Editorial: **Giving antiretrovirals in the peripartum period to prevent mother-to-child HIV transmission in low-income countries: only a short-term stopgap measure**

R. Colebunders¹, P. Kolsteren¹ and R. Ryder²

¹ Institute of Tropical Medicine, Antwerp, Belgium
² The North Carolina Center for Public Health Preparedness, Chapel Hill, NC 27599, North Carolina, USA

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Without interventions the rates of transmission of HIV from an infected mother to her child in Africa remain unacceptably high, ranging from 10% to 45% (The Working Group on Mother-to-Child Transmission of HIV 1995; Dabis & Ekpine 2002; Rollins et al. 2002). The intra-uterine transmission rate is estimated to be 5–10%, the intrapartum transmission rate 10–20% and the transmission rate through breastfeeding 10–20%. These rates vary according to maternal HIV viral load – the higher it is, the greater the infection rate. Viral load can now be successfully manipulated by an effective but expensive pharmacological intervention. In industrialized countries, where highly active antiretroviral treatment (HAART), caesarean section and artificial feeding are widely available, mother-to-child transmission (MTCT) rates of <3% are common (Beckerman 2002). In developing countries the same effective drugs are only rarely used because of their high cost. As a result of this economically driven imbalance, mother-to-child HIV transmission now occurs almost exclusively in resource-poor countries. How long can this injustice be tolerated?

Several ambitious efforts have recently been launched to ameliorate this unacceptable situation. Several large-scale MTCT prevention programmes were initiated such as those by UNICEF (2001) and the Elizabeth Glazer Pediatric AIDS Foundation (2002) (Kanshana & Simonds 2002), which represent an important step forward in making antiretrovirals (ARTs) universally available. So far however, these programmes had a relatively low cost–benefit ratio. For an MTCT HIV prevention programme to be successful, pregnant women must follow several, often difficult sequential steps: (1) presentation at an antenatal care unit equipped to conduct voluntary counselling and testing (VCT) and responsibly dispense ART; (2) accept pre-test counselling and HIV testing (only a relatively small number of these women will be HIV seropositive); (3) return for their test results; (4) accept therapy; (5) correctly receive and administer therapy; (6) agree to formula-feed their children if formula is available. At each step, losses will occur that will decrease the expected effectiveness. Although no data are available to estimate overall programme effectiveness, some indications of low performance can be deduced from the several MTCT trials that have now been conducted. A meta-analysis of 13 studies in Africa and Thailand found that the return rate, regardless of HIV status, fluctuated between 33% and 100%, with a median of 83% (Cartoux et al. 1998). There are two main factors that decrease overall programme effectiveness. First is the low participation rate of pregnant women (Cartoux et al. 1998; Msellati et al. 2001; Gaillard et al. 2002). Indeed, very little is offered to them and their partner. They remain untreated. The way most current MTCT programmes are structured decreases the incidence of perinatal transmission but increases the incidence of orphanage, hardly an effective long-term solution. Pregnant women are often afraid to be tested because of the stigma linked to HIV infection (Cartoux et al. 1998). They feel, quite understandably, that it is better to simply not know. These women may worry that the husband will discover that they are HIV seropositive; they may fear being abandoned or experiencing violence (Cartoux et al. 1998). Secondly, if artificial feeding is not an option, HIV transmission rates remain high (Nduati et al. 2000; Beckerman 2002). The long-term results of the Petra study have shown that 15–20% of infants who received short course zidovudine + lamivudine therapy were infected with HIV or dead by the age of 18 months (The Petra Study Team 2002). This long-term loss of benefit has been attributed to the transmission of HIV during breastfeeding. A retrospective study in South Africa suggested that exclusive breastfeeding might lower the risk of HIV transmission more than mixed feeding.
(Coutsoudis et al. 2001). However, these findings remain to be confirmed in prospective studies. Based on a pilot MTCT project in Thailand, where 80% of children born to HIV seropositive mothers received formula-feeding, and where the average risk for MTCT dropped from 30% to less than 10%, it was estimated that in Thailand 2500 infant HIV infections have been prevented each year (Kanshana & Simonds 2002).

In countries with limited resources, formula-feeding is not a safe option for most women with HIV infection (WHO 2001). In these settings, the most prudent course may be to start HAART in the third trimester of pregnancy, and continue it throughout the period of breastfeeding. This will decrease the viral load in the breast milk and thus significantly decrease the risk of post-natal HIV transmission. Women who need HAART for their own health [according to the recently proposed WHO (2002) criteria] should continue to receive such treatment without interruption after the breastfeeding period. For pregnant women who do not yet need HAART for their own health, we propose to start HAART in the third trimester and to continue it through the period of breastfeeding (≥6 months). If later these women develop HIV disease requiring treatment, HAART should be restarted.

However, anecdotal experience has suggested that it may not be possible to treat only HIV-positive mothers. All HIV-positive pregnant women had a recent sexual partner whose HIV status is likely to be unknown. These partners will also need counselling and testing. Initiating HAART in the post-partum period only for HIV-positive women will certainly induce domestic problems. Programmes seeking to implement ART treatment for women in the post-partum period will be under considerable pressure to also treat HIV-positive sex partner(s) (fathers) who meet the WHO criteria for initiating HAART.

Offering HAART to pregnant women and their partners has many advantages. It will improve the quality of life of HIV-infected parents (and thus improve their parenting efforts), decrease child mortality and the number of orphans because parents remain alive and healthy. In addition, less ART resistance will be induced than with the short-course mono- or bi-therapy regimens currently in use (Jackson et al. 2000; Eshleman et al. 2001). Providing HAART to women post-natally will also decrease stigmatization associated with HIV because women with HIV infection will be able to breastfeed their children just as healthy women do. Offering HAART to women and their partners will motivate people in the community to present for HIV testing and counselling, thus leading to increased awareness about HIV. Because HAART regimens are now offered at less than 1 US$ a day (Kumar 2001), our proposition is a realistic option for many pregnant women with HIV infection in developing countries in the near future. However, before implementation, we should identify optimal, cost-effective HAART regimens to achieve minimal viral loads in breast milk. A single 200-mg dose of nevirapine administered to pregnant women results in a nevirapine concentration in breast milk of >100 μg/l (10 times in vitro IC50 against wild-type HIV) (Musoke et al. 1999), but we have no information about drug levels in breast milk achieved by oral administration of other antiretrovirals. Pilot studies need to be conducted to measure ART levels in plasma and breast milk of mothers treated with different HAART regimens and in plasma from their children during breastfeeding. Moreover, children should be monitored for potential side-effects of the antiretroviral drugs.

Presently MTCT plus programmes are being planned in several centres in resource poor countries (Mailman School of Public Health at Columbia University 2002), which will provide HAART to mothers and their partners. We propose that these programmes make concerted efforts to assure that HAART will be given during breastfeeding.

References

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**Authors**

R. Colebunders, Department of Clinical Sciences, Institute of Tropical Medicine, Nationalestraat 155, 2000 Antwerp, Belgium. E-mail: bcoleb@itg.be

P. Kolsteren, Department of Public Health, Institute of Tropical Medicine, Nationalestraat 155, 2000 Antwerp, Belgium. E-mail: pkolsteren@itg.be

R. Ryder, University of North Carolina, Chapel Hill Department of Medicine/Epidemiology, Chapel Hill, NC 27599, USA. E-mail: Robert_Ryder@unc.edu