



HIV Care & PMTCT in Resource-Limited Settings

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prepared by the Bordeaux Working Group

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Number of citations selected for this issue: 13

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, **Subject Headings**

Subject headings / Subheadings indexing the selected references (by alphabetical order)

Adults / Women	Eastern Europe	Infant feeding / Breastfeeding	Prevention of Mother-To-Child Transmission (PMTCT) / AntiRetroViral (ARV)	Treatment impact and response
Children	Gynæcology	Infections (Others) / Prophylaxis	Prevention of sexual transmission	Treatment monitoring
Clinical manifestations (Others)	Hepatitis B infection (HBV)	Low Income Countries (LICs) / Africa, Asia, Carribean, South America	Randomized Controlled Trial (RCT)	Treatment programme
Comprehensive care	Hepatitis C infection (HCV)	Mother-To-Child Transmission (MTCT)	Termination of pregnancy / Abortion	Tuberculosis (TB) / Prophylaxis
Conference summary	Highly Active AntiRetroviral Treatment (HAART)	Natural history	Treatment adherence	Viral resistance
Contraception	Industrialized countries	Obstetrics	Treatment complications	Voluntary Counselling and Testing (VCT)

Alberti A, Clumeck N, Collins S, Gerlich W, Lundgren J, Palu G, Reiss P, Thiebaut R, Weiland O, Yazdanpanah Y, Zeuzem S. **Short statement of the first European consensus conference on the treatment of chronic hepatitis B and C in HIV co-infected patients.** Journal of Hepatology 2005;42(5):615-624.

Introduction. Despite recent advances in the management of hepatitis and HIV co-infection, there is no clear consensus among hepatology, infectious diseases and virology experts on treatment of co-infections and patient management. This encouraged the organisation of a European Consensus Conference to review current knowledge on the treatment of chronic hepatitis B and C in HIV co-infected patients, with the view to developing this consensus statement. An organising committee drafted questions to be addressed at the conference, and following 2-days of presentations and discussions, an independent Jury Panel assessed the evidence and prepared this statement with the aim of addressing eight questions: What are the reasons to treat viral hepatitis in HIV co-infected patients in the HAART era? How should viral hepatitis be diagnosed and how should disease severity be assessed in HIV-infected patients? What are the current treatment options? Which patients should be treated and when? How should co-infected patients be treated (treatment algorithms)? How should anti-hepatitis treatment be monitored? How should end-stage liver disease be managed? What are the most important areas for future research? This process essentially follows the consensus process used for preparing NIH Consensus Statements. This short version of the consensus summarises the main conclusions and recommendations from the conference.

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HBV, HCV, Industrialized countries

Berk DR, Falkovitz Halpern MS, Hill DW, Albin C, Arrieta A, Bork JM, Cohan D, Nilson B, Petru A, Ruiz J, Weinrub PS, Wenman W, Maldonado YA. **Temporal trends in early clinical manifestations of perinatal HIV infection in a population-based cohort.** JAMA 2005;293(18):2221-2231.

Abstr. Context The effect of early antiretroviral therapy (ART) on the early progression of perinatal human immunodeficiency virus (HIV) infection is not well defined. Objective To examine early disease progression and survival in a population-based cohort with perinatal HIV infection in relation to year of birth and use of ART. Design, Setting, and Patients Retrospective study of temporal trends in early progression of perinatal HIV infection among 205 HIV-infected children in Northern California born between January 1, 1988, and December 31, 2001, and followed up through age 3 years. Main Outcome Measures Prevalence of and age at progression to a first US Centers for Disease Control and Prevention category C diagnosis relative to year of birth, type of ART, and age at initiation of therapy. Results Of 205 children, 134 (65%) received ART and/or Pneumocystis jiroveci pneumonia prophylaxis. By age 3 years, 81 (40%) progressed to a category C diagnosis, 41 (51%) of whom died. Untreated children were significantly more likely to progress to a category C diagnosis (62% [44/71] untreated vs 28% [37/134] treated children, $P < .001$); none of 23 infants who received triple ART progressed to category C. However, even without triple ART, very early mono/dual ART (by age 2 months vs 3-4 months) was associated with delayed and decreased progression to category C ($P = .02$). Of 33 children born between January 1, 1996, and December 31, 2001, only 7 (21%) progressed to category C ($P = .02$ compared with 1988-1995), 6 of 7 of whom received no therapy. More recent year of birth and more advanced therapy were associated with improved survival. Conclusions This population-based cohort demonstrated decreased early HIV progression and improved survival at age 3 years, associated with more advanced therapy. Although limited by small sample size, the findings suggest that very early treatment, even without triple ART, was associated with improved outcome.

