PMTCT Intelligence Report
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Design of the bibliographic retrieval of this issue

Databases: Current Contents Life Sciences, Clinical Medicine, Social & Behavioral Sciences
(weeks # 28 to 32: to July 12, 2004 to August 9, 2004; coverage: journal and book citations)

Number of citations screened for this issue: 1379 + XV International AIDS Conference Proceedings

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

Number of citations selected for this issue: 12

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.
Abstr. (authors’ abstract) or Notes (prepared by the Bordeaux Working Group)
Author address, if available (for reprints)
Subject Headings

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**Abstr.** Context Timely testing of women in labor with undocumented human immunodeficiency virus (HIV) status could enable immediate provision of antiretroviral prophylaxis. Objectives To determine the feasibility and acceptance of rapid HIV testing among women in labor and to assess rapid HIV assay performance. Design, Setting, and Patients The Mother-Infant Rapid Intervention At Delivery (MIRIAD) study implemented 24-hour counseling and voluntary rapid HIV testing for women in labor at 16 US hospitals from November 16, 2001, through November 15, 2003. A rapid HIV-1 antibody test for whole blood was used. Main Outcome Measures Acceptance of HIV testing; sensitivity, specificity, and predictive value of the rapid test; time from blood collection to patient notification of results. Results There were 91707 visits to the labor and delivery units in the study, 7381 of which were by eligible women without documentation of HIV testing. Of these, 5744 (78%) women were approached for rapid HIV testing and 4849 (84%) consented. HIV-1 test results were positive for 34 women (prevalence=7/1000). Sensitivity and specificity of the rapid test were 100% and 99.9%, respectively; positive predictive value was 90% compared with 76% for enzyme immunoassay (EIA). Factors independently associated with higher test acceptance included younger age, being black or Hispanic, gestational age less than 32 weeks, and having had no prenatal care. Lower acceptance was associated with being admitted between 4 Pm and midnight, particularly on Friday nights, but this may be explained in part by fewer available personnel. Median time from blood collection to patient notification of result was 66 minutes (interquartile range, 45-120 minutes), compared with 28 hours for EIA (P<.001). Conclusions Rapid HIV testing is feasible and delivers accurate and timely test results for women in labor. It provides HIV-positive women prompt access to intrapartum and neonatal antiretroviral prophylaxis, proven to reduce perinatal HIV transmission, and may be particularly applicable to higher-risk populations.

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**Abstr.** NA

**URL free full text:** http://content.nejm.org/content/vol351/issue3/index.shtml

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**Abstr.** The aim of this study performed in Abidjan, Cote d'Ivoire, was to describe the distribution of CD4(+) T-cell lymphocytes (CD4) in HIV-1- infected (HIVE) pregnant women diagnosed during prenatal voluntary counseling and testing and to assess whether HIV-related immunodeficiency influenced the acceptance of an antiretroviral (ARV) package (zidovudine beginning at 36 weeks of amenorrhea plus intrapartum nevirapine) to prevent mother-to-child transmission. Between April and June 2002, a CD4 count was systematically performed in all HIV+ women (n = 221) in 5 antenatal clinics carrying out voluntary counseling and testing. No difference in CD4 count was found in HIV+ women who did not return for their test result (n = 50) and those who were informed of their positive serostatus (n = 171) (median CD4 count: 389/mm(3) vs. 420/mm(3); p = 0.19). We also found a lack of difference in CD4 count in those who accepted ARV (n = 72) and those who did not but knew their HIV status (n = 99) (median CD4 count: 405/mm(3) vs. 425/mm(3); P = 0.47). The overall uptake of the intervention (31.9%) appeared to be independent of the maternal immune status.

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**Abstr.** We compared nevirapine (NVP) resistance (NVPR) mutations in maternal plasma 7 days vs. 6-8 weeks after single-dose NVP prophylaxis. In the HIVNET 012 trial, Ugandan women received a single dose of NVP in labor for prevention of HIV-1 mother-to-child transmission. NVPR mutations were detected in 70 (25%) of 279 women 6-8
weeks after NVP. Samples collected 7 days after NVP were analyzed from a subset of those 279 women. Genotyping was performed with the ViroSeq HIV-1 Genotyping System. NVPR was analyzed using paired samples from 7 days and 6-8 weeks after NVP. Sixty-five women had genotyping results obtained for samples collected at both 7 days and 6-8 weeks post-NVP. Twenty-one (32%) of those women had NVPR mutations detected in one or both samples. This included three women with NVPR at 7 days only, seven with NVPR at 6-8 weeks only, and 11 with NVPR at both time points. Eight women had >1 NVPR mutation detected 7 days after NVP. Y181C was the most common NVPR mutation detected at 7 days, whereas K103N was the most common NVPR mutation detected at 6-8 weeks. We conclude that NVPR may be detected in women as early as 7 days after single-dose NVP. Complex patterns of NVPR are detected in some women. The Y181C NVPR mutation often fades from detection by 6-8 weeks. In contrast, the K103N mutation emerges more slowly, but often remains detectable 6-8 weeks after NVP.

