Published in final edited form as:
Curr Opin Pediatr. 2009 February ; 21(1): 94–101. doi:10.1097/MOP.0b013e32831ec353.

Update on successes and challenges regarding mother-to-child transmission of HIV

Elijah Paintsil[1,2] and **Warren A. Andiman**[1,3]

1 *Department of Pediatrics, Yale University School of Medicine, New Haven, Connecticut, USA*

2 *Department of Pharmacology, Yale University School of Medicine, New Haven, Connecticut, USA*

3 *Department of Epidemiology & Public Health, Yale University School of Medicine, New Haven, Connecticut, USA*

Abstract

Purpose of review—There is an unprecedented global commitment to reverse the pediatric HIV epidemic by making prevention of mother-to-child transmission (MTCT) services accessible in all countries. This review outlines the successes made and the challenges that remain.

Recent Findings—In resource-rich countries, MTCT rates of HIV as low as 1% has been achieved. The efficacy of short course antiretrovirals (ARVs) for the prevention of MTCT (PMTCT) in Africa is estimated at 50%. Co-infections with herpes simplex virus type 2 (HSV-2), other sexually transmitted infections resulting in genital ulcers, and endemic infectious diseases (e.g., malaria) may increase the risk of MTCT of HIV. Vertical transmission of drug-resistant viruses has been reported; the prevalence and effect of transmitted resistant virus on treatment outcomes are under investigation. Obstacles facing PMTCT in resources-limited countries include lack of health care infrastructure, limited manpower, and competing public health priorities with the limited health care budget.

Summary—While the birth of an HIV-infected child in a resource-rich country is now a sentinel health event, in most resource-limited countries the birth of an HIV-infected child continues to be the status quo. Comprehensive PMTCT including ARV treatment for HIV-infected women and HIV-infected children should be paramount in resource-limited countries.

Keywords

Prevention of mother-to-child transmission; HIV; antiretroviral drugs; resource-rich setting; resource-limited setting; drug-resistant virus

Introduction

Much progress has been made in containing the HIV epidemic, though it is unevenly applied among countries. The introduction of antiretroviral chemoprophylaxis to prevent mother-to-child transmission (MTCT) of HIV was an important milestone in pediatric HIV. In 2007, about 370 000 (330 000 – 410 000) children less than 15 years of age became infected with HIV; almost exclusively through MTCT (1). The United Nations General Assembly made a commitment in 2001 to reduce MTCT of HIV by 20% and 50% by 2005 and 2010, respectively (2). In this review, the successes at reaching these goals and the challenges that remain are discussed.

Correspondence to Elijah Paintsil, Yale University School of Medicine, Departments of Pediatrics and Pharmacology, 333 Cedar Street, New Haven, CT 06520-8064, USA Tel: +1 203 785 7119; fax: +1 203 785 6961; e-mail: Elijah.paintsil@yale.edu.

Basic principles of mother-to-child transmission of HIV

Without any intervention to prevent transmission, the rate of MTCT of HIV is estimated at 12–40% (3). MTCT of HIV can occur before, during, and after birth. The relative contribution of each of these modes of perinatal transmission is not well defined (4). The risk factors associated with MTCT are illustrated in Table 1. In resource-limited countries, breast feeding contributes significantly to MTCT.

Prevention of mother-to-child transmission

Current interventions to prevent MTCT target the late intrauterine and intrapartum periods, when most transmission events occurs. Administration of antiretroviral drugs to an HIV-infected mother and her infant, careful management of labor and delivery (with elective caesarean delivery for women with high HIV viral loads) and avoidance of breast feeding have reduced the rate of MTCT to less than 2%.

The containment of the HIV epidemic is inextricably linked to the socioeconomic, cultural and political milieu of a country. Therefore, the successes and challenges of the prevention of MTCT (PMTCT) of HIV are discussed under two headings: resource-rich countries (high income countries) and resource-limited countries (low and middle income countries).

