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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

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Subject Headings

Notes: Guiliano et al present in this study the selection of resistance mutations in pregnant women included in the Petra trial (IR 2002 #5). The aim of this study was to determine if the selection of resistance mutations occurs in mothers-baby pairs enrolled in arms A and B in which women were exposed for the longest prenatal periods to the combination of zidovudine (ZDV) and lamivudine (3TC). The timepoint to evaluate the presence of the mutation in women was enrolment (before drug administration), week 1 postpartum, and 3 months after delivery (only if a mutation was found at week 1). A total of 124 samples were processed. In women enrolled in arm A, the 3TC associated mutation M184V was detected in 6/50 samples (12%) one week after delivery. In this group, one women presented the mutation M41L at the three time points. Amongst women included in arm B, two presented the mutation V118I + V179E and one mutation V179D one week after delivery. No statistical difference was found amongst transmitting mothers and non-transmitting mothers. No sample of the HIV-infected child born to the M184V positive mother was available and the twins of one mother harbouring the V118I and V179E mutations showed the same resistance pattern. This short report confirms previous findings reported by Mandelbrot et al in the French ANRS 075 study concerning the use of 3TC in PMTC regimens (IR 2001 #1).

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PMTCT/ARV


Notes: There are several approaches to reduce the risk of HIV transmission through breastfeeding. One of the conceivable options consists in a shortened exposure to breastfeeding with avoidance of predominant or mixed breastfeeding. Yet, "the jury is still out" concerning the optimum duration of exclusive breastfeeding (EBF). Indeed, the shorter the duration of breastfeeding, the lower the risk of postnatal transmission, but this may be counter-balanced by the higher risks of child morbidity, mortality or growth problems induced by early weaning. This study throws new light on this issue in general terms as it was conducted among children born to HIV-uninfected mothers or to women of HIV unknown status in a country of low HIV prevalence in the general population. Indeed, the
authors investigated in the Republic of Belarus, Eastern Europe, the effects on infant health and growth of 3 compared with 6 months of EBF. Low weight-for-age z score (< -2) was rare in both groups at ages 6, 9 and 12 ; whereas low length-for-age z score was more common but did not differ significantly between children exclusively breastfed for 3 or 6 months. There was a protective effect of breastfeeding for the 6 month EBF group compared to the 3 month EBF one on the incidence of gastrointestinal infections in the 3 to 6 months of life period (adjusted incidence density rate ratio: 0.35 ; 95% CI: 0.13 - 0.96), but this effect did not persist between 6 and 12 months. There are no obvious overall differences between these two EBF strategies as far as morbidity and anthropometry indices are concerned.

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Infant feeding/breastfeeding

Notes: This pooled analysis of two randomized clinical trials (peri-partum zidovudine [ZDV] vs. placebo) conducted from 1995 to 1998 in Abidjan , Côte d'Ivoire, was designed to assess the postnatal transmission (PT) risk of HIV in a breastfeeding population after a maternal short course regimen of ZDV. Of the 479 infants eligible for analysis, 23/254 in the ZDV arm and 19/225 in the placebo arm became infected during the postnatal period, leading to a cumulative PT risk at 24 months of age of 9.8 and 9.1%, respectively. Thus, this study did not demonstrate any greater risk of PT due to a potential rebound in maternal viral load following a short course of ZDV aimed at the prevention of MTCT. The cumulative risk of PT was much higher among mothers with lower CD4 count (i.e. <500 compared with >500). Multivariate analysis revealed that at 24 months, the ZDV effect was non significant and that low maternal CD4 count and high maternal plasma viral load at study entry significantly increased the PT risk. In this context, the authors raise the issue that interventions to prevent PT should be urgently targeted in women with low CD4 count. This could include post-partum maternal HAART or alternatives to breastfeeding.
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PMTCT

