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 (weeks # 15 to 19: April 9 to May 7, 2001)
Coverage: Journal and book citations

Other sources: Journal contents (January to April, 2001):
Health Policy and Planning,
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News Groups
Conferences

Number of citations screened for this issue: 1 668
Number of citations selected for this issue: 18

Subject Headings

Contraception
Gynaecology
Infant feeding/Breastfeeding
MTCT (Mother-to-Child Transmission)
Obstetrics
PMTCT/ARV (Prevention of Mother-to-Child Transmission/AntiRetroVirals)
Primary prevention
Termination of pregnancy/Abortion

Citation format

Author(s). Title. Source.
Notes (prepared by the Bordeaux Working Group)
Author address, if available (for reprints)
URL, if available (link to author abstract or full text)
Subject Headings
**Bongertz V, Costa CI, Veloso VG, Grinsztejn B, Joao EC, Calvet G, Pilotto JH, Guimaraes ML and Morgado MG.**


**Notes:** An observational study carried out in Brazil between 1994 and 1998 looking for the role of neutralizing antibody in MTCT. Study population was 132 HIV-1 infected pregnant women, 24% of them being transmitters. MTCT decreased over time and was influenced by the use of ARVs during pregnancy. Neutralization at high titers of the reference isolate MN and of macrophage-tropic heterologous isolates was associated with lack of transmission. The generalizability and implications of these results are insufficiently discussed by the authors.

**Address:** Bongertz V, FIOCRUZ, IOC, Dept Imunol, AIDS & Imunol Mol Lab, Av Brasil 4365, BR-21045900 Rio De Janeiro, BRAZIL.


**MTCT**

**Coutsoudis A, Coovadia H, Pillay K and Kuhn L.**


**Notes:** A trial from Kenya reported recently (Durban AIDS Conference) that HIV-infected mothers who breastfed have a higher maternal mortality rate than those who formula-fed. Coutsoudis et al investigated this hypothesis using data from their Vitamin A intervention trial cohort implemented in Durban, South Africa: 2/410 (0.5%) HIV-infected women who ever breastfed died vs 3/156 (1.9%) among those who formula-fed (p=0.10). There was also no evidence of any increase of maternal morbidity among breastfeeders compared to formula-feeders. The authors conclude there is no deleterious effect of breastfeeding on the health of HIV-infected women and their feeding choice should continue on the basis of current WHO/UNAIDS recommendations. This is a reassuring report with good methodology and using appropriate data. This will be now the first published paper on this issue.

**Address:** Coutsoudis A, Univ Natal, Dept Paediat & Child Hlth, ZA-4001 Durban, SOUTH AFRICA

**URL:** NA

**Infant feeding/Breastfeeding**

**Desire N, Dehee A, Schneider V, Jacomet C, Goujon C, Girard PM, Rozenbaum W and Nicolas JC.**


**Notes:** A newly evaluated technology that has only been explored in adults in this paper but that could be relevant in the future for the early diagnosis of paediatric HIV infection in developing countries with PMTCT programmes.

**Address:** Desire N, Hop Rothschild, Microbiol Serv, 33 Blvd Picpus, F-75571 Paris 12, FRANCE


**MTCT**

**Dijkhuizen MA, Wieringa FT, West CE and Muherdiyantiningsih M.**


**Notes:** Prenatal and postnatal maternal nutritional status affect the quality of breast milk and neonatal health conditions. Deficiencies of vitamin A, iron and zinc coexist and have interacting effects. The results of this community-based study conducted in Indonesia show an almost three-fold greater risk of zinc deficiency in vitamin A-deficient infants, a positive effect of vitamin A supplementation on iron deficiency anaemia and the antagonistic effect of iron supplementation on zinc uptake. Interventions which include supplementation in multivitamins, iron and folates to women as well as paediatric micronutrient supplementation such as vitamin A, should consider the strong interrelation between the micronutrient status of the mother and infant when discussing combinations of micronutrients.

**Address:** West CE, Univ Wageningen & Res Ctr, Div Human Nutr & Epidemiol, POB 8129, NL-6700 EV Wageningen, NETHERLANDS

**URL:** http://www.ajcn.org/cgi/reprint/73/4/786.pdf

**Infant feeding/Breastfeeding**

**Goodburn E and Campbell O.**

**Reducing maternal mortality in the developing world: sector-wide approaches may be the key.** BMJ 2001; 322 (7291): 917-920.

