PMTCT Intelligence Report

prepared by the Bordeaux Working Group *


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Design of the bibliographic retrieval of this issue

Databases: Current Contents Life Sciences, Clinical Medicine, Social & Behavioral Sciences
(weeks # 15 to 19: April 12, 2004 to May 10, 2004; coverage: journal and book citations)

Number of citations screened for this issue: 1320

News Groups: AFRO-NETS, AMEDEO, CABA, Kaiser, Medscape, ProCAARE, RHO, UNAIDS e-Workspaces

Number of citations selected for this issue: 14

Subject Headings/Subheadings
Conference summary
Contraception
Gynaecology
Infant feeding/Breastfeeding
MTCT (Mother-to-Child Transmission)
Obstetrics
PMTCT/ARV (Prevention of Mother-to-Child Transmission/AntiRetroVirals)
Primary prevention of sexual transmission/VCT (Voluntary Counselling and Testing)
Termination of pregnancy/Abortion

Citation format (by alphabetical order of the authors)
Author(s). Title. Source.
Notes (prepared by the Bordeaux Working Group)
Author address, if available (for reprints)
URL, if available (link to author abstract/full text/journal TOC)
Subject Headings

**Abstr.** Mother-to-child transmission of HIV through breast-feeding is the remaining challenge facing mothers in resource-poor settings with a high HIV prevalence. Nearly all infants in developing countries are initially breast-fed, and most children continue to receive some breast-feeding until at least 6 months of age but frequently into the 2nd year of life, especially in sub-Saharan Africa and Asia. In December 2002, international researchers convened in Ghent, Belgium, to discuss mechanisms for, rates and risk factors of, and approaches to prevention of HIV transmission through breast-feeding. Four papers were compiled bringing together the presentation and discussions during this workshop, while the fourth paper also benefits from presentation made during an earlier workshop on vaccines in the prevention of mother-to-child transmission. These papers summarize the current state of knowledge and highlight the outstanding issues that will need to be addressed in the very near future before research advances can be translated into public health practice.

**Address:** Centre for Paediatric Epidemiology and Biostatistics, Institute of Child Health, University College, London, UK.

**Infant feeding/Breastfeeding**


**Abstr.** Background: Nevirapine (NVP) is widely prescribed in resource-poor settings to pregnant women for treatment and prevention of HIV infection. High rates of misreported adherence, however, have compelled clinicians to find alternative methods to ensure systemic drug exposure. This report describes a fast, inexpensive thin-layer chromatography (TLC) method to detect the presence of NVP in human plasma. Methods: Human plasma was spiked with various concentrations of NVP. NVP was subsequently isolated using solid-phase extraction and visualized with TLC. Clinical samples with NVP concentrations predetermined by high-performance liquid chromatography were used to validate the TLC method. Results: NVP was detected at concentrations as low as 60 ng/mL. The lower limit of detection was set at 100 ng/mL due to the clear spot definition at this concentration. The turnaround time for assay results averages several hours, and costs associated with the assay are considerably below standard drug quantitation techniques. Conclusion: TLC provides a rapid, sensitive, and economical tool to qualitatively measure NVP in plasma. This method offers clinicians in resource-poor settings an alternative approach for measuring adherence, particularly in developing-world regions where NVP use is common and there is an immediate need to prevent mother-to-child HIV transmission.

**Address:** Division of Clinical Pharmacology, Department of Obstetrics and Gynecology, University of Alabama at Birmingham School of Medicine, USA.

**PMTCT/ARV**


**Abstr.** The participation of HIV-1-infected pregnant women in a programme of prevention of mother-to-child transmission (MTCT) of HIV in Abidjan is described. Prenatal counselling with a rapid HIV test was proposed to 14 067 pregnant women, and acceptance was 89.4%. The return rate for results was 74.2%. The HIV-1 prevalence was 11.1%, and 26.2% of HIV-infected women started the prevention of MTCT programme. To increase the uptake, we recommend community mobilization and the strengthening of male involvement.