Notes: Conventional testing algorithms involve venipuncture collection of blood for testing using Enzyme ImmunoAssay (EIA) and confirmation of positive test results using Western Blot (WB) analysis. These methods may have several limitations that may act as barriers to testing: invasive procedure and inconvenience of follow-up. The authors of this report after stating the potential benefits of rapid testing assessed the performance of the Hema-Strip HIV-1/2 capillary flow immunoassay (Saliva Diagnostic Systems, Vancouver, WA). This is a whole-blood finger-stick rapid test that uses immunochromatography to assess presence of anti-HIV antibodies. The study was done in a prospective cohort of Thai women assessing incidence of HIV infection. Women of childbearing age were recruited from family planning clinics and a postpartum ward (n=804). The article examines how demographic, reproductive health and risk behaviour variables are correlated with test acceptability. Test acceptability was assessed at the first 6-month follow-up visit through four open questions and categorized through a five-point scale. More than half (56.2%) of the women preferred having blood taken from the fingertip rather than from the arm. Most of the women (80%) preferred learning the test result during the same clinic visit rather than returning for the result at a later date. The majority (78.7%) preferred the rapid test method over typical test methods. Those aged 26 to 35 years were more likely than those aged 16 to 25 years to prefer the finger-stick test (OR = 1.6; 95% CI: 1.1-2.1, p <0.01). Women with a household income greater than or equal to 5 000 baht per month significantly preferred the rapid finger-stick test (OR = 1.7, 95% CI: 1.1-2.7, p <0.05). Multivariate analysis showed that age and education were independently associated with preference for taking blood from the fingertip versus the arm. The study documents the utility and high acceptability of a rapid whole-blood finger-stick HIV test among women in an area of moderate HIV prevalence in Chiang Rai, Thailand. The use of rapid tests with easily collected specimens can greatly enhance the expanding global efforts to prevent HIV transmission and provide care for people living with AIDS.

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Primary prevention of sexual transmission/VCT


Notes: This paper investigates the nevirapine (NVP) concentration in neonates in order to assess whether the two-dose intrapartum neonate NVP regimen achieves its goal, i.e. maintaining NVP concentrations of more than 100 ng/mL in the newborn throughout the first week of life. The authors obtained 109 plasma samples for NVP assay from cord blood and 149 just prior to the neonatal NVP dose given 48 to 72 hours after birth. This study was conducted in a subset of infants participating to the PACTG 316 trial (IR 2002, #8). The authors showed that NVP concentrations were below the target concentration of 100 ng/mL in eight (7%) of 109 cord blood, and 23 (15%) of the 149 predose samples. The distribution of those 23 infants according to time between maternal NVP dosing and birth was as follows: 100% (12/12) of infants born one hour or less after dosing, 29% (5/17) of those born between one and two hours after dosing, 13% (3/24) of those born between two and four hours after dosing, 5% (2/38) of those born between four and six hours after dosing, and 2% (1/58) of those born more than six hours after dosing. The authors conclude that, with no danger for the infant health or major additional cost, infants born less than two hours after maternal NVP intake during labor should receive a dose of NVP immediately after birth in addition to the standard infant dose given at 48 to 72 hours. This important addendum to the commonly used guidelines should be followed when using the two-dose intrapartum neonate NVP regimen for PMTCT in resource-poor settings.


Notes: This paper aims to describe the association between maternal plasma HIV-1 RNA viral load and cervico-vaginal fluid HIV-1 DNA with transmission outcome in a cross sectional study in Botswana. This study was run using a cross-sectional design, not very appropriate to the question of predicting perinatal transmission. It is unfortunate that no PMTCT program was in place in the population where the study was conducted mid-99.


Notes: Recent reports have demonstrated a high maternal mortality rate associated with tuberculosis in HIV-infected patients in South Africa. HIV markedly increases the risk of tuberculosis. Furthermore, tuberculosis preventive therapy has been shown to be effective in reducing the incidence of tuberculosis in HIV-infected, tuberculin skin test (TST)-positive individuals. The authors report the prevalence of undiagnosed active tuberculosis in HIV-infected, TST-positive participants to a PMTCT programme in Soweto, South Africa. Of 438 tuberculin-tested HIV-infected patients, 157 (49%) had a ≥5mm induration, 120 (76%) underwent complete tuberculosis screening of whom 213 (11%) were found to have active tuberculosis (3% of the total population). Nachega et al underline the need to undertake active tuberculosis case-finding to prevent mortality and transmission, and preventive therapy for latent tuberculosis infection. The development of innovative ways of integrating tuberculosis prevention and treatment services and HIV care including PMTCT is a priority.