**Notes:** Maternal ill health is the largest contributor to the disease burden affecting women in developing countries. The authors state that maternal and child health interventions implemented up to now have failed. To improve this, there is a need to create a functioning health infrastructure, mainly through the improvement of the coverage and...
quality at the district level. This process needs to be linked to the existing Safe Motherhood Initiative. The article presents an overview of the advantages and drawbacks of three options for funding large scale activities considering technical scope and management: a) vertical maternal health project approach; b) reproductive health programme approach and c) sector-wide approach. They conclude that sector-wide approaches are likely to have a sustainable impact on maternal mortality. A sector-wide approach will help link policy and implementation, giving the possibility to identify priorities at different levels. Nevertheless, this approach will demand political endorsement for long term sustainability, a common approach across sectors and capacity in the Ministries of Health who need to become actively involved through the development of health policies to guide donors. Other issues to look over will be the possibility of an effective decentralisation process, the need for the development of a monitoring system to show impact and the possibility of overload at the local level.

Address: Elizabeth Goodburn, Centre for Sexual and Reproductive Health, John Snow International (UK), London NW5 1TL.
URL: http://bmj.com/cgi/reprint/322/7291/917.pdf

Obstetrics


Notes: This is the first publication on per-contact probability of HIV-1 transmission from representative heterosexual discordant couples in sub-Sahara Africa. The transmission probability per coital act increased significantly with HIV viral load, being highest in younger individuals between 15 and 29 years and if genital ulcer disease was reported by the HIV-1-positive partner (p=0.02). Nevertheless, the study had limited power to detect STD cofactor associations. A higher transmission probability per act from women to men than from men to women was found, although not statistically significant, in contrast to studies in Europe and USA. Low condom use within marriage was reported, despite the fact that condoms and counselling were offered free of charge and promoted by the project. Interventions to reduce viral load could reduce transmission. In addition, better understanding of sexual behaviour including barriers for not using condoms continue to be a priority as behavioural and social change is the primary tool of HIV prevention. No specific data is provided in this report on the risk of transmission in the pre-partum and post-partum lactating periods.

Address: Gray RH, Johns Hopkins Univ, Sch Hyg & Publ Hlth, Dept Populat & Family Hlth Sci, Suite 4030, 615 N Wolfe St, Baltimore, MD 21205 US

Primary prevention


Notes: P. Jha et al state that the global response to the HIV/AIDS epidemic has been inadequate particularly in developing countries. The authors remind us of the need to implement interventions at a wide enough scale to have significant impact, and the necessity to prioritise interventions, proposing the following criteria: a) to consider the importance of the intervention in relation to HIV spread (heterosexual intercourse), b) feasibility of success of the intervention in accessible populations (make sexual contacts safer to avert such contacts, the need of a well-functioning health care system), c) cost effectiveness (unprotected sex within core groups i.e. peer mediated education programmes among female sex workers). The article highlights the most important interventions available to reduce HIV transmission in developing countries: improved case management of STI, short course ARV drugs to prevent MTCT, voluntary counselling and testing (recognising that a sustained effect on behaviour remains uncertain and that high-risk individuals might avoid such services), male circumcision, mass media information and communication programs and the need of evidence-based interventions on their effect and targeting youth through primary prevention. Rigorous evaluation of behavioural analysis interventions focusing on high-risk groups is considered here a first priority. Finally, a research agenda is proposed: microbicides, cost-effective behavioural interventions for high-risk men and youth, to support the vaccine initiative and to enhance monitoring and evaluation of interventions. No specific recommendations for research on PMTCT is provided.