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PMTCT/ARV


Abstr. BACKGROUND: A single intrapartum dose of nevirapine for the prevention of mother- to-child transmission of human immunodeficiency virus (HIV) leads to the selection of resistance mutations. Whether there are clinically significant consequences in mothers who are subsequently treated with a nevirapine-containing regimen is unknown. METHODS: We randomly assigned 1844 women in Thailand who received zidovudine during the third trimester of pregnancy to receive intrapartum nevirapine or placebo. In the postpartum period, 269 of the women with a CD4 count below 250 cells per cubic millimeter began a nevirapine-containing antiretroviral regimen. Plasma samples were obtained 10 days post partum and analyzed for resistance mutations. Plasma HIV type 1 (HIV-1) RNA was measured before the initiation of therapy and three and six months thereafter. RESULTS: After six months of therapy, the HIV-1 RNA level was less than 50 copies per milliliter in 49 percent of the women who had received intrapartum nevirapine, as compared with 68 percent of the women who had not received intrapartum nevirapine (P=0.03). Resistance mutations to nonnucleoside reverse-transcriptase inhibitors were detectable in blood samples obtained 10 days post partum from 32 percent of the women who had received intrapartum nevirapine; the most frequent mutations were K103N, G190A, and Y181C. Among the women who had received intrapartum nevirapine, viral suppression was achieved at six months in 38 percent of those with resistance mutations and 52 percent of those without resistance mutations (P=0.08). An HIV-1 RNA level at or above the median of 4.53 log(sub 10) copies per milliliter before therapy and intrapartum exposure to nevirapine were independently associated with virologic failure. After six months of therapy, there was no significant difference between groups in the CD4 count (P=0.65). CONCLUSIONS: Women who received intrapartum nevirapine were less likely to have virologic suppression after six months of postpartum treatment with a nevirapine-containing regimen. Our data suggest the need for strategies to maximize the benefits of both antiretroviral prophylaxis against mother-to-child transmission of HIV and antiretroviral therapy for mothers.

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PMTCT/ARV


Abstr. Objective To determine the rate and factors associated with perinatal transmission among women infected with HIV-1. Design Cohort study. Setting Centro Municipal de Atendimento ern DST/AIDS is a major reference centre for HIV treatment in Porto Alegre city, southern Brazil. Population Pregnant and puerperal women infected with HIV-1. Methods Women were enrolled during pregnancy and seen monthly at the antenatal care centre. Those detected at delivery that presented at the centre within the first 10 days of postpartum were included. Maternal, obstetric and infant-related characteristics were ascertained and testing for CD4 cell count, HIV PCR/RNA assay, anti- HCV, HBsAg and syphilis were performed. Antiretrovirals and formula were provided free of charge following Brazilian guidelines. Main outcome measure HIV-1 infection status in the infant. Results Perinatal transmission was assessed in 343 children (95% of the whole sample). Overall, the transmission rate was 3.2% (95% CI: 1.7-5.8%). Perinatal transmission rates increased with maternal viral load (greater than or equal to10,000 copies/mL; RR: 11.27;
95% CI: 1.38-92.23). In multivariate analyses, the only independent risk factor for perinatal transmission was the maternal viral load at baseline (OR = 2.72 per log increase in the number of copies; 95% CI: 1.17-6.50). Conclusion Perinatal transmission rate was low among HIV-1 infected women in clinical care and on antiretroviral therapy despite poor socio-economic conditions. Viral load was the only independent predictor of perinatal transmission. It is possible to prevent HIV-1 perinatal transmission in a developing country if we provide antiretrovirals and formula.

