PMTCT Intelligence Report
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prepared by the Bordeaux Working Group *

* by alphabetical order:

Design of the bibliographic retrieval of this issue

Databases: Current Contents Life Sciences, Clinical Medicine, Social & Behavioral Sciences
(weeks # 15 to 19: April 15, 2002 to May 13, 2002; coverage: journal and book citations)

Journal contents: Health Policy and Planning, MMWR, Social Science and Medicine, Tropical
Medicine and International Health (April to May, 2002)

Number of citations screened for this issue: 1422

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

Number of citations selected for this issue: 10

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

Notes: This article presents the results of a randomised, double-blind placebo-controlled trial which took place between September 1998 and June 2000 in Mombasa (Kenya) to assess the effect of vitamin A supplementation on vaginal shedding of HIV-1. The study, conducted among 400 HIV-1 infected women, shows no significant difference neither in the prevalence of HIV-1 DNA (p= 0.40) nor in the median vaginal HIV-1 RNA concentration (p=1.0) between women receiving vitamin A supplementation and the placebo arm. The authors then list a certain number of possible explanations for this lack of association: statistical power, vitamin A dosage, length of the intervention, HIV-1 infection stage, severity of vitamin A deficiency and lastly the fact that the relationship between serum vitamin A and vaginal HIV-1 shedding is not present in all populations. Overall, according to this study, there is no role for vitamin A supplementation in reducing infectivity or preventing transmission of HIV-1, sexually or from mother to child.

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PMTCT, Primary prevention of sexual transmission


Notes: This second report of the Erice 2001 PMTCT Workshop reviews the issue of vaccination as a means of prevention of postnatal transmission of HIV-1. Vaccinating actively the newborn or immunizing him (her) passively are being considered but the relevance of this research avenue might be modified by the ongoing studies on prevention of postnatal transmission by antiretrovirals. Therapeutic vaccination of HIV-infected pregnant women is a less realistic approach at this stage.

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PMTCT


Notes: Ekpini et al describe in this paper changes in maternal HIV-1 plasma viral load and CD4 cell count associated with a short course of oral ZDV during pregnancy and study also zidovudine (ZDV) resistance. 49 women were included at random (34 in the ZDV group and 15 in the placebo group) among 84 women for whom blood specimens and follow up data during 12 weeks postpartum were available. The two treatment groups were similar according to age, viral load and CD4 T cell count at baseline. These women were classified into three groups (2, 4, and 6 weeks) on the basis of the duration of treatment. In the placebo, no significant difference of viral load was found between the baseline and follow up levels. At delivery, CD4 cell count increased by 157 cell/ml, and was significantly higher than CD4 value at baseline (p=0.03), then declined gradually during postpartum period.

In the ZDV group, after two weeks of treatment the median maternal viral load was 0.48 log10 copies/ml lower than at baseline (p=0.02) and remained between 0.17 and 0.21 log10 copies/ml lower at the postpartum visits. After initiation of treatment CD4 cell counts were significantly higher (p<0.001) than at baseline and higher than corresponding values in the placebo group (p<0.001)

This study assessed also ZDV resistance in 20 women, no mutations associated with ZDV resistance were identified. This reassuring study found no significant overshoot in viral load after the women stopped taking medication and showed also no significant difference of CD4 and viral load during postpartum period in women receiving placebo and ZDV.

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PMTCT/ARV

**Notes:** The present study explores the relation between retinol deficiency, which affects women's mucosal integrity, and perinatal transmission of HIV-1. The authors find no significant correlation (p=0.87) between serum concentrations of retinol and quantified HIV-1 RNA measured in the genital secretions of 301 HIV-infected women enrolled in the New-York WHIS cohort, and thus no association between retinol status and perinatal transmission. Among the factors explaining this lack of relation, the authors mention the lack of severity of retinol deficiency in their study population, linked to a favourable epidemiological and nutritional situation, and thus the low impairment of the women's mucosal integrity.

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**Notes:** This group of primatologists has demonstrated that neonatal macaques (Macaca nemestrina) exposed to HIV-2 (287) constituted an appropriate animal model to study replication in the presence or absence of antiretroviral agents aiming to reduce HIV vertical transmission.

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**Notes:** In this paper, a panel of South African researchers advocates for the strengthening of policy and practice for preventing paediatric HIV/AIDS. They review the major advances in the field of PMTCT, the efficacy of the various antiretroviral regimens, their cost-effectiveness, their side effects, the resistance induced, and the issue of breastfeeding practices in relation to infant and maternal mortality. This article also argues for the operational capacity and the ethical necessity of implementing PMTCT activities in South Africa. The authors indeed underline the inadequacy between the public health urgency of PMTCT and the weak political support and recommendations for such programmes. They call for an increased commitment of the South African government in developing programmes for AIDS prevention and care, within which specific actions to reduce MTCT. NB: Progress has been announced by the South African government since the publication of this paper. (see next Intelligence Report).

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**Notes:** A phylogenetic analysis of HIV-1 sequences from 141 American infected children enrolled in PACTG 377, a randomized trial of four regimens of HAART. Two of these children born in the USA, had subtype D (1) and A/G CRF02 recombinant virus (1) acquired from their mother. Early versions of Amplicor Roche assay underestimated the child HIV plasma viral load in one case. The authors speculate this could have implications for PMTCT in the USA. These recombinant viruses are becoming highly prevalent in Africa; however MTCT is preventable by antiretrovirals in this other epidemiological context.