PMTCT successes in resource-rich countries

In 1994, a landmark Pediatric AIDS Clinical Trials Group study (PACTG 076) demonstrated a 67% reduction in perinatal HIV transmission with the administration of a combination of prenatal, intrapartum, and neonatal zidovudine (ZDV) (5). The US Public Health Task Force adopted the study's finding and recommended that all pregnant women should be offered HIV testing and that those women who were identified as HIV-infected should be given the 3-part ZDV regimen (i.e., the PACTG 076 regimen). There is an increase in the acceptance and completion of rapid HIV testing in resource-rich countries (6*).

Perinatal transmission rates as low as 1% has been achieved as a result of the use of the PACTG 076 regimen (Table 2)(7), HAART regimens, and appropriate management of labor and delivery. Therefore, the birth of an infected child in a resource-rich country is now a sentinel health event signaling a chain of missed opportunities and barriers to available PMTCT programs (8). The CDC estimates that 100 to 200 infants with HIV infection are born in the U.S. annually. The rate of mother to child transmission of HIV continues to decrease; in 2005, only about 67 HIV-infected infants were born in the US (9).

PMTCT challenges in resource-rich countries

There are ongoing issues that may reverse or threaten the gains achieved in PMTCT of HIV in resource-rich countries.

Late access to MTCT prevention services

In a French study, it was observed that pregnant women who have emigrated from sub-Saharan African countries had delayed access to HIV testing and antenatal care compared with French-born pregnant women (10**). In the US, racial/ethnic differences in the time to initiation of HAART has been observed among HIV-infected pregnant women; 42% of white women started therapy prior to pregnancy compared with 29% of Hispanic and 27% of black women (11). Moreover, the number of teenagers who were perinatally-infected and who are non-adherent to their HAART regimens who access care very late in pregnancy is on the rise.

Non adherence to HIV testing guidelines during pregnancy by providers

There are some providers who continue to offer routine HIV testing during pregnancy solely to women they consider at high risk, rather than to all pregnant women. There are cases of infected infants born to women who tested negative in early pregnancy but who seroconverted later in pregnancy, presumably as a result of recent acquisition of primary infection.

Herpes simplex virus type 2 co-infection and the risk of MTCT of HIV

Genital ulcer diseases, including herpes simplex virus type 2 (HSV-2) and syphilis, facilitate sexual transmission and acquisition of HIV. HSV-2 co-infection with HIV results in increased genital shedding of HIV (12). It is postulated that HSV-2 co-infection may increase the risk of MTCT of HIV. In a case-control study of HIV-infected women enrolled in an MTCT trial in Zimbabwe, HSV-2 infection was associated with increased intrapartum MTCT of HIV [adjusted odds ratio (OR), 1.50; 95% CI, 1.09–2.08] (13**). The administration of valaciclovir (which suppresses subclinical and clinical reactivation of HSV-2) to HIV-infected women reduced their genital and plasma HIV viral loads (14**). Further research is needed to determine if treatment of HSV-2 co-infection in HIV-infected pregnant women will result in further reduction of MTCT of HIV.

Effect of perinatal antiretroviral exposure on the infant

There are limited data on the short-term and long-term toxicities associated with exposure of an infant to ARV drugs in utero and during infancy. In long-term study (4 to 6 years), no adverse events were observed with in utero exposure to ZDV; however, there were occasional episodes of transient and self-limiting anemia (15). The women and infants transmission study (WITS) group recently reported small but significant differences in several hematologic parameters in the first 24 months of life between infants exposed and unexposed to perinatal ARVs (16). There is a need for continuous surveillance of infants exposed in utero to combination ARV therapy for emergence of adverse events.

Drug-resistant HIV and its impact on MTCT

In a recent study (PACTG P1030), about a quarter of a cohort of recently infected US-born infants were infected with drug-resistant HIV (17). Moreover, postnatal treatment of an infant to prevent MTCT may select for drug resistant HIV acquired from the mother (18). Resistant virus may be archived in the resting CD4+ T cells of the infants within the first 6 months (17). Though, not statistically significant, the children with drug-resistant virus tended to have a poor treatment outcome. Moreover, poor virologic response to nevirapine (NVP)-containing HAART regimens in the postpartum period has been observed in HIV-infected women exposed to intrapartum NVP (19).