**Address:** Project ANRS Ditrame Plus, Programme PACCI, Abidjan, Cote d'Ivoire.

**PMTCT/ARV, Infant feeding/Breastfeeding**


**Abstr.** The major remaining challenge in the prevention of mother-to-child transmission is the reduction of the risk in settings where breast-feeding is common. This review gives an update on ongoing or planned antiretroviral intervention studies in resource-limited settings that are aimed at reducing the risk of mother-to-infant HIV transmission during lactation. These strategies include antiretroviral therapy given to the mother to reduce viral load in plasma and breast milk as well as antiretroviral regimens providing prophylaxis to uninfected infants during the period of breast-feeding. The rationale for the interventions based on animal models and human studies is described as well as the study designs of clinical trials. Potential risks and benefits of these interventions to mothers and infants...
are also highlighted. Laboratory studies nested within several of these trials will provide a better understanding of the pathogenesis of postnatal HIV transmission and its potential prevention using antiretroviral drugs.

**Address:** World Health Organization, Reproductive Health and Research, Geneva, Switzerland

**Infant feeding/Breastfeeding, PMTCT/ARV**


**Abstr.** Breast-feeding substantially increases the risk of HIV-1 transmission from mother to child, and although peripartum antiretroviral therapy prophylaxis significantly decreases the risk of mother-to-child transmission around the time of delivery, this approach does not affect breast-feeding transmission. Increased maternal RNA viral load in plasma and breast milk is strongly associated with increased risk of transmission through breast-feeding, as is breast health, and it has been suggested that exclusive breast-feeding could be associated with lower rates of breast-feeding transmission than mixed feeding of both breast- and other milk or feeds. Transmission through breast-feeding can take place at any point during lactation, and the cumulative probability of acquisition of infection increases with duration of breast-feeding. HIV-1 has been detected in breast milk in cell-free and cellular compartments; infant gut mucosal surfaces are the most likely site at which transmission occurs. Innate and acquired immune factors may act most effectively in combination to prevent primary HIV-1 infection by breast milk.

**Address:** Department of Medicine, University of Washington, USA.

**Infant feeding/Breastfeeding, MTCT**


**Abstr.** Zidovudine monotherapy is used to reduce perinatal HIV transmission in women with low viral loads. There are few data on the risk of drug resistance in this select cohort of women. We determined the prevalence of newly acquired mutations conferring reduced sensitivity to zidovudine after exposure during pregnancy, and found that the development of mutations was uncommon and was restricted to women treated before 1998 who had higher baseline viral loads than those currently recommended monotherapy.

**Address:** Department of Genitourinary Medicine, Virology Section, Guys, Kings and St Thomas' School of Medicine, London, UK.

**PMTCT/ARV**


**Abstr.** NA

**URL:** [http://www.who.int/entity/bulletin/volumes/82/3/en/161.pdf](http://www.who.int/entity/bulletin/volumes/82/3/en/161.pdf)

**Address:** NA

**Infant feeding/Breastfeeding**

McNamara PJ and Abbashi M. **Neonatal exposure to drugs in breast milk.** Pharmaceut Res 2004; 21 (4): 555-566.

**Abstr.** There are many benefits of breast-feeding both for the infant and for the mother. Nursing mothers who are also taking medications or exposed to environmental hazards may be confronted with a difficult choice to discontinue nursing or maternal medication or risk potential harm to the infant. Frequently, these decisions are made without sufficient information or understanding of the factors influencing exposure. The current review explores two indices of exposure, together with their pharmacokinetic determinants. Both of the indices include the milk to serum (M/S) concentration ratio for a given drug and the volume of milk consumed. The first exposure term, EI(Dose), expresses neonatal dose as a percentage of maternal dose and is inversely related to the maternal systemic clearance. By contrast, the second exposure term, EI(Conc), expresses infant concentration as a percentage of maternal concentration and is inversely related to the infant systemic clearance. Issues related to intersubject variation in M/S (e.g., colostrum vs. Mature milk, fore vs. Hind milk) and infant clearance (e.g., ontogeny of elimination pathways, pharmacogenetics) and their role in modulating exposure are also discussed.