Address: Plummer FA, Univ Manitoba, Dept Med Microbiol, Winnipeg, MB R3E 0W3, CANADA
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Primary prevention, MTCT

Notes: A study of the relationship between maternal plasma RNA levels and MTCT of HIV-1 in African breastfed children in Cote d'Ivoire and Burkina Faso. The design was a nested case-control study within a randomised trial assessing the efficacy of short maternal ZDV to reduce MTCT vs placebo (Pl). Patients were 55 transmitting mothers (23 ZDV, 32 Pl) and 117 non transmitting mothers (47 ZDV, 70 Pl) with maternal RNA levels available and measured at inclusion and day 8 after delivery. The results showed a higher maternal viral load in transmitting mothers compared to non transmitters (4.6 log10 vs 3.7 log10, p<10^-3). In logistic regression, the odds ratio for MTCT was 8.7 for one log increase of maternal RNA at inclusion. This report describes the role of high viral load in overall MTCT of HIV-1 in an African breastfed population.

Address: Leroy V, Univ Bordeaux 2, INSERM U330, IPSED, 146 Rue Leo Saignat, F-33076 Bordeaux, FRANCE


Notes: One of the first studies to look at the relationship between vitamin A levels and sexual transmission of HIV. The results of this case-control study are somewhat paradoxical as lower vitamin A levels may protect against transmission, or vitamin A may increase susceptibility to HIV, especially in case of genital ulcers. No parallel can be drawn with findings from studies looking at the relation between vitamin A and MTCT.

Address: MacDonald KS, Mt Sinai Hosp, Dept Microbiol, Room 1484, 600 Univ Ave, Toronto, ON M5G 1X5, CANADA


Notes: A landmark study of PMTCT by the lamivudine-zidovudine (3TC-AZT) combination both in terms of design and findings. This non-randomised open-label intervention cohort enrolled in France (ANRS 075 Study) in 1997-1998 showed in the absence of breast-feeding a residual transmission of 1.6% at 18 months (95% Confidence Interval [CI]: 0.7-3.3%), or seven cases in total. The 445 HIV-infected pregnant women were treated with the standard 076 AZT regimen plus 3TC starting at 32 week's gestation (150 mg bid). Children received AZT (076 regimen) plus 3TC 2 mg/ kg bid for six weeks. A reference group of 899 women and children treated by AZT alone in the preceding three years had a transmission rate of 6.8% (CI: 5.1-8.7%) (p<0.001). Median maternal plasma HIV-1 viral load decreased by 1.2 log between enrolment in the cohort and delivery (p=0.01). The M184V lamivudine resistance mutation was observed in 52/132 (39.4%, CI: 31.1-47.7%) of maternal samples at six weeks post-delivery. There were 65 discontinuations of 3TC in 451 neonates, 40 of them for adverse effects (8.9%). Among these, 30 hematologic disorders were documented, neutropenia or anaemia, requiring blood transfusion in nine cases. Two deaths of uninfected children with neurological complications related to mitochondrial dysfunction were documented. The authors are not entirely clear on the usefulness of their findings for updating guidelines in industrialized countries, considering cases averted and safety issues. They provide however an excellent example of the use of a non-randomised study design in the context of the evaluation of PMTCT interventions.

Address: Mandelbrot L, Hop Cochin, Dept Obstet Gynecol, 123 Blvd Port Royal, F-75014 Paris, FRANCE

MTCT, PMTCT/ARV

Notes: A preliminary report discussing a study design and early results of the evaluation of a PMTCT programme.

Address: NA
URL: NA

PMTCT

Perinatal HIV Guidelines Working Group Members. Public Health Service Task Force recommendations for use of antiretroviral drugs in pregnant HIV-1 infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United Sates.[Visited: 05/11/2001].

Notes: The May 4, 2001 revision of the previously published guidelines (January 24, 2001). Limited changes are proposed: extension of the use of the 076 ZDV regimen to all HIV-infected previously untreated pregnant women regardless of plasma HIV RNA copy number; no further recommendation is provided to monitor lactate levels in the neonatal period in the absence of new information on their clinical significance; details on the components of comprehensive postpartum follow-up of HIV-infected women are outlined; long-term follow-up of exposed infants is recommended up to six years and mitochondrial dysfunction remains a concern. Safety, pharmacokinetics and mechanisms of action of ARV combination regimens require more research, including resistance studies.