PMTCT successes in resource-limited countries

In resource-limited countries, a number of randomized trials have assessed the efficacy of short-course ARV (sc-ARV) to reduce of MTCT of HIV (Table 2)(7). WHO recommends either the use of combination antiretroviral treatment (usually including NVP) for pregnant women in need of treatment for their own health or the administration of sc-ZDV followed by single-dose NVP (SDNVP) during labor, as well as a 7-day postpartum short-course of ZDV and lamivudine (3TC) if antiretroviral treatment is not yet indicated (20). However, SDNVP administered to the mother at labor and to the infant within 48 to 72 h or life is the most popular regimen, due to ease of administration and low cost (Table 2).

Increased coverage of ARV to HIV-positive pregnant women

Through the global initiative to scale-up ARV access in resource-limited countries, the proportion of HIV-positive pregnant women receiving ARV increased from 9% in 2004 to 33% in 2007 (1).

Efficacy of short-course ARV regimens to prevent MTCT

The efficacy of sc-ARV varies from country to country due to differences in PMTCT coverage, components and available ARV regimens (Table 2). In a meta-analysis of published clinical trials on PMTCT in Africa, the efficacy of sc-ARV to prevent MTCT was estimated at 50% (21**). The combined effect estimate of using ARVs was 10.6% (95% CI: 8.6–13.1) transmission at 4–6 weeks compared to 21% (95% CI: 15.5–27.7) transmission without ARVs (21). In a study involving 48 sub-Saharan African countries, about 31 472 infant-HIV infections and deaths were averted due to use of sc-ARV to prevent MTCT in the years 2004 and 2005 (22*).

The Drug Resource Enhancement against AIDS and Malnutrition (DREAM) program demonstrated that PMTCT outcomes can be improved significantly if programs to protect the unborn child are accompanied by ARV treatment of the mother's infection (23). Transmission rates were compared between two cohorts of pregnant women. The first cohort gave supplemental formula to their infants for the first 6 months after delivery and the second cohort received HAART during the first six months while exclusively breast feeding (24**). The MTCT rates were 4/341 (1.2%) and 7/809 (0.8%) among formula fed and breast fed infants at one of month of age, respectively. Tonwe-Gold et al. evaluated a two-tiered PMTCT strategy in which treatment was selected based on maternal medical status (as indicated by CD4+ T cell count and WHO clinical staging) in pregnant women enrolled in Abidjan, Cote d'Ivoire, in the MTCT-Plus initiative (25*). The first cohort included 107 women who received HAART (ZDV+3TC+NVP) at a median gestational age of 30 weeks and continued treatment postpartum. The second cohort of 143 women, were not eligible for HAART and they received sc-ARV (ZDV+3TC with SDNVP during labor) for prevention of MTCT. The rate of peripartum HIV transmission was 2.2%, the cumulative rate of infant HIV infection at 12 months was 5.7%, and the 12-month HIV-free survival was 88.3%, without significant difference between the two groups.

Thailand's national PMTCT program established in 2000 is the most successful in a resource-limited setting (26). Plipat et al. assessed the effectiveness of the PMTCT program in Thailand using a registry of children born to HIV-infected mothers from 2001 to 2003 in six provinces (27*). They found a transmission risk of 6.8% (95% CI: 5.2–8.9%) among 761 mother-infant pairs in whom the mothers received ZDV during pregnancy and labor and the infants received ZDV after birth. With the mother-infant pairs who received PMTCT ZDV combined with other ARVs (usually NVP), the transmission risk was 3.9% (CI: 2.2–6.6%) (27). These studies and others continue to demonstrate that a comprehensive PMTCT program (including provision of ARV to the mothers for their infection) in resource-limited countries could achieve MTCT rates as low as currently observed in resource-rich countries (24,25,27,28*).