**Address:** College of Pharmacy, University of Kentucky, Lexington, Kentucky 40536, USA.

**pmcnmara@email.uky.edu**

**Infant feeding/Breastfeeding, PMTCT/ARV**

**Abstr.** Objective: The purpose of this study was to evaluate the effect of elective cesarean delivery plus a lamivudine-zidovudine prophylaxis regimen on non-breastfeeding mothers with human immunodeficiency virus type 1 and their infants. Study design: Forty-six antiretroviral-naive, pregnant women with human immunodeficiency virus type 1 were included. The prophylactic regimen was a lamivudine-zidovudine tablet (150 mg/300 mg) twice daily, from week 34 of pregnancy until cesarean delivery at week 38 of gestation, preoperative intravenous zidovudine, and neonatal zidovudine syrup for 4 weeks. Results: At weeks 34 and 38 of gestation, the median maternal viral loads were, respectively, 3.65 Log(10) copies/mL (range, 2.34-4.70 log(10) copies/mL) and 2.51 log(10) copies/mL (range, 2.04-3.66 log(10) copies/mL; P < .001), respectively. The viral reduction was 1.12 log(10) copies/mL (range, -0.16 to -2.60 log(10) copies/mL), and the CD4(+) cell counts increased from 335 cells/mm(3) (range, 57-974 cells/mm(3)) to 420 cells/mm(3) (range, 84-1,083 cells/mm(3); P = .002). No mother or infant had a serious adverse event. Two infants were infected (4.3%; 95% CI, 0.5%-15.7%); 1 infant had intrapartum infection. Conclusion: Elective cesarean delivery plus short-course lamivudine-zidovudine is safe but does not eliminate mother-to-child transmission of human immunodeficiency virus type 1. (C) 2004 Elsevier Inc. All rights reserved.

**Address:** Department of Obstetrics and Gynaecology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.

PMTCT/ARV


**Abstr.** Objective Little is known about the nutritional adequacy and feasibility of breastmilk replacement options recommended by WHO/UNAIDS/UNICEF. The study aim was to explore suitability of the 2001 feeding recommendations for infants of HIV-infected mothers for a rural region in KwaZulu Natal, South Africa specifically with respect to adequacy of micronutrients and essential fatty acids, cost, and preparation times of replacement milks. Methods Nutritional adequacy, cost, and preparation time of home-prepared replacement milks containing powdered full cream milk (PM) and fresh full cream milk (FM) and different micronutrient supplements (2 g UNICEF micronutrient sachet, government supplement routinely available in district public health clinics, and best available liquid paediatric supplement found in local pharmacies) were compared. Costs of locally available ingredients for replacement milk were used to calculate monthly costs for infants aged one, three, and six months. Total monthly costs of ingredients of commercial and home-prepared replacement milks were compared with each other and the average monthly income of domestic or shop workers. Time needed to prepare one feed of replacement milk was simulated. Findings When mixed with water, sugar, and each micronutrient supplement, PM and FM provided <50% of estimated required amounts for vitamins E and C, folic acid, iodine, and selenium and <75% for zinc and pantothenic acid. PM and FM made with UNICEF micronutrient sachets provided 30% adequate intake for niacin. FM prepared with any micronutrient supplement provided no more than 32% vitamin D. All PMs provided more than adequate amounts of vitamin D. Compared with the commercial formula, PM and FM provided 8-60% of vitamins A, E, and C, folic acid, manganese, zinc, and iodine. Preparations of PM and FM provided 11% minimum recommended linoleic acid and 67% minimum recommended alpha-linolenic acid per 450 ml mixture. It took 21-25 minutes to optimally prepare 120 ml of replacement feed from PM or commercial infant formula and 30-35 minutes for the fresh milk preparation. PM or FM cost approximately 20% of monthly income averaged over the first six months of life; commercial formula cost approximately 32%. Conclusion No home-prepared replacement milks in South Africa meet all estimated micronutrient and essential fatty acid requirements of infants aged <6 months. Commercial infant formula is the only replacement milk that meets all nutritional needs. Revisions of WHO/UNAIDS/UNICEF HIV and infant feeding course replacement milk options are needed. If replacement milks are to provide total nutrition, preparations should include vegetable oils, such as soybean oil, as a source of linoleic and alpha-linolenic acids, and additional vitamins and minerals.


**Address:** Africa Centre for Health and Population Studies, Mtabutuba, KwaZulu Natal, South Africa.

ppapathakis@mrc.ac.za

Infant feeding/Breastfeeding

Abstr. Approaches to reducing or preventing the risk of postnatal transmission through breast-feeding include the avoidance of all breast-feeding and the use of exclusive replacement feeds or exclusive breast-feeding for a limited duration with early and rapid cessation of breast-feeding around 4-6 months of age. The efficacy and safety of the latter approach have not been established and studies are in progress to provide further information. In addition, inactivation of HIV in breast milk would allow breast-feeding to continue while reducing the risk of postnatal transmission of HIV and may be usefully applied in certain circumstances, such as for premature infants or while a mother recovers from mastitis. In this review, experience is reported from clinical trials or studies additional to their main objective of assessing rates and risk factors for mother-to-child transmission. This may inform policy, programming, and training options and may be especially valuable in the absence of conclusive data on the efficacy of the interventions to be applied during the breast-feeding period.