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Notes: Recent studies have highlighted the importance of postnatal transmission (PT) of HIV-1 through breastfeeding (an absolute risk of 16% at two years with 44% of all mother-to-child-transmission [MTCT] attributable to PT). This study, the first of its kind, assessed the 24 month efficacy of a maternal short course regimen of oral zidovudine in reducing the overall risk of MTCT in breastfeeding populations and evaluated risk factors for MTCT. Methodology consisted in the analysis of pooled individual data from two randomized double-blinded placebo-controlled trials: DITRAME ANRS-049 conducted in Abidjan, Cote d'Ivoire and Bobo-Dioulasso, Burkina Faso and RETRO-CI conducted in Abidjan. Leroy et al report that by 24 months of age, of the total number of live-born children included in the efficacy analysis (n=641), the overall risk of MTCT was 7.8% lower in the zidovudine arm than in the placebo arm (95% CI for the risk difference 0.7-14.9%), a significant 26% reduction in the risk of MTCT (95% CI 2-44%). The efficacy of zidovudine was greater in children born to women with higher CD4 cells counts at enrolment. Indeed, among children born to women with CD4 cell count of less than 500 cells/ml at enrolment, the estimated cumulative risk of HIV-1 infection at age 24 months in the zidovudine group (36.6%) was nearly equal to the corresponding 41.3% risk in the placebo group. This 4% reduction in risk (95% CI -30 to 29%) was not statistically significant. In contrast, among children born to women with CD4 cell counts of 500 cells/ml or greater, the estimated cumulative risks of HIV-1 infection in the zidovudine group were 6.0% at age 2 weeks, 8.8% at 6 months and 9.1% at 24 months. The corresponding risks in the placebo group were 14.7, 19.2 and 22.0%. Main conclusions of this study are: a) peripartum zidovudine regimens can reduce MTCT of HIV-1 despite prolonged breastfeeding; b) at all ages, treatment effects strongly depend on the baseline maternal CD4 cell count; c) advanced maternal HIV-1 disease is a strong determinant of overall MTCT including PT; d) there is a need to determine the optimal maternal CD4 cell count for defining high versus low efficacy. The authors highlight the challenge there is to further reduce both peripartum and postnatal MTCT of HIV-1 and cite possible strategies: to extend the duration of prenatal treatment, combine zidovudine with other antiretroviral regimens, alternatives to breastfeeding and continued antiretroviral therapy for mothers and infants; especially for mothers with low CD4 cell counts. If efficacy of short-course antiretroviral regimens to prevent MTCT depend on maternal immune status, recent WHO/UNAIDS recommendations on the use of these drugs for PMTCT may need to be updated.

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Notes: The aim of this study, conducted between February and October 2000 in three public maternity wards in Rio de Janeiro, Brazil, was to assess a rapid HIV test strategy during labour. For this, two rapid HIV tests (Determine and Double Check) were systematically performed at labour on 858 patients. Test acceptance and performance (confirmation of positive and discordant results by a standard ELISA and Western blot [WB] tests) and HIV prevalence were measured. Of the 841 patients tested (98% acceptance), 13 were positive by both tests, i.e. 1.5% HIV-1 prevalence, and all were confirmed by ELISA and WB analyses. Seven samples gave discordant results by the rapid tests. The positive predictive value for samples that were positive simultaneously by the two rapid tests was 100%. The authors conclude on the acceptance and efficiency of using two rapid HIV tests in labour wards. This is one of the first reports exploring this issue for HIV testing in labour.

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Primary prevention of sexual transmission/VCT

Notes: The PETRA trial was aimed to assessed the efficacy of three short-course regimens of a combination of zidovudine and lamivudine in a randomized, double blind, placebo-controlled trial in South Africa, Uganda, and Tanzania. Between June 1996 and January 2000, HIV-1 infected mothers were randomized to one of the four following regimens: placebo, regimen A, zidovudine plus lamivudine starting at 36 weeks gestation, followed by oral intrapartum dosing and by 7 days postpartum dosing of mothers and infants; regimen B, as regimen A, but without the prepartum component; regimen C, intrapartum zidovudine and lamivudine only. From February 18, 1998 onward, women were only randomized to one of the active treatment groups. Overall, 1797 HIV-infected women were enrolled. It was concluded to the loss of efficacy at 18 months of age of the arms A and B, which were previously reported in conference presentations to significantly reduce the risk of MTCT compared to the placebo at age six weeks. This overall lack of long term efficacy was interpreted by the authors as due to the high risk of subsequent postnatal transmission (PT).

This important study deserves some comments on the interpretation of the findings. First, at 18 months, about 30% of the children died or were lost to follow up without HIV diagnosis, leading to a potential and unmeasured bias if those lost to follow up are not equally distributed for their PT risk between arms. Second, the authors did not provide specific estimates of PT risk in their paper and those may have differed between arms. But assuming that the lack of long term efficacy is due to a high PT, several explanations could be raised: it is possible that PT would be greater after a regimen of several antiretroviral drugs than after a single drug regimen as in ZDV trials conducted in West Africa and Thailand. This is possible if the combination regimen results in a higher postpartum viral load than prior to therapy, and thus a higher PT risk, differential between treatment arm (Van de Perre et al, AIDS 2001;1:658).

Lastly, it is important to note that the characteristics of the PETRA population were quite different from other sites in Africa: higher rate of C-section, higher rate of formula feeding. Also, the maternal immunodeficiency could have been deeper in the PETRA population leading to a higher PT risk as shown in West Africa (see Leroy et al in the same issue of this report). Thus, the PETRA results are important but should be further investigated. Nevertheless, the authors lead to a reasonable conclusion that introduction of short course regimens to prevent MTCT in less-developed countries should be accompanied by interventions to minimise the risk of subsequent transmission via breastfeeding. Note an accompanying editorial by Beckerman, (Lancet 2002; 359:1168) claiming that PMTCT should be viewed as part of a global response and not isolated.

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PMTCT/ARV