PMTCT challenges in resource-limited countries

The obstacles facing PMTCT programs in resources-limited countries are multifaceted; lack of health care infrastructure, slow integration of PMTCT programs to traditional maternal child health (MCH) services, limited manpower, limited donor funding, and competing public health priorities with limited health care budget (29–31).

Low coverage of antiretroviral treatment and MTCT programs

At the end of 2007, 55 of 136 (40.4%) countries had less than 25% coverage of ARVs to adults and children with advance AIDS (1). Moreover, 61 of 113 resource-limited countries had less than 25% coverage of ARVs for prevention of MTCT (Table 3) (1). Some of the reasons for the low coverage of PMTCT in these countries are; lack of integration of MCH services with PMTCT (29*), lack of knowledge about HIV and PMTCT (30*), and health system failures leading to missed opportunities, i.e., non-availability of counselors, supplies such as HIV test kits, health staff giving incorrect instruction and short supply of ARV drugs (31*). Routine offer of antenatal HIV counseling and testing ("opt-out" approach) and availability of rapid HIV kits in ANC and labor ward could improve coverage and uptake of PMTCT among pregnant women (32*,33*).

Development of drug-resistant HIV to PMTCT antiretroviral agents

A 5-year follow-up study of the HIVNET 012 trial to examine the persistence of the mutation at codon 103 of the reverse transcriptase gene from 'Lysine' to 'Asparagine' (K103N) in women who received SDNVP found that of the 60 women who harbored the K103N mutation, 16, 43, 55, and 55 women demonstrated fading of the mutation by 2, 3, 4, and 5 years, respectively (34*). The K103N mutation confers resistance to HIV non nucleoside analogs. For women who were re-exposed to SDNVP for PMTCT, the detection of K103N was independently associated with its detection at 6–8 weeks after the first SDNVP exposure and pre-NVP viral load (35*). Recent studies suggest that treatment with an NNRTI-based regimen may still be effective in SDNVP-exposed women, provided that treatment is not initiated too soon (< 6 months) after SDNVP exposure (36*,37*). Combination of other antiretrovirals with SDNVP reduces the emergence of NNRTI-resistance mutations. The addition of intrapartum plus 4 to 7 days of maternal postpartum ZDV/3TC significantly reduced the prevalence of NNRTI-associated resistant mutations (38). Moreover, the addition of a single intrapartum dose of tenofovir/emtricitabine (TDF/FTC) to sc-ZDV plus SDNVP significantly reduced the prevalence of NNRTI-associated mutations in mothers at 6 weeks' post partum (39*). Further studies are needed to determine the optimal time for treatment initiation with NNRTI-based HAART and the effect of NNRTI-associated mutations on subsequent treatment with HAART.

Malaria co-infection and the risk of MTCT in resource-limited countries

The risk of MTCT of HIV associated with HSV-2 co-infection or other STIs (e.g., infections resulting in genital ulcers) described above apply also to transmissions in resource-limited settings. Moreover, in some resource-limited countries there are endemic infectious diseases that may have an impact on MTCT of HIV. There are conflicting reports on the effect of malaria during pregnancy on MTCT. A recent study, found that placental malaria was associated with increased MTCT, even at low maternal viral loads (40**). The authors suggested that prevention of malaria during pregnancy in malaria endemic areas should be part of PMTCT programs. Further research is needed to characterize the association between malaria and MTCT.

Feeding practices and MTCT

The WHO recommends exclusive breastfeeding in settings where replacement feeding is not acceptable, feasible, affordable, sustainable, and safe (20). Breast feeding is known to offer protection against diarrheal and respiratory diseases that contribute to the high rates of infant mortality in resource-limited countries. To balance the protective effect of breast feeding with the potential risk of transmission of HIV, there have been several studies on the optimum duration of breast feeding. In a mathematical model based on data from Uganda and Kenya, researchers found that reducing exclusive breast feeding delayed the time to death rather than reducing it altogether; breast feeding reduced mortality at very young ages, however, the infants

who got infected progressed rapidly to AIDS with most dying by two years of age (41*). Lehman et al. found that sc-ARVs used in PMTCT reduced the cell-free virus in the breast milk to a greater extent than the cell-associated virus in breast milk (42**). These and other ongoing studies will have impact on future recommendations on appropriate feeding practices in resource-limited settings to prevent MTCT.

