



## HIV Care & PMTCT in Resource-Limited Settings

### Monthly Intelligence Report

### 2005, Vol 1, Issue 9

[Available on line](#)

#### prepared by the Bordeaux Working Group

**Members:** Elise Arrivé, Renaud Becquet, François Dabis (Coordinator), Valériane Leroy, Dominique Marchand, Evelyne Mouillet (Coordinator), Joanna Orne-Gliemann, Freddy Perez, Charlotte Sakarovitch, Catherine Seyler, Besigin Tonwe-Gold.

**Number of citations selected for this issue: 31 + IAS Conference Proceedings**

**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)

Becquet R, Ekouevi DK, Sakarovitch C, Bequet L, Viho I, Tonwe Gold B, Dabis F, Leroy H. **Knowledge, attitudes, and beliefs of health care workers regarding alternatives to prolonged breast-feeding (ANRS 1201/1202, Ditrane Plus, Abidjan, Cote d'Ivoire).** Journal of Acquired Immune Deficiency Syndromes 2005;40(1):102-105.

**Abstr.** The Ditrane Plus project conducted in Abidjan, Cote d'Ivoire, is aimed at the prevention of mother-to-child transmission of HIV in combining perinatal antiretroviral interventions with a systematic proposal of alternatives to prolonged breast-feeding: formula feeding from birth, or exclusive breast-feeding for 3 months then early cessation of breast-feeding. We surveyed all health care workers involved in this project in November 2003 using a self-administered anonymous questionnaire to investigate their knowledge, attitudes, and beliefs regarding the infant feeding interventions proposed since March 2001. Their knowledge regarding infant practices proposed within the study was consistent and their attitude was in accordance with the study protocol. However, proposing alternatives to prolonged breast-feeding causes difficulties for health care workers that should be taken into account when tailoring such complex interventions.

**Address:** Becquet, R; Univ Bordeaux 2; INSERM; 146 Rue Leo Saignat; F-33076 Bordeaux; France.  
[Renaud.Becquet@isped.u-bordeaux2.fr](mailto:Renaud.Becquet@isped.u-bordeaux2.fr)

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

Bentwich Z. **CD4 measurements in patients with HIV: are they feasible for poor settings?** Plos Medicine 2005;2(7):595-596.

**Abstr.** Measurement of peripheral blood CD4 T lymphocytes is probably the most important laboratory assay for evaluation and monitoring of patients with HIV. The CD4 count is critical for determining the clinical stage of HIV infection, for deciding when to start antiretroviral therapy (ART), for evaluating the efficacy of treatment, and for changing the medications when necessary. Most HIV treatment decisions are therefore based upon the CD4 count.

**Address:** Bentwich, Z; Hebrew Univ Jerusalem; Sch Med; IL-91905 Jerusalem; Israel.  
[zbentwich@rosettagenomics.com](mailto:zbentwich@rosettagenomics.com)

**Free full text :** [http://medicine.plosjournals.org/archive/1549-1676/2/7/pdf/10.1371\\_journal.pmed.0020214-S.pdf](http://medicine.plosjournals.org/archive/1549-1676/2/7/pdf/10.1371_journal.pmed.0020214-S.pdf)

**LICs, Treatment monitoring**

Bharucha KE, Sastry J, Shrotri A, Sutar S, Joshi A, Bhore AV, Phadke MA, Bollinger RC, Shankar AV. **Feasibility of voluntary counselling and testing services for HIV among pregnant women presenting in labour in Pune, India.** International Journal of Std and AIDS 2005;16(8):553-555.