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**PMTCT/ARV**


**Abstr.** BACKGROUND: Although zidovudine prophylaxis decreases the rate of transmission of the human immunodeficiency virus (HIV) type 1 substantially, a large number of infants still become infected. We hypothesized that the administration, in addition to zidovudine, of a single dose of oral nevirapine to mothers during labor and to neonates would further reduce transmission of HIV. METHODS: We conducted a randomized, double-blind trial of three treatment regimens in Thai women who were receiving zidovudine therapy during the third trimester of pregnancy. In one group, mothers and infants received a single dose of nevirapine (nevirapine-nevirapine regimen); in another, mothers and infants received nevirapine and placebo, respectively (nevirapine-placebo regimen); and in the last, mothers and infants received placebo (placebo-placebo regimen). The infants also received one week of zidovudine therapy and were formula-fed. The end point of the study was infection with HIV in the infants, established by virologic testing. RESULTS: Between January 15, 2001, and February 28, 2003, a total of 1844 Thai women were enrolled. At the first interim analysis, the independent data monitoring committee stopped enrollment in the placebo-placebo group. Among women who delivered before the interim analysis, the as-randomized Kaplan-Meier estimates of the transmission rates were 1.1 percent (95 percent confidence interval, 0.3 to 2.2) in the nevirapine-nevirapine group and 6.3 percent (95 percent confidence interval, 3.8 to 8.9) in the placebo-placebo group (P«0.001). The final per-protocol transmission rate in the nevirapine-nevirapine group, 1.9 percent (95 percent confidence interval, 0.9 to 3.0), was not significantly inferior to the rate in the nevirapine-placebo group (2.8 percent; 95 percent confidence interval, 1.5 to 4.1). Nevirapine had an effect within subgroups defined by known risk factors such as viral load and CD4 count. No serious adverse effects were associated with nevirapine therapy. CONCLUSIONS: A single dose of nevirapine to the mother, with or without a dose of nevirapine to the infant, added to oral zidovudine prophylaxis starting at 28 weeks’ gestation, is highly effective in reducing mother-to-child transmission of HIV.

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**PMTCT/ARV**


**Abstr.** Context Antenatal counseling and human immunodeficiency virus (HIV) testing are not universal in Africa; thus, women often present in labor with unknown HIV status without receiving the HIVNET 012 nevirapine (NVP) regimen (a single oral dose of NVP to the mother at the start of labor and to the infant within 72 hours of birth). Objective To determine risk of mother-to-child transmission of HIV when either standard use of NVP alone or in combination with zidovudine (ZDV) was administered to infants of women tested at delivery. Design, Setting, and Participants A randomized, open-label, phase 3 trial conducted between April 1, 2000, and March 15, 2003, at 6 clinics in Blantyre, Malawi, Africa. The trial included all infants born to 894 women who were HIV positive, received NVP intrapartum, and were previously antiretroviral treatment-naive. Infants were randomly assigned to NVP (n=448) and NVP plus ZDV (n=446). Infants were enrolled at birth, observed at 6 to 8 weeks, and followed up through 3 to 18 months. The HIV status of 90% of all infants was established at 6 to 8 weeks. Intervention Mothers received a 200-mg single oral dose of NVP intrapartum and infants received either 2- mg/kg oral dose of NVP or NVP (same dose) plus 4 mg/kg of ZDV twice per day for a week. Main Outcome Measures HIV infection of infant at birth and 6 to 8 weeks, and adverse events. Results The mother-to-child transmission of HIV at birth was 8.1% (36/445) in infants administered NVP only and 10.1% (45/444) in those administered NVP plus ZDV (P=.30). A life
All the abstracts of the studies quoted below are available on the conference web site at XV International AIDS Conference Bangkok Thailand 11–16 July 2004.

In the context of access to care for all, Okong et al reported in Uganda their experience of using HAART in pregnancy within the MTCT Plus initiative (abstract ThPeB7136). HIV-infected pregnant women with WHO clinical stage 3 or 4 or CD4 cell counts ≤200 received a combination of zidovudine (ZDV), lamivudine (3TC) and nevirapine (NVP) starting antenatally. Women who were less immuno-compromised received single-dose NVP in labour. The rate of transmission was not reported, 4/12 (33%) HAART-treated women experienced severe anaemia, on average 83 days after treatment initiation. The use of HAART is one option to reduce significantly the MTCT rate in low resource settings as recommended now by WHO (see below). Teeraratkul et al described the maternal viral load (VL) response and the risk of intrapartum HIV transmission after starting ZDV (34-36 weeks) + NVP single-dose intrapartum in Thailand (abstract ThOrB1349). A total of 97 women were enrolled; their median VL at baseline was 4.33 log, and median duration of ZDV prophylaxis was 29 days. The median reduction in VL at delivery was -0.71 log compared to baseline (p<0.001), and -1.56 log one week after delivery (p<0.001). VL at 1 and 4 months postpartum increased to higher than baseline levels (median log difference +0.11 and +0.07 log, respectively; p<0.05). The Kaplan-Meier estimation of the transmission rate was 6.3% (95% CI 2.9%-13.7%). The intrauterine to intrapartum infection ratio was 1:2. The authors concluded that short-course ZDV + NVP single-dose suppressed well maternal VL, the VL reduction being the greatest at one week postpartum. The subsequent rebound to higher than baseline levels could be of concern in the context of potential postnatal risk of HIV exposure via breastfeeding (this was not the case in Thailand) and access to HAART for maternal treatment.