Lack of PCR-based diagnosis for Pediatric HIV

In most resource-limited countries, PCR-based assays are not available for the early diagnosis of pediatric HIV. The high mortality rate of pediatric HIV in resource-limited countries is partly due to lack of early diagnosis and low coverage of pediatric HAART treatment. There is an urgent need to integrate low-cost and accessible viral nucleic acid based assays (43*,44*).

Conclusions

Much progress has been made in the prevention of MTCT; however, challenges remain that threaten to reverse the gains. Resource-rich countries should be unrelenting in their efforts to provide access to HIV testing to all women and PMTCT to HIV-infected pregnant women. Furthermore, access to comprehensive PMTCT including ARV treatment for HIV-infected women and HIV-infected children should be paramount in resource-limited countries.

Acknowledgements

EP is supported by grants from the National Institute of Health (K08AI074404), and Yale Child Health Research Center Award (K12HD001401-08).

References

Papers of particular interest, published within the annual period of review, have been highlighted as:

*of special interest

**of outstanding interest

1. Report on the global AIDS epidemic; executive summary. 2008 [cited 9/13/2008]; Available from: http://data.unaids.org/pub/GlobalReport/2008/JC1511_GR08_ExecutiveSummary_en.pdf
2. Action Guide for the united nations Country Teams. United Nations Special Session on HIV/AIDS. New York: United Nations General Assembly; 2001. Implementing the Declaration of Commitment on HIV/AIDS.
3. De Cock KM, Fowler MG, Mercier E, et al. Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice. JAMA 2000;283:1175–82. [PubMed: 10703780]
4. Kourtis AP, Lee FK, Abrams EJ, et al. Mother-to-child transmission of HIV-1: timing and implications for prevention. Lancet Infect Dis 2006;11:726–32. [PubMed: 17067921]
5. Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. N Engl J Med 1994;331:1173–80. [PubMed: 7935654]
6*. Stokes SH, McMaster P, Ismail KM. Acceptability of perinatal rapid point-of-care HIV testing in an area of low HIV prevalence in the UK. Arch Dis Child 2007;92:505–8. [PubMed: 17293365]The authors describe the high acceptance and completion of antenatal HIV testing among pregnant women and midwives in the UK.
7. Paintsil E, Andiman WA. Care and management of the infant of the HIV-1-infected mother. Semin Perinatol 2007;31:112–23. [PubMed: 17462496]

8. Mofenson LM. Can perinatal HIV infection be eliminated in the United States? JAMA 1999;282:577–9. [PubMed: 10450721]

9. HIV/AIDS Surveillance Report, 2005. Vol. 17. Rev.ed. Atlanta:. 2005 [cited September 13, 2008]; Available from: http://www.cdc.gov/hiv/topics/surveillance/resources/reports/2005report/

10**. Jasseron C, Mandelbrot L, Tubiana R, et al. Prevention of mother-to-child HIV transmission: similar access for sub-Sahara African immigrants and for French women? AIDS 2008;22:1503–11. [PubMed: 18614874]This French study describes a phenomenon that may be common in other resource-rich countries; pregnant immigrant-women having late access to HIV testing and PMTCT services.