**Abstr.** Factors affecting the eligibility and acceptability of voluntary counselling and rapid HIV testing (VCT) were examined among pregnant women presenting in labour in Pune, India. Of the 6702 total women appearing at the delivery room from April 2001 to March 2002, 4638 (69%) were admitted for normal delivery. The remaining women presented with obstetrical complications, delivered immediately or were detected to be in false labour. Overall, 2818 (61%) of the admitted women had been previously tested for HIV during their pregnancy. If previously seen in the hospital's affiliated antenatal clinic, the likelihood of being previously tested was 89%, in contrast to 27% of women having prenatal care elsewhere. Of the admitted women, 3436 (74.3%) were assessed for their eligibility for rapid HIV VCT in the delivery room. Only 1322 (38%) of these women were found to be in early labour and without severe pain or complications, and therefore eligible for rapid HIV screening in the delivery room (DR). Of those 1322 eligible women, only 582 (44%) consented and were tested for HIV, of whom nine (1.6%) were found to be HIV-infected. Of the 1674 women arriving in the DR with no evidence of previous HIV testing, through this DR screening programme, we identified four women with HIV who could now benefit from treatment with ART. Given the high rates of HIV testing in the antenatal clinic at this site and the challenges inherent to conducting DR screening, alternatives such as post-partum testing should be considered to help reduce maternal to infant transmission in this population.

**Address:** Shankar, AV; Johns Hopkins Univ; Bloomberg Sch Publ Hlth; 615 N Wolfe St; Baltimore; MD 21205; USA. [avshanka@jhspu.edu](mailto:avshanka@jhspu.edu)

**LICs / Asia, Voluntary Counselling and Testing (VCT), PMTCT**

Breen RAM, Smith CJ, Cropley I, Johnson MA, Lipman MCI. **Does immune reconstitution syndrome promote active tuberculosis in patients receiving highly active antiretroviral therapy?** AIDS 2005;19(11):1201-1206.

**Abstr.** Objectives: To assess whether highly active anti-retroviral therapy (HAART) contributes to the presentation of active tuberculosis (TB). Design: Retrospective single-centre cohort study. Methods: A total of 111 HIV-infected individuals with active TB were identified at an urban teaching hospital between February 1997 and April 2004. Those receiving HAART at the time of TB diagnosis were assessed. Results: Nineteen of 111 (17%) were receiving HAART when TB developed. Within this group there appeared to be two distinct populations. Thirteen of 19, 12 from ethnic or social groups with high background rates of TB, developed

disease a median of 41 days (range, 7-109) after starting HAART ('early TB' group). In six of 19 ('late TB' group), TB occurred a median of 358 days after HAART initiation (range, 258-598). The 'early TB' group had lower CD4 cell counts when starting HAART in comparison with the 'late TB' group (median; 87 versus 218 x 106 cells/l; P = 0.04); however no difference was observed in the rate of change of CD4 cell count (P = 0.5) or HIV load. Paradoxical reaction rate in the 'early TB' group was significantly greater than in the 'late-TB' group (62 versus 0%, P = 0.02) and greater than in a similar control population who started HAART while taking anti-TB therapy (62 versus 30%, P = 0.05). Conclusions: These data suggest anti-HIV treatment may amplify the presentation of active TB. This has implications for antiretroviral programmes in countries with high TB rates and warrants prospective investigation of a larger cohort. (c) 2005 Lippincott Williams and Wilkins.

**Address:** Breen, RAM; Royal Free Hosp; Dept Thorac & HIV Med; Pond St; London NW3 2QG; England. [r.breen@rfc.ucl.ac.uk](mailto:r.breen@rfc.ucl.ac.uk)

#### **HAART, TB**

Bulterys M, Weidle PJ, Abrams EJ, Fowler MG. **Combination antiretroviral therapy in African nursing mothers and drug exposure in their infants: New pharmacokinetic and virologic findings** [Editorial commentary]. *Journal of Infectious Diseases* 2005;192(5):709-712.