Address: NA
URL: http://www.hivatis.org/guidelines/perinatal/May03_01/PerinatalMay04_01.pdf

PMTCT/ARV


Notes: One of the rare studies to estimate directly and comparatively the risk of postpartum morbidity according to the mode of delivery. The US-based Women and Infants Transmission Study cohort was used, with 8-week postpartum documentation of 1186 deliveries of singleton births, 4.7% of them with a scheduled C-section. The cumulative incidence of postpartum morbidity was 15.0%. This risk was associated with scheduled C-section (adjusted odds ratio: 2.6 compared to spontaneous vaginal delivery, CI: 1.6-4.2). This relation was particularly well documented for fever without infection and urinary tract infection. The authors appropriately recommend informing HIV-infected women of these risks before choosing PMTCT interventions in industrialized countries.

Address: Read JS, NICHD, Adolescent & Maternal AIDS Branch, NIH, Execut Bldg, Room 4B11F, 6100 Execut Blvd MSC 7510, Bethesda, MD 20892 USA

Obstetrics


Notes: A comparative non-randomized intervention study looking at recurrence, persistence and progression of cervical intraepithelial neoplasia (CIN) after initial excisional therapy among 56 HIV-infected women with or without HAART with a protease inhibitor (PI) and 62 HIV-negative control women. HIV infection was significantly associated with progression, persistence or recurrence of the lesions, as already documented in the literature. Among HIV-infected women, HAART with PI decreased statistically the frequency of these three adverse outcomes.

Address: Robinson WR, Harrington Canc Ctr, 1500 Wallace Blvd, Amarillo, TX 79106 USA

Gynaecology


Notes: The editorial accompanying the paper by Mandelbrot et al is generally favourable to the study, its design and its main conclusions, especially on efficacy, resistance and haematologic toxicity. This commentary reminds us that serious adverse events were not observed in excess in the AZT-3TC group compared to the zidovudine cohort and that mitochondrial dysfunction has not been seen in the US. The author is quite cautious on the clinical and public health significance of the resistance data. He suggests further exploring the use of 3TC in pregnant women.
excluding the neonatal treatment, in comparison to AZT and nevirapine monotherapy in developing countries, while continuing the implementation of the already proven and simple ARV regimens.

**Address:** Shaffer N, CDC & Prevent, MTCT Unit, Global AIDS Program, MS E-41, 1600 Clifton Rd, Atlanta, GA 30333 USA

**URL:** NA

**PMTCT/ARV**


**Notes:** The authors hypothesised that ARV combinations of several drugs could be less long term effective in reducing MTCT of HIV in breastfeeding populations than one drug due to a higher maternal viral load rebound after the ARV discontinuation while breastfeeding. This hypothesis was based on the observation of MTCT rates (assessed with different judgement criteria) in evaluating the long term efficacy in four African ARV trials aimed to prevent MTCT. This needs to be further investigated with appropriate data sets including prospective maternal viral load assessments and standardised methods of comparison of outcomes in such trials.

**Address:** Van de Perre P, Ctr Muraz, 01 BP 153, Bobo Dioulasso, BURKINA FASO

**URL:** NA

**PMTCT/ARV**


**Notes:** A cost-effectiveness analysis concluding that in the US, genotypic antiretroviral resistance is valuable for patients acquiring drug resistance through failed treatment (secondary resistance). The interest of genotyping is still limited for patients infected with resistant virus (primary resistance) as long as its prevalence remains low. This paper does not address the issue of the treatment of pregnant women and their neonates for PMTCT, although the issue of resistance in this context should not be neglected in the future.

**Address:** Weinstein MC, Harvard Univ, Sch Publ Hlth, Ctr Risk Anal, 718 Huntington Ave, Boston, MA 02115 USA


**PMTCT/ARV**


**Notes:** An in-depth US study of 14 HIV-infected women before and after treatment of cervical intra-epithelial neoplasia lesions. RNA shedding increased 1.0 to 4.4 log_{10} (10,000 fold) when cervix was inflamed and ulcerated by treatment. Genotypic analysis suggested local viral replication. The authors consider these findings compatible with the hypothesis of increased transmissibility of HIV in case of STD. Although not stated, this is a relevant conclusion in case of MTCT.

**Address:** Wright TC, Columbia Univ Coll Phys & Surg, Dept Pathol, 630 W 168th St, Room 16-428, P&S Bldg, New York, NY 10032 US


**Gynaecology, MTCT**