11. Cunningham CK, Balasubramanian R, Delke I, et al. The impact of race/ethnicity on mother-to-child HIV transmission in the United States in Pediatric AIDS Clinical Trials Group Protocol 316. J Acquir Immune Defic Syndr 2004;36:800–7. [PubMed: 15213563]

12. Mbopi-Keou FX, Legoff J, Gresenguet G, et al. Genital shedding of herpes simplex virus-2 DNA and HIV-1 RNA and proviral DNA in HIV-1- and herpes simplex virus-2-coinfected African women. J Acquir Immune Defic Syndr 2003;33:121–4. [PubMed: 12794542]

13**. Cowan FM, Humphrey JH, Ntozini R, et al. Maternal Herpes simplex virus type 2 infection, syphilis and risk of intra-partum transmission of HIV-1: results of a case control study. AIDS 2008;22:193–201. [PubMed: 18097221]The risk of increased MTCT of HIV in women with HSV-2 coinfection is well described in this study in Zimbabwe.

14**. Nagot N, Ouedraogo A, Foulongne V, et al. Reduction of HIV-1 RNA levels with therapy to suppress herpes simplex virus. N Engl J Med 2007;356:790–9. [PubMed: 17314338]Treatment with valaciclovir reduces HIV viral load; implication for prevention of MTCT of HIV.

15. Mofenson LM, Munderi P. Safety of antiretroviral prophylaxis of perinatal transmission for HIV-infected pregnant women and their infants. J Acquir Immune Defic Syndr 2002;30:200–15. [PubMed: 12045684]

16**. Pacheco SE, McIntosh K, Lu M, et al. Effect of perinatal antiretroviral drug exposure on hematologic values in HIV-uninfected children: An analysis of the women and infants transmission study. J Infect Dis 2006;194:1089–97. [PubMed: 16991083]The findings of the women and infants study (WITS) group are consistent with previous French study with regard to possible long-term adverse events resulting from in utero exposure to antiretroviral drugs. The authors emphasize the need of continuous surveillance for adverse events.

17**. Persaud D, Palumbo P, Ziemniak C, et al. Early archiving and predominance of nonnucleoside reverse transcriptase inhibitor-resistant HIV-1 among recently infected infants born in the United States. J Infect Dis 2007;195:1402–10. [PubMed: 17436219]The study describes the transmission of drug resistant HIV variants from mother to child and the archiving of the resistant mutation in the resting CD4+ T-cells. This will have implication on the choice and efficacy of antiretroviral treatment for the child.

18. Nolan M, Fowler MG, Mofenson LM. Antiretroviral prophylaxis of perinatal HIV-1 transmission and the potential impact of antiretroviral resistance. J Acquir Immune Defic Syndr 2002;30:216–29. [PubMed: 12045685]

19. Lallemant M, Jourdain G, Le Coeur S, et al. Single-dose perinatal nevirapine plus standard zidovudine to prevent mother-to-child transmission of HIV-1 in Thailand. N Engl J Med 2004;351:217–28. [PubMed: 15247338]

20. World Helath Organization. Antiretroviral drugs for treating pregnant women and preventing HIV infection in infant: towards universal acess. Recommendations for a public health approach. 2006 [cited September 13, 2008]; Available from: http:/www.who.int/hiv/pub/guidelines/pmtctguidelines3.pdf

21**. Chigwedere P, Seage GR, Lee TH, Essex M. Efficacy of antiretroviral drugs in reducing mother-to-child transmission of HIV in Africa: a meta-analysis of published clinical trials. AIDS Res Hum Retroviruses 2008;24:827–37. [PubMed: 18544018]The authors, in a meta-analysis of published clinical trials on PMTCT in Africa, established that ARVs are efficacious in reducing MTCT in Africa.

22*. Boeke CE, Jackson JB. Estimate of Infant HIV-Free Survival at 6 to 8 Weeks of Age Due to Maternal Antiretroviral Prophylaxis in Sub-Saharan Africa, 2004–2005. J Int Assoc Physicians AIDS Care (Chic Ill) 2008;7:133–40. [PubMed: 18460695]The authors used the most recent and complete data

(2004 and 2005) from UNICEF, WHO, and UNAIDS to estimate the number of infants born to HIV-positive mothers in sub-Saharan Africa who were alive and HIV-free at 6 to 8 weeks of age due to the use of NVP and other sc-ARV to prevent MTCT of HIV.