**Introduction.** Africa's HIV/AIDS epidemic has reached crisis proportions and calls for a rapid expansion of both prevention and treatment services, particularly among young women and children. Mother-to-child transmission (MTCT) is the most important source of HIV-1 infection in children, and prolonged breast-feeding is associated with a near doubling of the risk of MTCT. In resource-limited settings, the majority of HIV-1-infected mothers choose to breast-feed because of cultural norms, the high cost of formula, the lack of a safe water supply, and the stigma associated with not breast-feeding. Reducing HIV-1 transmission during lactation remains a pressing global health dilemma confronting HIV-1-infected women, health-care providers, and policy makers. Clinical trials are currently under way to assess whether the use of highly active antiretroviral therapy (HAART) during late pregnancy and during the first 6 months of lactation, followed by early weaning, can substantially reduce the risk of HIV-1 transmission among breast-feeding women. In addition, it is anticipated that eligible HIV-1-infected nursing mothers in sub-Saharan Africa will increasingly be able to receive HAART for the maintenance of their own health. In this issue of the *Journal of Infectious Diseases*, Shapiro et al. present data on the pharmacokinetics of antiretroviral (ARV) drugs among lactating women and on the effect of HAART on breast milk HIV-1 RNA and DNA. These studies are of vital importance for both biological understanding and health policy. In the first report, detailed pharmacokinetic findings are presented on the magnitude of infant ARV drug exposure from breast milk. Although it was based on a relatively modest sample size (20 mother-infant pairs), this is the first published study to evaluate ARV drug concentrations in breast-feeding infants of women receiving HAART in Africa and is the largest study to date of ARV drug concentrations in breast milk. In the second report, the authors demonstrate that HAART effectively reduces HIV-1 RNA load, but not DNA load, in breast milk. Both studies were conducted in Botswana, where these findings are particularly relevant, given the government's sustained commitment to a nationwide program for MTCT prevention, as well as to the rapid implementation of combination ARV treatment to all those who need it.

**Address:** Bulterys, M; Ctr Dis Control & Prevent Zambia; Global AIDS Program; Amer Embassy, Independence Ave, POB 31617; Lusaka; Zambia. [bulterysm@cdczm.org](mailto:bulterysm@cdczm.org)

**Free full text :** <http://www.journals.uchicago.edu/JID/journal/issues/v192n5/34546/34546.html>

**Adults / Women, Children, HAART, Infant feeding / Breastfeeding, LICs / Africa, MTCT, Viral resistance**

Chokephaibulkit K, Chaisilwattana P, Vanprapar N, Phongsamart W, Sutthen R. **Lack of resistant mutation development after receiving short-course zidovudine plus lamivudine to prevent mother-to-child transmission.** *AIDS* 2005;19(11):1231-1233.

**Abstr.** A short-course regimen of zidovudine plus lamivudine starting from 34 weeks' gestation in pregnant women to prevent mother-to-child HIV infection, and discontinued after delivery, was evaluated for the development of resistance at 6 weeks postpartum. No resistant mutation was found in 32 women. One of the three infected infants carried the M184V and K219Q mutations.

**Address:** Chokephaibulkit, K; Mahidol Univ; Siriraj Hosp; Bangkok 10700; Thailand

#### **PMTCT / ARV**

Dabis F, Leroy V, Newell ML, Read JS, Coutoudis A, Fawzi W, Gaillard P, et al. **Mortality among HIV-1-infected women according to children's feeding modality An individual patient data meta-analysis.** *Journal of Acquired Immune Deficiency Syndromes* 2005;39(4):430-438.

**Abstr.** Background: Two recent analyses of HIV-1-infected mothers' mortality according to their children's feeding modality have produced conflicting results. Methods: An individual patient data meta-analysis was conducted using data regarding HIV-1-infected women from eligible clinical trials. Analyses included Cox

proportional hazards regression modeling, with children's feeding modality treated as a time-dependent covariate. Results: Of 4237 HIV-1-infected women, 162 (3.8%) died within 18 months after delivery. The risk of mortality during the 18-month period after delivery did not differ significantly by children's feeding modality (ever vs. never breast-fed), with or without adjustment for maternal CD4(+) count. Treating children's feeding modality as a time-dependent covariate, the risk of mortality was lower among women still breast-feeding (hazard ratio = 0.05, 95% confidence interval. 0.03, 0.09; P < 0.0001) than among those who had ceased, with similar results observed with adjustment for maternal CD4(+) count. Conclusions: HIV-1-infected women with lower CD4(+) counts were less likely to initiate breast-feeding. Mothers' mortality during the 18-month period after delivery did not differ significantly according to children's feeding modality (ever vs. never breast-fed). Of those women who initiated breast-feeding, the lower mortality risk among those still breast-feeding compared with those not breast-feeding likely represents better overall maternal health (with healthier women being able to breast-feed longer).