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Children, Industrialized countries, PMTCT /ARV

Brogly S, Williams P, Seage GR, Oleske JM, Van Dyke R, McIntosh K. **Antiretroviral treatment in pediatric HIV infection in the United States - From clinical trials to clinical practice.** JAMA 2005;293(18):2213-2220.

Abstr. Context Antiretroviral therapy (ART) for pediatric human immunodeficiency virus (HIV) infection has evolved from simple nucleoside reverse transcriptase inhibitor (NRTI) regimens to complex combination therapies based largely on evidence from clinical trials. However, the integration of novel ART into the clinical care of pediatric HIV infection has not been examined. Objectives To describe changes in the treatment of pediatric HIV infection in the United States from 1987-2003, to assess concordance of initial regimens with US pediatric guidelines, and to identify predictors of the first regimen switch. Design, Setting, and Participants The study population included 766 perinatally HIV-infected children in the Pediatric AIDS Clinical Trials Group 219C cohort born before January 1, 2004, who had not participated in an ART clinical trial at 219C enrollment or during follow-up. Main Outcome Measures Proportion of children receiving specific ART regimens, proportion of children initiating ART according to pediatric guidelines, and time to first regimen switch (risk of switching). Results Single and dual NRTI regimens were used most frequently through 1997. In 1998, 2 years

after protease inhibitors were approved for adult HIV infection and at the time pediatric guidelines were issued, regimens of highly active antiretroviral therapy including a protease inhibitor became most frequently used. From 1998-2003, 22% of children initiated ART with a regimen not recommended by pediatric guidelines. In multivariate regression, the risk of switching decreased with age at ART initiation (hazard ratio [HR], 0.96; 95% confidence interval [CI], 0.94-0.99) and increased with year of initiation (HR, 1.28; 95% CI, 1.23-1.33). The risk of switching was higher in children who started with 1 NRTI (HR, 8.05; 95% CI, 5.80-11.18), 2 NRTIs (HR, 4.08; 95% CI, 3.08-5.40), or an unconventional regimen (HR, 6.23; 95% CI, 3.36-11.54) vs children who started with a protease inhibitor-containing regimen; and in children who initiated ART at CD4 T lymphocyte percentages less than 15 vs 15 or greater (HR, 2.90; 95% CI, 1.03-8.13). Conclusions There was a short lag between the identification of novel ART and its adoption in the pediatric community. A variety of regimens were used, including some unorthodox therapies. Important predictors of first regimen switch were identified.

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Children, HAART, Industrialized countries

Costello C, Nelson KE, Jamieson DJ, Spacek L, Sennun S, Tovananubutra S, Rungruenthanakit K, Suriyanon V, Duerr A. **Predictors of low CD4 count in resource-limited settings - Based on an antiretroviral-naive heterosexual Thai population.** Journal of Acquired Immune Deficiency Syndromes 2005;39(2):242-248.

Abstr. A barrier to the appropriate provision of antiretroviral therapy to treat immunosuppressed HIV-infected persons in resource-poor countries is identifying who requires treatment. The World Health Organization (WHO) has suggested using a clinical algorithm combined with a total lymphocyte count (TLC) < 1200 cells/mm³ as a surrogate for a CD4 count less than 200 cells/mm³ when it is not possible to measure the CD4 count. We evaluated various TLC levels, anemia, and body mass index and compared our data with the WHO criteria to develop a more sensitive algorithm to predict CD4 counts of <200 cells/mm³ and <350 cells/mm³ in 839 men and women from Thailand infected with HIV-1 subtype E (CRF01_AE). The December 2003 WHO guidelines had a sensitivity of 34.1% in men and 31.8% in women to detect persons with a CD4 count <200 cells/mm³ in this HIV-infected population from Thailand. The use of a TLC < 1500 cells/mm³ or TLC <2000 cells/mm³ combined with anemia or WHO stage II infection doubled the sensitivity to detect persons with a CD4 count <200 (63.0% in men, 68.2% in women) with less than a 6% decrease in specificity.