In resource limited settings the development of early biological tests for infant HIV diagnosis is crucial. In this context, Singh et al reported on the diagnostic utility of the p24 antigen assay as a potential inexpensive and reliable tool for early HIV-1 diagnosis and estimation of the timing of MTCT (abstract MoPeB3112). The assay used had quasi-perfect sensitivity and specificity at six months. However, the reliability of the test was age-dependant. Optimal sensitivity was 71.4% at six weeks and 100% at six months (p<0.05). Other investigations are required to develop the reliable alternative method that is needed in Africa to identify HIV infection earlier than with serology, as discussed by WHO during this conference (see below).

Perhaps the most important PMTCT data presented during this meeting was an interim analysis from the ongoing Treatment Options Preservation Study (TOPS) in South Africa. During this late breaker presentation by McIntyre et al (abstract LbOrB09), it was reported that supplementing NVP single-dose for the mother and infant with either a four or a seven-day course of ZDV and 3TC (given as Combivir®) for the mother and the baby caused a five-fold reduction in the proportion of women who had evidence of postpartum NVP resistance after six weeks of follow-up, compared to those who by randomization had been exposed to NVP single-dose only. At the time of this interim analysis 156 women had entered the trial and six week resistance data was available for 61 mothers: 18, 20 and 23

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mothers in the NVP single-dose, NVP single-dose + 4 days Combivir® and NVP single-dose + 7 days Combivir® groups (arms 1, 2 and 3, respectively). All women in this analysis had clade C HIV-1 infection. At 6 weeks postpartum, resistance was detected in 53.3% of group 1 mothers, 5.0% in group 2 and 13.6% in group 3, respectively (9.3% of those receiving NVP single-dose + Combivir® irrespective of the duration of the exposure) (p=0.001). The most frequently detected NVP mutations were K103N and Y181C. There was no resistance detected in relation to either ZDV or 3TC exposure. The trial was not powered to look at efficacy but out of the 68 evaluable infants, four were infected through intrauterine transmission and one peri- or post-partum in the NVP single-dose alone group. The final results of the TOPS trial are now eagerly awaited to see whether a difference can be detected between arms 2 and 3, as enrolment in arm 1 has now been stopped considering these very promising interim results. Another study on NVP mutations in HIV-infected women exposed to NVP single-dose in Thailand was presented (abstract WeOrB1289) and confirmed the previously reported data on this subject. It is available now in two back to published articles by Lallemant et al and Jourdain et al (see this IR issue).

5. HIV and Infant feeding:
We acknowledge Ted Greiner, Peggy Koniz-Booher, and Jay Ross who selected and organized under several key themes a first selection of 90 abstracts related to HIV and infant feeding. Among those, the Bordeaux Working Group decided to highlight the following studies. Two prospective studies conducted in Zimbabwe and Côte d'Ivoire presented their results on HIV transmission through breastmilk, the first one in untreated women (abstract MoPpB2008) and the second one in women and children exposed perinatally to ARVs (MoPpB2007). A study conducted in Zambia compared maternal mortality between long and short term breastfeeding exposure (abstract ThPeB7010). The role of partner participation in VCT and couple counselling in the uptake of interventions to prevent postnatal transmission was investigated within a Kenyan study (abstract ThOrC1415). Studies conducted in Côte d'Ivoire, Botswana and South Africa investigated knowledge, attitude and practices of health-care workers concerning infant feeding practices aimed at reducing breastmilk HIV transmission (abstracts ThPeC7294, ThPeB7111 and ThPeE7969).

In a satellite symposium organized with the Ghent International AIDS Society Working Group on HIV in Women and Children, WHO announced the release of the 2004 PMTCT ARV guidelines that are now available on their web site (see this IR issue). During the same symposium, a progress report was presented on the development of guidelines on the early diagnosis of HIV infection. All the material reported is available on the Ghent Group web site (http://www.ghentgroup.org).


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