**Address:** Read, JS; NICHHD; Pediat Adolescent & Maternal AIDS Branch; Execut Bldg, Room 4B11F, 6100 Execut Blvd MSC 7510; Bethesda; MD 20892; USA. [jennifer\\_read@nih.gov](mailto:jennifer_read@nih.gov)

**Adults / Women, Infant feeding / Breastfeeding**

Diaz T, De Cock K, Brown T, Ghys PD, Boerma JT. **New strategies for HIV surveillance in resource-constrained settings: an overview.** AIDS 2005;19 Suppl. 2:S1-S8.

**Abstr.** Additional funding recently became available to help resource-constrained countries scale up their HIV treatment and prevention activities. This increased funding is accompanied by an increased demand for accountability from stakeholders. Many countries will need to make substantial improvements in their current HIV surveillance methods to monitor the collective national impact of these treatment and prevention initiatives. However, whereas most resource-constrained countries have monitored the prevalence of HIV, they have collected little information on other events in the HIV disease process, such as HIV incidence, rate of HIV drug resistance, number of deaths due to AIDS and only modest emphasis has been placed on AIDS reporting in generalized epidemics, resulting in severe underreporting. In addition, data on mortality trends are often not gathered. Furthermore, less than half of the countries with low-level/concentrated epidemics have tailored their surveillance systems to the local epidemic, behavioral surveillance is often not present, an integrated analysis of data is not widespread, and data are rarely used to inform policy. In January 2004, a conference was convened in Addis Ababa, Ethiopia, to examine new strategies for surveillance in resource-constrained countries, and their use in monitoring and evaluating HIV activities. This supplement summarizes the newest approaches and lessons learned for HIV/AIDS surveillance, based on presentations and discussions from that conference. This article provides an overview of HIV/AIDS surveillance in resource-constrained settings and discusses the history, current approaches, and future directions for HIV/AIDS surveillance in generalized and low-level/concentrated epidemics.

**Address:** Diaz, T; Ctr Dis Control & Prevent; Global AIDS Program; MS E-30,1600 Clifton Rd; Atlanta; GA 30033; USA. [txd1@cdc.gov](mailto:txd1@cdc.gov)

**LICs Treatment monitoring**

Dinh TH, Detels R, Nguyen MA. **Factors associated with declining HIV testing and failure to return for results among pregnant women in Vietnam.** AIDS 2005;19(11):1234-1236.

**Introduction.** In a cross-sectional study, 53.2% of 500 antenatal attendees at Hai-Phong Hospital accepted HIV testing and 55.3% returned for results. Factors associated with declining included opinions about providing testing or that only high-risk pregnant women need testing, intention to decline testing, being a housewife, perception of poor healthcare support, and worry about husband's disapproval. Low educational level was associated with not returning for results. Testing programmes need to address husbands' attitudes, low education levels, and perceptions of risk.

**Address:** Dinh, TH; Univ Calif Los Angeles; Sch Publ Hlth; Los Angeles; CA 90024; USA

**LICs / Asia, PMTCT, Voluntary Counselling and Testing (VCT)**

Eshleman SH, Guay LA, Mwatha A, Brown E, Musoke P, Mmiro F, Jackson JB. **Comparison of mother-to-child transmission rates in Ugandan women with subtype A versus D HIV-1 who received single-dose nevirapine prophylaxis.** HIV Network for Prevention Trials 012. Journal of Acquired Immune Deficiency Syndromes 2005;39(5):593-597.