Address: Africa Centre for Health and Population Studies, Mtubatuba, South Africa.

Infant feeding/Breastfeeding, PMTCT


Abstr. Antiretroviral therapy can profoundly reduce the risk of mother-to-child transmission (MTCT) of HIV, but the drugs have a relatively short half-life and should thus be administered throughout breast-feeding to optimally prevent postnatal infection of the infant. The potential toxicities and the development of resistance may limit the long-term efficacy of antiretroviral prophylaxis, and a safe and effective active/passive immunoprophylaxis regimen, begun at birth, and potentially overlapping with interpartum or neonatal chemoprophylaxis, would pose an attractive alternative. This review draws on data presented at the Ghent Workshop on prevention of breast milk transmission and on selected issues from a workshop specifically relating to immunoprophylaxis held in Seattle in October 2002. This purpose of this review is to address the scientific rationale for the development of passive (antibody) and active (vaccine) immunization strategies for prevention of MTCT. Data regarding currently or imminently available passive and active immunoprophylaxis products are reviewed for their potential use in neonatal trials within the coming 1-2 years.

Address: Elizabeth Glaser Pediatric AIDS Foundation, Department of Pediatrics, David Geffin School of Medicine, University of California, Los Angeles, USA. jeff@pedaids.org

Infant feeding/Breastfeeding, PMTCT


Abstr. This study aimed to find out whether genetic polymorphisms were present in positions potentially affecting susceptibility to antiretrovirals in non-B subtypes from HIV-1-infected patients in Rwanda. Viral pol gene diversity was investigated by direct sequencing in 43 treatment-naive women. In addition, 10 DNA sequences from uncultured peripheral blood mononuclear cells were analyzed 6 weeks after a single dose of nevirapine (prevention of mother-to-child transmission program). Phylogenetic analyses have shown 34 subtype A1, 6 subtype C, and 2 subtype D strains. In addition, an A/C recombinant between the protease (PR) (subtype A1) and the reverse transcriptase (RT) (subtype C) was identified. In the PR coding region, high numbers of polymorphisms were found, including substitutions in secondary PR resistance sites. PR 35D, 361, and 37N were always present within subtype A as were PR 93L in subtype C strains. PR 101V, 20R, 33F, and 77V were found in subtype A whereas PR 361 was highly prevalent in subtype C strains. The A/C recombinant displayed substitutions related to resistance (PR 10, 33, 36 and RT 118). One nevirapine resistance mutation (RT 181Y/C) was found in proviral DNA after 6 weeks. In conclusion, subtypes A and C are predominant in this cohort in Rwanda. Substitutions similar to secondary protease inhibitor resistance mutations are common before treatment whereas major resistance mutation may be archived after a single dose of nevirapine. Accordingly, the hypothesis of a genetic background effect in non-B strains has to be further addressed in programs of introduction of antivirals in Africa.

Address: Treatment Research AIDS Center, Kigali, Rwanda. rwa21@rwandal.com

PMTCT/ARV

**Abstr.** Background: There is a continuing need to evaluate sustainable interventions for prevention of mother-to-child transmission (MTCT) of HIV type 1. We evaluated different concentrations (0.25%, 1%, and 2%) of chlorhexidine (CHX) for perinatal maternal and infant washes to identify the maximum tolerable concentration of CHX for such an intervention. Methods: Women were enrolled during their third trimester at the maternity unit of the Chris Ham Baragwanath Hospital in Soweto, South Africa, and perinatal maternal and infant washes were completed. Subjective maternal symptoms as well as infant examinations were used to assess tolerability of the washes. Results: The 0.25% concentration of CHX was well tolerated by the mothers (n = 29). Ten of 79 women (13%) with 1% CHX washes complained of mild vaginal area burning or itching, and washes were stopped in 5 (6%). Twenty-three of 75 women (31%) in the 2% CHX wash group had subjective complaints, and the washes were stopped in 12 (16%). There were no clinical indications of toxicity of the CHX washes among infants. Conclusion: A 1% solution of CHX appears to be a safe and tolerable concentration of CHX for consideration in an MTCT prevention trial.

**Address:** Department of Pediatrics, University of Alabama at Birmingham, Birmingham, Alabama 35294, USA. cwilson@uab.edu

PMTCT, Obstetrics