23*. Marazzi MC, Bartolo M, Emberti Gialloreti L, et al. Improving adherence to highly active antiretroviral therapy in Africa: the DREAM programme in Mozambique. Health Educ Res 2006;21:34–42. [PubMed: 15947022]The paper describes the components of a comprehensive PMTCT program

24**. Palombi L, Marazzi MC, Voetberg A, Magid NA. Treatment acceleration program and the experience of the DREAM program in prevention of mother-to-child transmission of HIV. Aids 2007;21(Suppl 4):S65–71. [PubMed: 17620755]The study demonstrates that a comprehensive PMTCT program (including provision of ARV to the mothers for their infection) in resource-limited countries could achieve MTCT rates as low as currently observed in resource-rich countries.

25**. Tonwe-Gold B, Ekouevi DK, Viho I, et al. Antiretroviral treatment and prevention of peripartum and postnatal HIV transmission in West Africa: evaluation of a two-tiered approach. PLoS Med 2007;4:e257. [PubMed: 17713983]The authors demonstrated that the use of two-tiered strategy is safe and effective for short- and long-term PMTCT in resource-limited setting.

26. Amornwichet P, Teeraratkul A, Simonds RJ, et al. Preventing mother-to-child HIV transmission: the first year of Thailand's national program. JAMA 2002;288:245–8. [PubMed: 12095391]

27*. Plipat T, Naiwatanakul T, Rattanasuporn N, et al. Reduction in mother-to-child transmission of HIV in Thailand, 2001–2003: Results from population-based surveillance in six provinces. AIDS 2007;21:145–51. [PubMed: 17197804]The success story of Thailand PMTCT is illustrated in this paper.

28**. Leroy V, Ekouevi DK, Becquet R, et al. 18-month effectiveness of short-course antiretroviral regimens combined with alternatives to breastfeeding to prevent HIV mother-to-child transmission. PLoS ONE 2008;3:e1645. [PubMed: 18286200]The paper describes the effectiveness of short course ARV for PMTCT in a resource-limited setting.

29*. Ginsburg AS, Hoblitzelle CW, Sripipatana TL, Wilfert CM. Provision of care following prevention of mother-to-child HIV transmission services in resource-limited settings. AIDS 2007;21:2529–32. [PubMed: 18025890]The paper discusses some of the reasons for low coverage of PMTCT in resource-limited countries.

30*. Creek T, Ntumy R, Mazhani L, et al. Factors Associated with Low Early Uptake of a National Program to Prevent Mother to Child Transmission of HIV (PMTCT): Results of a Survey of Mothers and Providers, Botswana, 2003. AIDS Behav 2007;610.1007/s10461-007-9322-8The paper discusses some of the reasons for low coverage of PMTCT in resource-limited countries.

31*. Nkonki LL, Doherty TM, Hill Z, et al. Missed opportunities for participation in prevention of mother to child transmission programmes: simplicity of nevirapine does not necessarily lead to optimal uptake, a qualitative study. AIDS Res Ther 2007;4:27. [PubMed: 18034877]The paper discusses missed opportunities to provide PMTCT to pregnant women in resource-limited countries.

32*. Chandisarewa W, Stranix-Chibanda L, Chirapa E, et al. Routine offer of antenatal HIV testing ("opt-out" approach) to prevent mother-to-child transmission of HIV in urban Zimbabwe. Bull World Health Organ 2007;85:843–50. [PubMed: 18038074]The authors discuss the need for routine offer of antenatal HIV testing to help increase coverage of PMTCT of HIV.

33*. Pai NP, Barick R, Tulsky JP, et al. Impact of round-the-clock, rapid oral fluid HIV testing of women in labor in rural India. PLoS Med 2008;5:e92. [PubMed: 18462011]The use of round-the-clock rapid HIV testing has improved PMTCT coverage in a labor ward in rural India.

34*. Flys TS, Donnell D, Mwatha A, et al. Persistence of K103N-containing HIV-1 variants after single-dose nevirapine for prevention of HIV-1 mother-to-child transmission. J Infect Dis 2007;195:711–5. [PubMed: 17262714]The time to fading of K103N mutations resulting from the use of nevirapine for prevention of MTCT is discussed.