**Abstr.** Objective: To compare the rate of mother-to-child transmission (MTCT) in women with subtype A versus D HIV-1 who received single-dose nevirapine (NVP). which was also apparent among women whose infants were infected after 8 weeks of age. Methods: The MTCT rates were compared in women with subtype A versus D at birth and at 8 weeks and 18 months of age of the infants. The rate of late MTCT (after 8 weeks of age) was also analyzed. Results: HIV-1 subtypes were determined for 300 of 306 women who received NVP in the HIV Network for Prevention Trials 012 study (158 women with subtype A and 105 women with subtype D).

Infant infection status was known for 297 women. The cumulative rate of MTCT at 18 months was 13.2% for subtype A and 18.3% for subtype D (P = 0.34). The rate of late transmission was 3.8% for subtype A and 7.6% for subtype D (P = 0.28). Maternal baseline viral load was a significant predictor of MTCT, but maternal baseline CD4 cell count and subtype were not. Conclusions: No significant difference was observed in the rate of MTCT in women with subtype A versus D. There was a trend toward a higher rate of MTCT among women with subtype D, however, which was also apparent among women whose infants were infected after 8 weeks of age.

**Address:** Eshleman, SH; Johns Hopkins Med Inst; Dept Pathol; Ross Bldg 646,720 Rutland Ave; Baltimore; MD 21205; USA. [seshlem@jhmi.edu](mailto:seshlem@jhmi.edu)

**LICs / Africa, PMTCT / ARV, Viral resistance**

Gill CJ, Hamer DH, Simon JL, Thea DA, Sabin LL. **No room for complacency about adherence to antiretroviral therapy in sub-Saharan Africa.** AIDS 2005;19(12):1243-1249.

**Abstr.** Medication adherence is essential to successful treatment of HIV/AIDS. Maintaining high adherence will likely prove a major challenge in Africa—just as it has in developed nations. Despite early reports suggesting that adherence would not pose a major barrier to treatment success, more recent research shows that adherence rates in Africa are quite variable and often poor. Given the large number of patients whose disease will progress if adherence is suboptimal, research is urgently needed to determine patient-level behavioral barriers to adherence and the most effective and appropriate methods for assessing adherence in African cohorts.

**Address:** Gill, CJ; Boston Univ; Sch Publ Hlth; 85 E Concord St; Boston; MA 02118; USA. [cgill@bu.edu](mailto:cgill@bu.edu)

**LICs / Africa, Treatment adherence**

Goicoechea M, Haubrich R. **CD4 lymphocyte percentage versus absolute CD4 lymphocyte count in predicting HIV disease progression: An old debate revisited [Editorial commentary].** Journal of Infectious Diseases 2005;192(6):945-947.

**Introduction.** Even before the first effective antiretroviral therapy (ART) became available nearly 20 years ago, various staging systems were used to predict HIV disease progression, and, subsequently, these systems have been used to guide initiation of therapy. They are based on measurements of CD4 lymphocytes, including the absolute CD4 lymphocyte count, the percentage of lymphocytes that are CD4 positive (CD4 lymphocyte percentage), and the CD4 : CD8 lymphocyte ratio. In this issue of the Journal of Infectious Diseases, Hulgath et al. present data that suggest that the baseline CD4 lymphocyte percentage may be an additional predictor of disease progression in a subset of individuals who have absolute CD4 lymphocyte counts >350 cells/mm<sup>3</sup> but have low CD4 lymphocyte percentages. Although absolute CD4 lymphocyte counts and CD4 lymphocyte percentages provide similar information and are highly correlated, these correlations are not perfect; in one study, the correlation coefficient between the 2 markers was 0.5. Differences between absolute CD4 lymphocyte count and CD4 lymphocyte percentage may represent a type of immune discordance. A relatively high absolute CD4 lymphocyte count and a low CD4 lymphocyte percentage may occur in 8%–10% of untreated HIV-infected patients. This has potentially important clinical implications. Current guidelines for initiation of therapy for asymptomatic individuals with HIV RNA levels <100,000 copies/mL are based on the absolute CD4 lymphocyte count and recommend initiating ART at a count 350 cells/mm<sup>3</sup>. For minimally symptomatic patients, a CD4 lymphocyte count <200 cells/mm<sup>3</sup> is used as a guide in resource-limited settings. Given that response to therapy is dependent on disease stage, if a significant number of HIV-infected patients present with this type of discordance, it may partially explain why some individuals who initiate therapy with moderate disease have suboptimal virologic and immunologic responses.