**Notes:** Poirier et al. studied long-term mitochondrial toxicity in children born to HIV-uninfected (ZDV-/HIV-; n=30) and HIV-infected women receiving no antiretroviral drug (ZDV-/HIV+; n=20) or Zidovudine (ZDV+/HIV+; n=10) during pregnancy. Infant leukocytes for biomarkers related to mitochondrial integrity (mtDNA quantity) and telomere length in infants at birth and age 1 year and 2 years have been examined. The analysis showed a significant reduction in mtDNA levels of the ZDV-/HIV+ group in comparison with the ZDV-/HIV- group. Mitochondrial integrity was altered with the use of ZDV during pregnancy. However, telomere length measures at birth and age 1 year were not altered in relation to the HIV status of the mother or ZDV exposure. The authors concluded that the children of HIV+ mothers are at risk for mitochondrial damage that is further increased in infants of mothers receiving ZDV during pregnancy. The authors suggest to follow for long periods of time children born to HIV-infected mothers receiving prenatal nucleoside analogues-containing PMTCT regimens because it is possible that the depletion in mtDNA levels observed may comprise their overall health later in life.

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**PMTCT/ARV**


**Notes:** This Harvard-based group has focused on the development of a simian model of passive immunization in newborn macaques with human neutralizing monoclonal antibodies (nmAbs). These antibodies were isolated from HIV clade B infected individuals. They were shown to target conserved functionally important epitopes. The triple or quadruple nmAbs combinations were administered intravenously to neonatal animals in the first week of life, preceded (n=4) or not (n=12) by another intravenous administration of nmAbs prior to and three days after delivery to the female macaques. After challenging the 16 neonates with different chimeric simian-human immunodeficiency viruses, the authors observed a complete protection in 11 instances. Furthermore, the quadruple nmAbs combination they developed neutralized in vitro primary isolates of clades A, B, C and D. It is possible therefore that this passive immunization approach can be used for preventing transmission of non-clade B viruses via breastfeeding. Plans are now well under way to move this approach to clinical research in South Africa based on these in vitro and animal findings.

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**PMTCT**


**Notes:** In Lusaka, Zambia, 40 000 babies are born each year, of these, one in four infants is delivered to an HIV-infected mother. A nevirapine (NVP) based perinatal HIV prevention program was initiated in all clinics in the Lusaka district in November 2001. This report describes progress and challenges in the first year of bringing these services to scale in a large, urban centre with high HIV prevalence in sub-Sahara Africa. The package of services included a training program on voluntary counselling and testing, an initial general pregnancy-orientated health talk followed by individual voluntary counselling and rapid testing, NVP-based perinatal HIV prevention scheme and recommended six-month exclusive breastfeeding to all postpartum mothers including HIV-infected women. Serology HIV testing was done at 15-18 months for pediatric HIV diagnosis. The program began in two clinics performing 150 deliveries per-month each, with progressive expansion to satellite clinics. Results showed that the program was successfully integrated into existing antenatal services in the Lusaka district, 17 263 pregnant women were counselled for HIV, 12 438 (72%) were tested, and 2 924 (24%) were found to be infected with HIV. NVP was taken by 1 654 (57%) HIV-infected mothers and 1 157 (40%) babies. The authors estimate that at least 190 infants have been spared from HIV infection (11 per 1000 counselled women or 65 per 1000 identified HIV-infected women). The cost of the programme over a 12-month period was calculated to be US$ 221,170. Stringer et al. conclude that the early experience in Lusaka suggests that a large-scale NVP-based perinatal HIV prevention program is feasible, cost-effective and sustainable. Nevertheless, patient attrition and non-adherence represent a
major source of program inefficiency, which requires to be systemically addressed. The need to find ways to integrate antiretroviral therapy into these programs will become increasingly important.

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**PMTCT/ARV**

Van de Perre P. **Transfer of antibody via mother's milk.** Vaccine 2003; 21 (24): 3374-3376.

**Notes:** A litterature review of the investigation of the milk-excreted antibodies in animal species and humans. The author concludes that protection against HIV, a virus that can be transmitted via a mucosal portal of entry, may be at least in part antibody-mediated.

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**MTCT**