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Adults, LICs / Asia, Natural history

Dieye TN, Vereecken C, Diallo AA, Ondoa P, Diaw PA, Camara M, Karam F, Mboup S, Kestens L. **Absolute CD4 T-Cell counting in resource-poor settings - Direct volumetric measurements versus bead-based clinical flow cytometry instruments.** Journal of Acquired Immune Deficiency Syndromes 2005;39(1):32-37.

Abstr. Flow cytometry is an accurate but expensive method to determine absolute CD4 cell counts. We compared different methods to measure absolute CD4 counts in blood samples from HIV-infected and uninfected subjects using a research/clinical flow cytometer (FACScan); a dedicated clinical instrument (FACSCount); and a volumetric, mobile, open-system flow cytometer equipped with 3 fluorescence and 2 light scatter detectors (Cyflow SL blue). The FACScan and Cyflow were used as single-platform instruments, but they differ in running cost, which is a central factor for resource-poor settings. Direct volumetric and bead-based CD4 measurements on the Cyflow were compared with 2 bead-based single-platform CD4 measurements on the FACSCount and on FACScan (TruCount) in "Le Dantec" Hospital, Dakar, Senegal, using whole blood samples from 102 HIV+ and 28 HIV- subjects. The agreement between the various measurement methods was evaluated by Bland-Altman analysis. Volumetric CD4 measurements on the Cyflow using a no-lyse-no-wash (NLNW) procedure and a lyse-no-wash (LNW) procedure correlated well with each other (R² = 0.98) and with CD4 measurements on the FACSCount (R² = 0.97) and FACScan (R² = 0.97), respectively. Red blood cell lysis had no negative effect on the accuracy of absolute CD4 counting on the Cyflow. An excellent correlation was observed between bead-based CD4 measurements on the Cyflow and CD4 measurements on the FACSCount (R² = 0.99) and FACScan (R² = 0.99). Rigid internal and external quality control monitoring and adequate training of technicians were considered essential to generate accurate volumetric CD4 measurements on the Cyflow.

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Adults, LICs / Africa, Treatment monitoring

Kagaayi J, Dreyfuss ML, Kigozi G, Chen MZ, Wabwire Mangen F, Serwadda D, Wawer MJ, Sewankambo NK, Nalugoda F, Kiwanuka N, Kiddugavu M, Gray RH. **Maternal self-medication and provision of nevirapine to newborns by women in Rakai, Uganda.** Journal of Acquired Immune Deficiency Syndromes 2005;39(1):121-4.

Abstr. To assess the effectiveness of maternal self-administration of nevirapine for prevention of mother-to-child transmission (MTCT) of HIV, we conducted a program to provide maternal and newborn doses of nevirapine to pregnant women in rural Uganda. Women provided blood for HIV testing and were offered Voluntary counseling and testing (VCT) during annual community HIV surveys. HIV-positive women who accepted VCT were offered nevirapine tablets and syrup. Blood samples were collected postpartum from women and their babies. Infants were tested for HIV by polymerase chain reaction (PCR), and a subsample of maternal and infant blood was assayed for nevirapine. Among the 981 women tested for HIV, 900 (91.7%) accepted VCT, of whom 105 (11.7%) were HIV-positive. Ninety-three women accepted nevirapine, of whom 81 (87.1%) were followed postpartum; 75 (92.6%) reported receipt of the drug, and 69 reported taking the tablets (85.2%). There were 81 liveborn babies (3 sets of twins), and 67 (84.8%) received the syrup. In a subsample of 25 mothers reporting receipt of the drug, nevirapine was detected in 22 (88.0%) and 24 (96.0%) babies tested. PCR of 67 infant blood samples identified 5 HIV-positive (MTCT rate = 7.5%, 95% confidence interval [CI]: 0.3% 16.6%). Mothers can administer nevirapine to themselves and their newborns and can achieve low rates of perinatal HIV infection.