**Free full text available at:** <http://www.journals.uchicago.edu/JID/journal/issues/v192n6/35173/35173.html>

**Address:** Haubrich, R; Univ Calif San Diego; Antiviral Res Ctr; 150 W Washington St, Ste 100; San Diego; CA 92103; USA. [rhaubrich@ucsd.edu](mailto:rhaubrich@ucsd.edu)

**Treatment monitoring**

Gray GE, Urban M, Chersich MF, Bolton C, van Niekerk R, Violari A, Stevens W, McIntyre JA. **A randomized trial of two postexposure prophylaxis regimens to reduce mother-to-child HIV-1 transmission in infants of untreated mothers.** AIDS 2005;19(12):1289-1297.

**Abstr.** Background: Single-dose nevirapine (NVP) prophylaxis to mother and infant is widely used in resource-constrained settings for preventing mother-to-child transmission (MTCT) of HIV-1. Where women do not access antenatal care or HIV testing, post-exposure prophylaxis to the infant may be an important preventative strategy. Methods: This multicentre, randomized, open-label clinical trial (October 2000 to September 2002) in South Africa compared single-dose NVP with 6 weeks of zidovudine (ZDV), commenced within 24 h of delivery among 1051 infants whose mothers had no prior antiretroviral therapy. HIV-1 infection rates were ascertained at birth, and at 6 and 12 weeks of age. Kaplan-Meier survival methods were used to estimate HIV-1 infection rates in an intention-to-treat analysis. Results: Overall, 6 week and 12 week MTCT probability was 12.8% [95% confidence interval (CI), 10.5-15.01 and 16.3% (95% CI, 13.4-19.2), respectively. At 12 weeks, among infants

who were not infected at birth, 24 (7.9%) infections occurred in the NVP arm and 41 (13.1 %) in the ZDV arm (log rank  $P = 0.06$ ). Using multivariate analysis, factors associated with infection following birth were ZDV use [odds ratio (OR), 1.8; 95% CI, 1.1 -3.2;  $P = 0.032$ ], maternal CD4 cell count  $< 500 \times 10^6$  cells/l (OR, 2.5; 95% CI, 1.3-5.0;  $P = 0.007$ ), maternal viral load  $> 50\,000$  copies/ml (OR, 3.6; 95% CI, 2.0-6.2;  $P < 0.0001$ ) and breastfeeding (OR, 2.2; 95% CI, 1.3-3.8;  $P = 0.006$ ). Conclusion: A single-dose of NVP given to infants offers protection against HIV-1 infection and should be a strategy used in infants of mothers with untreated HIV infection.

**Address:** Gray, GE; Univ Witwatersrand; Chris Hani Baragwanath Hosp; POB 114; ZA-1864 Johannesburg; South Africa. [gray@pixie.co.za](mailto:gray@pixie.co.za)  
**LICs / Africa, PMTCT / ARV**

Hulgan T, Raffanti S, Kheshti A, Blackwell RB, Rebeiro PF, Barkanic G, Ritz B, Sterling TR. **CD4 lymphocyte percentage predicts disease progression in HIV-infected patients initiating highly active antiretroviral therapy with CD4 lymphocyte counts  $>350$  lymphocytes/mm<sup>3</sup>.** Journal of Infectious Diseases 2005;192(6):950-957.