35*. Flys TS, Mwatha A, Guay LA, Nakabiito C, Donnell D, Musoke P, et al. Detection of K103N in Ugandan women after repeated exposure to single dose nevirapine. AIDS 2007;21:2077–82. [PubMed: 17885298]The detection of K103N mutation with repeated use of nevirapine for prevention of MTCT was independently associated with its detection at first exposure.

36*. Chi BH, Sinkala M, Stringer EM, et al. Early clinical and immune response to NNRTI-based antiretroviral therapy among women with prior exposure to single-dose nevirapine. AIDS

2007;21:957–64. [PubMed: 17457089]The authors discuss the effect of SDNVP use in PMTCT on efficacy of subsequent NNRTI-based regimen.

37*. Lockman S, Shapiro RL, Smeaton LM, et al. Response to antiretroviral therapy after a single, peripartum dose of nevirapine. N Engl J Med 2007;356:135–47. [PubMed: 17215531]The authors discuss the effect of SDNVP use in PMTCT on efficacy of subsequent NNRTI-based regimen.

38*. Arrive E, Newell ML, Ekouevi DK, et al. Prevalence of resistance to nevirapine in mothers and children after single-dose exposure to prevent vertical transmission of HIV-1: a meta-analysis. Int J Epidemiol 2007;36:1009–21. [PubMed: 17533166]The addition of intrapartum plus 4 to 7 days of maternal postpartum ZDV/3TC reduced the prevalence of NNRTI-associated mutations.

39**. Chi BH, Sinkala M, Mbewe F, et al. Single-dose tenofovir and emtricitabine for reduction of viral resistance to non-nucleoside reverse transcriptase inhibitor drugs in women given intrapartum nevirapine for perinatal HIV prevention: an open-label randomised trial. Lancet 2007;370:1698–705. [PubMed: 17997151]Addition of single dose of TDF/FTC to PMTCT regimens reduced the prevalence of NNRTI-associated mutations.

40**. Brahmbhatt H, Sullivan D, Kigozi G, et al. Association of HIV and malaria with mother-to-child transmission, birth outcomes, and child mortality. J Acquir Immune Defic Syndr 2008;47:472–6. [PubMed: 18332766]The authors provide evidence in support of the association between placental malaria and the risk of MTCT of HIV.

41*. Atashili J, Kalilani L, Seksaria V, Sickbert-Bennett EE. Potential impact of infant feeding recommendations on mortality and HIV-infection in children born to HIV-infected mothers in Africa: a simulation. BMC Infect Dis 2008;8:66. [PubMed: 18485200]The effect of different infant feeding practices on transmission of HIV is discussed.

42**. Lehman DA, Chung MH, John-Stewart GC, Richardson BA, Kiarie J, Kinuthia J, et al. HIV-1 persists in breast milk cells despite antiretroviral treatment to prevent mother-to-child transmission. AIDS 2008;22:1475–85. [PubMed: 18614871]ARVs used to PMTCT of HIV are less effective on cell-associated virus in breast milk.

43*. Creek T, Tanuri A, Smith M, et al. Early diagnosis of human immunodeficiency virus in infants using polymerase chain reaction on dried blood spots in Botswana's national program for prevention of mother-to-child transmission. Pediatr Infect Dis J 2008;27:22–6. [PubMed: 18162933]The need for early diagnosis of pediatric HIV in resource-limited countries using PCR-based assay is reiterated.

44*. Zhang Q, Wang L, Jiang Y, et al. Early infant human immunodeficiency virus type 1 detection suitable for resource-limited settings with multiple circulating subtypes by use of nested three-monoplex DNA PCR and dried blood spots. J Clin Microbiol 2008;46:721–6. [PubMed: 18077639] The need for early diagnosis of pediatric HIV in resource-limited countries using PCR-based assay is reiterated.