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Children, LICs / Africa, PMTCT / ARV

Kuhn L, Trabattoni D, Kankasa C, Semrau K, Kasonde P, Lissoni F, Sinkala M, Ghosh M, Vwalika C, Aldrovandi GM, Thea DM, Clerici M. **alpha-defensins in the prevention of HIV transmission among breastfed infants.** Journal of Acquired Immune Deficiency Syndromes 2005;39(2):138-142.

Abstr. alpha-Defensins have been observed to have anti-HIV activity but have not been investigated in relation to mother-to-child HIV transmission. We measured the concentration of alpha-defensins in breast milk of HIV-positive mothers and tested whether the concentrations were associated with HIV transmission. A nested case-control study of 32 HIV-positive women who transmitted HIV to their infants and 52 randomly selected HIV-positive women who did not transmit HIV to their infants was conducted in Lusaka, Zambia. a-Defensins were detected in most (79%) of the milk samples tested. Concentrations of a-defensins increased as breast milk HIV RNA quantity increased, and breast milk HIV RNA quantity was, in turn, a strong and significant predictor of HIV transmission. After adjustment for milk HIV RNA quantity, however, a-defensin concentration was significantly associated with a decreased risk of intrapartum and postnatal HIV transmission (odds ratio = 0.3, 95% confidence interval: 0.09-0.93). Our data suggest that there may be a role for a-defensins in prevention of HIV transmission to breastfed infants.

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Infant feeding / Breastfeeding, LICs / Africa, MTCT, PMTCT

Kupka R, Garland M, Msamanga G, Spiegelman D, Hunter D, Fawzi W. **Selenium status, pregnancy outcomes, and mother-to-child transmission of HIV-1.** Journal of Acquired Immune Deficiency Syndromes 2005;39(2):203-210.

Abstr. Background: Among HIV-infected pregnant women, low selenium status may increase risk of mother-to-child transmission (MTCT) of HIV and poor pregnancy outcomes (low birthweight, small for gestational age, preterm birth, and fetal death) through several mechanisms, such as by promoting maternal HIV disease progression, viral shedding in the genital tract, and development of mastitis. However, there is no direct epidemiologic evidence on these relations among HIV-infected pregnant women. Objective: To investigate the association between selenium status during pregnancy and pregnancy outcomes, MTCT of HIV, and child mortality. Design: Baseline plasma selenium measurements from HIV-positive pregnant women (n = 670) were obtained between 12-27 weeks of gestation and mother-child pairs were followed prospectively until 24 months after delivery. Results: Low plasma selenium levels were associated with increased risks of fetal death, child death, and HIV transmission through the intrapartum route. Low selenium status, was not associated with risks of low birthweight or preterm birth but was associated with an apparently lower risk of small for gestational age. Conclusion: Adequate selenium status may be beneficial for some but not all pregnancy outcomes. Further studies are needed to better understand the role of selenium status in pregnancy outcomes, HIV transmission, and child health.

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LICs / Africa, MTCT

Mbaye AD, Sy HS, Gueye NRD, Ba A, Sylla A, Diouf S, Diagne I, Sarr M, Sow HD. **Epidemiological and clinical aspects of paediatric HIV infections in Albert-Royer Paediatric hospital (Dakar, Senegal).** Archives de Pédiatrie 2005;12(4):404-409.

Abstr. Human Immunodeficiency Virus (HIV) infection prevalence rate is estimated at 1.4% in Senegal, and about 3,000 children could be infected. HIV positive children are followed up since 2000 in Albert Royer Hospital (Dakar, Senegal). Objectives. - To describe clinical and epidemiological aspects of HIV paediatric infection, and to evaluate the implementation of high active antiretroviral therapy in HIV positive children in our country. Population and methods. - Over a period of three years, the medical reports of 98 infected patients have been collected, 96% with HIV I infection. Results. - Most of the patients had a maternally transmitted HIV infection (99%). At their enrolment, the median age was 60 months; malnutrition (79%), persistent lymphadenopathy (65%) and skin lesions (64%) were the common clinical manifestations. Thirty-nine percent of the patients were in class C (CDC) and 81% had CD4 cell count \leq 25%. Median viral load were 421,852 copies/ml at presentation. Seven infants had a rapid progressive disease with encephalopathy. Thirty-six patients received high active antiretroviral therapy with high observance and good tolerance. Conclusion. - This study allowed to define clinical and biological profile of paediatric HIV infection in our country and to update the implementation of high active antiretroviral therapy. (c) 2005 Publie par Elsevier SAS.