**Abstr.** Background. The optimal timing of highly active antiretroviral therapy (HAART) in human immunodeficiency virus (HIV)-infected patients with  $\geq 200$  absolute CD4 lymphocytes/mm<sup>3</sup> is unknown. CD4 lymphocyte percentage could add prognostic information. Methods. Persons who initiated HAART between 1 January 1998 and 1 January 2003, received  $\geq 30$  days of therapy, and had baseline CD4 lymphocyte data available were included in the study. The log-rank test for time to event and Cox proportional hazards models were used to determine predictors of a new acquired immunodeficiency syndrome - defining illness or death. Results. A total of 788 patients met the inclusion criteria. At baseline, subjects had a median of 225 CD4 lymphocytes/mm<sup>3</sup> and 17% CD4 lymphocytes. Subjects with  $\geq 17\%$  CD4 lymphocytes had earlier disease progression, compared with subjects with  $< 17\%$ , both in the entire cohort ( $P < .001$ ) and of those subjects with  $> 350$  absolute CD4 lymphocytes/mm<sup>3</sup> at baseline ( $P = .03$ ). CD4 lymphocyte percentage  $< 17\%$  was the strongest predictor of disease progression among subjects in this latter group (hazard ratio, 3.57;  $P = .045$ ). Conclusions. In this cohort, CD4 lymphocyte percentage predicted disease progression in HIV-infected subjects who initiated therapy with  $> 350$  CD4 lymphocytes/mm<sup>3</sup>. This information may help identify persons who will derive the greatest benefit from initiation of HAART.

**Free full text available at:** <http://www.journals.uchicago.edu/JID/journal/issues/v192n6/33585/33585.html>

**Address:** Hulgan, T; Vanderbilt Univ; Sch Med; 345 24th Ave N Ste 105; Nashville; TN 37203; USA. [todd.hulgan@vanderbilt.edu](mailto:todd.hulgan@vanderbilt.edu)

**Industrialized countries, Treatment monitoring**

Idigbe EO, Adewole TA, Eisen G, Kanki P, Odunukwe NN, Onwujekwe DI, Audu RA, Araoyinbo ID, Onyewuche JI, Salu OB, Adedoyin JA, Musa AZ. **Management of HIV-1 infection with a combination of nevirapine, stavudine, and lamivudine. A preliminary report on the Nigerian antiretroviral program.** Journal of Acquired Immune Deficiency Syndromes 2005;40(1):65-69.

**Abstr.** Objective: To evaluate treatment outcome in the first 12 months among HIV positive patients managed with a combination of nevirapine + stavudine + lamivudine under the current national antiretroviral (ARV) program in Nigeria. Design: This was a prospective observational, cohort study on 50 ARV naive patients who met the inclusion criteria for the program and had given informed consent. All patients were in stage 2 or stage 3 periods of infection based on World Health Organization clinical classification. The patients were treated with the generic brands of ARVs and treatment consisted of oral nevirapine (Nevimal, Cipla, Mumbai, India), 200 mg daily, lamivudine (Lamivir, Cipla), 150 mg twice daily, and stavudine (Stavir, Cipla), 40 mg twice daily. Prior to initiation of treatment, the clinical history and baseline data for each patient were documented. The levels of plasma HIV-1 RNA, CD4(+) cell counts, frequency of opportunistic infections, and estimated body mass index were recorded at baseline and subsequently at intervals during treatment. Data obtained at the various sampling times for each parameter were compared against their baseline values. Results: Data on the plasma HIV-1 RNA levels indicated that between baseline and week 24, the median viral load of the patients decreased by 1.79 log<sub>10</sub> copies/mL. Equally between baseline and week 48 the median CD4(+) cell counts increased by 186  $\times 10^6$  cells/L, the frequency of opportunistic infections decreased by 82%, the median body mass index increased by 4.8 kg/m<sup>2</sup>, and 36% experienced side effects, which were minor and transient. The most prevalent side effect recorded was skin rash associated with nevirapine. Good adherence to this triple regimen was recorded in  $> 85\%$  of the patients. Conclusions: The overall results within the 12-month treatment period indicated an effective suppression of viral replication, the reconstitution of the immune system, and improvement of the physical well-being of the study population. Though there may be differences in global distribution of the infecting HIV-1 subtypes, the clinical and biologic results of this study compared favorably to those documented

in cohorts treated with branded and generic ARV drugs in some developed and developing countries. The cumulative data in this study further confirmed that the correct use of generic brands of ARVs is a feasible option in HIV care and support programs in resource-poor countries.

