prevent the continuing growth of local and national epidemics[5,6].

Antenatal screening

Because effective interventions are now available to prevent most infants becoming infected from their mothers, all pregnant women in the UK are encouraged to have an HIV test as an integral part of their antental care. Screening pregnant women is essential so that infected women can be identified and MTCT prevention measures appropriately targeted. Since the late 1990s there has been a year-on-year increase in the number of infants born in the UK and Ireland to HIV-infected women, with over 1000 births in 2003. Since 2002, most HIV-

Number of people living with HIV in 2005	**Total**	**40.3 million (36.7-45.3 million)**
	Adults	38.0 million (34.5-42.6 million)
	Women	17.5 million (16.2-19.3 million)
	Children under 15 years	2.3 million (2.1-2.8 million)
People newly infected with HIV in 2005	**Total**	**4.9 million (4.3-6.6 million)**
	Adults	4.2 million (3.6-5.8 million)
	Children under 15 years	700,000 (630,000-820,000)
AIDS deaths in 2005	**Total**	**3.1 million (2.8-3.6 million)**
	Adults	2.6 million (2.3-2.9 million)
	Children under 15 years	570,000 (510,000-670,000)

TABLE 1 Global summary of the AIDS epidemic, December 2005. *Courtesy of UNAIDS/WHO AIDS epidemic update: December 2005*[1].

infected pregnant women have been diagnosed prior to delivery and the majority of these have taken advantage of interventions to reduce the risk of mother-to-child transmission of the virus. Consequently the proportion of infants who are themselves infected has been significantly reduced[7]. Just 64 children were diagnosed last year with maternally-acquired HIV infection in the UK, most of them over the age of one year at diagnosis. However, many of these children were infected abroad, mainly in Africa, where there is a higher HIV prevalence than in the UK[8].

Consequences of infection

HIV infects a variety of important immune system cells, especially a subgroup of T-lymphocytes known as $CD4^+$ T-cells. Within these and other similar cells, HIV aggressively replicates and billions of new viruses explode out of infected cells every day, invading, infecting and ultimately destroying more and more vulnerable cells. During this chronic infection, there is progressive damage to immune function as measured by the continual loss of more and more $CD4^+$ T-cells (CD4 count) matched by a corresponding relentless and persistent increase in the level of HIV in the blood (viral load) (**FIGURE 1**). The lower the CD4 count and the higher the viral load, the greater the risk of transmitting infection and the more likelihood of progression to end-stage HIV disease, i.e. AIDS[4].

Risk of MTCT-HIV

Several factors influence the risk of HIV-pregnant women transmitting the virus to their newborn infant, the most important of which are the level of maternal viral load and CD4 cell count and whether or not the newborn child is breastfed. Without treatment, the risk of transmission is between 12-25% in countries in the developed world, and between 20-45% in resource-limited settings in the developing world countries. Breastfeeding greatly increases the risk of maternal transmission[4].

Interventions to prevent MTCT-HIV

Antiretroviral therapy (ART) for infected mothers and/or neonatal antiretroviral chemoprophylaxis, elective caesarean section delivery, and modifications in infant feeding practices can all significantly protect infants and young children from the risk of MTCT HIV infection. Although all of these interventions are available in the UK and other western European countries, they are not widely available in developing world countries where children are at the greatest risk[2].

Antiretroviral treatment during pregnancy

All HIV-infected women, including pregnant women, need to be assessed for specific ART for their own health. In the UK, treatment guidelines[9] generally recommend treatment when women present with late disease and/or symptomatic HIV infection with a CD4 T-cell count consistently below 200 cells/mm^3, or who have been diagnosed with AIDS or severe/recurrent HIV related illnesses or tumour, at any CD4 count. In women with earlier disease, treatment is usually recommended when the CD4 T-cell count is between 200 and 350 cells/mm^3. The exact timing of starting ART is dependent upon individual factors, such as symptoms, patient preference, likely adherence to therapy and potential toxicity. ART consists of a combination of different types of anti-HIV drugs, all focused on inhibiting viral replication. Most drug regimens used in pregnancy contain the antiretroviral drug zidovudine (ZDN or Retrovir™).

Effective ART will significantly lower the plasma viral load (often to below the level of detection) which considerably reduces the risk of maternal transmission. The long term safety of exposure to antiretroviral drugs to infants in the womb and early in life is not known. However, there is little evidence that these drugs cause significant risk of serious abnormalities.

More specific information of ART can be reviewed on the National AIDS Manual website[10] and the website of the British HIV Association[11].

Antiretroviral chemoprophylaxis

A three-part ZDN regimen is used as the standard chemoprophylaxis in Europe to prevent MTCT[12]. ZDN is given during pregnancy, during labour and in the neonatal period, commencing at 28-32 weeks' gestation. This protocol, known as PACTG 076, is based upon data from the Pediatric AIDS Clinical Trials Group (PACTG) demonstrating a potential to reduce the risk of MTCT by 70%[11] following its introduction over ten years ago[13]. Other drugs may be used in combination with ZDN in modifications

- Remove the financial barriers that prevent girls from going to school.
- End violence against women.
- Implement laws to safeguard women's property and inheritance rights.
- Delay child marriage.
- Provide voluntary HIV testing and counselling in a sensitive environment, before pregnancy and during antenatal care.
- Improve access to general health, prevention, sexual and reproductive services for all women, including people living with HIV and members of vulnerable groups with specific needs, such as young brides.
- Ensure that male and female condoms are more cheaply and readily available and promote their use.

TABLE 2 Reducing women's vulnerability to HIV infection[5,6].

of this protocol, e.g. nevirapine, lamivudine[12].