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Children, HAART, LICs / Africa, Natural history

Mirochnick M, Stek A, Acevedo M, Keller M, Holland D, Capparelli E, Connor J, Huang S, Hughes M, Watts H, Mofenson L, Bryson Y. **Safety and pharmacokinetics of nelfinavir coadministered with zidovudine and lamivudine in infants during the first 6 weeks of life.** Journal of Acquired Immune Deficiency Syndromes 2005;39(2):189-194.

Abstr. The safety and pharmacokinetics of nelfinavir coadministered with zidovudine and lamivudine were studied in 26 infants during the first 6 weeks of life. Cohort 1 infants (n = 7) received 10 mg/kg 3 times a day, and cohort 2 infants (n = 19) received 40 mg/kg twice a day. Two cohort 1 infants at week 1 and none at week 6 exceeded the target 24-hour area under the curve (AUC) of 30 μ g center dot h/mL, equal to the 10th percentile of the AUC for adults receiving standard nelfinavir dosing. In cohort 2, the median 24-hour AUC was 38 μ g center dot h/mL at both time points, with considerable variability among the infants. Three of 11 cohort 2 infants at week 1 and 4 of 11 at week 6 did not meet the AUC target. Median nelfinavir oral clearance was 2.1 L/h/kg at weeks 1 and 6. The median ratio of the plasma concentrations of the nelfinavir metabolite M8 to unchanged nelfinavir increased from 0.16 (range: 0-0.38) during week 1 to 0.56 (range: 0.4-1.47) during week 6 (P < 0.01). There were no significant differences in any of the other pharmacokinetic parameters when week 1 and week 6 results were compared. Few adverse event, were attributed to nelfinavir. These data suggest that nelfinavir is well tolerated in infants at these doses, but exposure was frequently less than that seen in adults taking standard nelfinavir dosing. Further investigations of larger doses, such as 75 mg/kg twice a day, should be undertaken.

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Children, HAART, Industrialized countries

Indian Journal of Medical Research. **Special Issue on HIV/AIDS**, 2005;121(4).

Introduction. The HIV epidemic has reached an important threshold in India. India has the world's second largest burden of HIV-infected persons. One of every six new HIV infections occurs in India. Two Indians become HIV-infected every minute and HIV is expected to exacerbate a number of other important public health problems in India. India's DOTS programme for control of tuberculosis has been a model of success. Yet, India also now has the largest number of HIV-TB co-infected persons in the world. In addition to increasing the number of active TB cases, HIV can be expected to increase TB associated mortality in India, challenging the continued success of the national DOTS programme. In a setting of an expanding feminization of the HIV epidemic, Indian women are already overburdened with high maternal mortality and limited access to health care. Indian women endure high rates of many other health problems, including the world's highest rates of cervical cancer, which would be expected to increase further due to HIV infection. At least 500,000 Indians have already died of HIV-associated illnesses and most of these deaths have occurred in the past 5 yr. HIV-associated morbidity and mortality will put an increasing, costly burden on public and private medical care systems, which are already coping with major challenges. Finally, recent publicity of episodes of violence and discrimination towards adults and children with HIV in India, reflect significant stigmatization of the victims of HIV infection, in many segments of society.

Free full text available at: http://www.icmr.nic.in/ijmr/2005/April/apr_contents.htm

LICs / Asia

Journal of Acquired Immune Deficiency Syndromes. **Special issue on Fertility Regulation and Systemic Hormones in HIV-Infected and At-Risk Women - Conference Proceedings**, 2005;38(Suppl 1).

Abstr. Why is fertility an issue for HIV-infected and at-risk women? The issues discussed include social and behavioral, programme and implementation, and biological and clinical.

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Adults / Women, Conference summary, Contraception, Gynaecology

Journal of Neurovirology. **Special Issue on NeuroAIDS in the developing world**, 2005;11(Suppl 1).

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Clinical manifestations (others), LICs