In the resource-limited areas in the developing world where PACTG 076 approaches are unaffordable, the World Health Organization (WHO) recommend a less-effective but less expensive short-course ZDN regimen[14]. Various regimens using other drugs, including lamivudine and single dose nevirapine to the mother about an hour prior to birth and to the infant shortly after birth, are also used[14, 15].

Elective caesarean section delivery

There is considerable evidence demonstrating the high risk of MTCT during birth, including observations that HIV transmission rates are lower in second-born twins compared to first-born twins and following elective caesarean section compared to vaginal delivery[16, 17]. HIV has been found in the vaginal and cervical secretions of pregnant women and also in gastric secretions of infants born to HIV-infected women[18, 19].

Neonates can become infected during vaginal delivery when they are exposed to HIV-contaminated birth fluids, either through ingestion into the gastrointestinal tract or from the close contact their skin and mucous membranes have with birth fluids. Ruptured membranes of greater than 4 hours are significantly associated with increased risk of intrapartum transmission to infants born by caesarean section or vaginal delivery, as the neonates have been exposed to infectious material for longer[20].

Current European recommendations acknowledge that elective caesarean section delivery carried out before labour at 38 weeks' gestation, significantly reduces the risk of MTCT[12]. However, this benefit may be less important in mothers who have a low or undetectable plasma viral load.

Modifications in infant feeding practices

There are immense benefits to both mother and infant in breastfeeding, especially during the early months of life. Breastfeeding protects against respiratory infections and diarrhoea disease, two of the most important causes of childhood mortality, and has significant economical, social, psychological and family planning advantages. Nevertheless, in infected mothers, HIV is found in breast milk at any point during lactation and the risk of HIV transmission to breastfed infants can be considerable. In Africa, where prolonged breastfeeding is common, breastfeeding can be responsible for 42% of HIV infections in infants and young children. Overall, an estimated 5 to 20% of infants born to HIV-infected mothers are infected postnatally from breastfeeding[21].

In the UK and in other countries in Europe and throughout the developed world, guidelines recommend that HIV-infected women should refrain from breastfeeding and use formula feed[12, 22]. Elsewhere, the WHO and the United Nations Children's Fund (UNICEF) also recommend that HIV-infected mothers completely avoid breastfeeding when replacement feeding is acceptable, feasible, affordable, sustainable and safe. However, this option is not available to most women in resource-limited settings where formula feed is frequently unaffordable and associated with increased health risks, e.g. gastroenteritis.

An observational study from South Africa reported that mixed feeding (defined as breast milk plus water, other fluids and foods) in the first three months of life was associated with increased risk of infant HIV infection when compared with exclusive breastfeeding[23]. Further information from this study showed that, at 15 months of age, the lowest rates of infant infection were found in the never-breasted group, followed by the exclusively breastfed groups and that the rates in the mixed-fed group were the highest[24]. Accordingly, WHO, UNICEF and the Joint United Nations Programme on AIDS (UNAIDS) recommend exclusive breastfeeding for those HIV-infected women who choose to breastfeed[25].

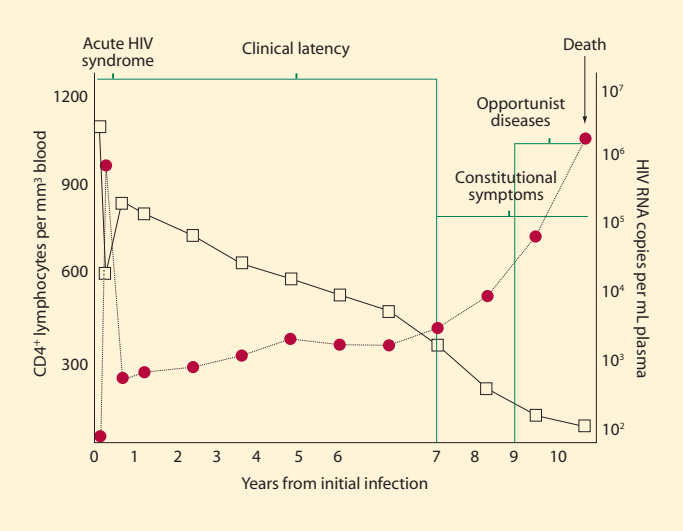

FIGURE 1 The clinical course of HIV infection and disease in relation to the CD4+ T-lymphocyte cell count (□) and the viral load (●).
From: Pratt R.J. et al. Tuberculosis: A foundation for nursing and healthcare practice. London: Hodder-Arnold. 2005.

Infant feeding – implications for practice

Despite the advances in prevention and treatment of MTCT-HIV, not all women are screened during pregnancy. Women newly arrived in the UK and those who book late or arrive in labour should be encouraged to undergo screening, even after delivery. For those identified as HIV-infected, formula feeding offers the best protection against MTCT, yet many women will feel a loss at not being able to breastfeed, particularly where this is a cultural norm. These mothers will require considerable support, including help with creating a reason for not breastfeeding, in order to protect their confidentiality from friends and family. This is particularly important where baby friendly policies that promote exclusive breastfeeding are in place. On discharge from hospital it is important to ensure that the mother has a sufficient supply of formula milk, knows how to use it and where and how to obtain further supplies.

Summary

As long as women remain vulnerable to HIV infection, the risk of MTCT will remain. Antiretroviral treatment and/or chemoprophylaxis, caesarean delivery and modifications in infant feeding practices are all highly effective in reducing the risk of maternally transmitted HIV infection to infants and young children. Nurses and other healthcare professionals are uniquely placed to provide accurate information, encourage antenatal screening for HIV infection and support parents and families in making the right choices for them and their newborn child. The prime factor that drives their decisions should be the

protection of the child from avoidable chronic disease and early death.

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