**Address:** Idigbe, EO; Nigerian Inst Med Res; PMB 2013; Lagos; Nigeria. [oniidigbe@yahoo.com](mailto:oniidigbe@yahoo.com)

**HAART, LICs / Africa**

Lawn SD, Bekker LG, Wood R. **How effectively does HAART restore immune responses to Mycobacterium tuberculosis? Implications for tuberculosis control** [Editorial review]. *AIDS* 2005;19(11):1113-1124.

**Abstr.** Use of highly active antiretroviral treatment (HAART) has had a major impact on HIV-associated morbidity and mortality in industrialized countries. Access to HAART is now expanding in low-income countries where tuberculosis (TB) is the most important opportunistic disease. The incidence of TB has been fuelled by the HIV epidemic and in many countries with high HIV prevalence current TB control measures are failing. HAART reduces the incidence of TB in treated cohorts by approximately 80% and therefore potentially has an important role in TB control in such countries. However, despite the huge beneficial effect of HAART, rates of TB among treated patients nevertheless remain persistently higher than among HIV-negative individuals. This observation raises the important question as to whether immune responses to Mycobacterium tuberculosis (MTB) are completely or only partially restored during HAART. Current data suggest that full restoration of circulating CD4 cell numbers occurs only among a minority of patients and that, even among these, phenotypic abnormalities and functional defects in lymphocyte subsets often persist. Suboptimal restoration of MTB-specific immune responses may greatly reduce the extent to which HAART is able to contribute to TB control at the community level because patients receiving HAART live much longer and yet would maintain a chronically heightened risk of TB.

**Address:** Lawn, SD; Univ Cape Town; Fac Hlth Sci; Anzio Rd; ZA-7925 Cape Town; South Africa. [stevelawn@yahoo.co.uk](mailto:stevelawn@yahoo.co.uk)

**HAART, TB**

McIntyre J. **Preventing mother-to-child transmission of HIV: successes and challenges** [Review]. *Bjog an International Journal of Obstetrics and Gynaecology* 2005;112(9):1196-1203.

**Abstr.** Mother-to-child transmission of HIV continues to be a major cause of infant morbidity and mortality in resource-poor settings. Intrapartum and postpartum nevirapine-based regimens have been introduced in many settings. New research has shown that better efficacy can be achieved with the addition of single-dose nevirapine to short course zidovudine regimens, and that selection of nevirapine-resistant virus can be reduced with a short postpartum combination antiretroviral cover. Women who need antiretroviral therapy for their own health should receive it in pregnancy, and access for pregnant women needs to be expanded urgently. The reduction of transmission through breastfeeding remains a challenge.

**Address:** McIntyre, J; Univ Witwatersrand; Perinatal HIV Res Unit; POB 114; ZA-1864 Johannesburg; South Africa

**PMTCT**

Morris AB, Dobles AR, Cu Uvin S, Zorrilla C, Anderson J, Harwell JI, Keller J, Garb J. **Protease inhibitor use in 233 pregnancies.** *Journal of Acquired Immune Deficiency Syndromes* 2005;40(1):30-33.

**Abstr.** Background: In the United States, as most highly active antiretroviral therapy (HAART) regimens used during pregnancy in HIV-infected women include a protease inhibitor (PI), it is important to determine the effects of PIs specifically rather than all HAART regimens. Prospective trials employing HAART during pregnancy are ongoing. Objective: To better understand the effects of PI use during pregnancy on prematurity, maternal and infant adverse events, and infant outcomes. Results: A total of 233 pregnancies in which PIs were used were reported, including 5 sets of twins and 1 set of triplets. Perinatal transmission is documented in 2 of 221 infants for a rate of 0.9% (95% CI, 0%-2.2%). Both HIV-positive infants were delivered by cesarean section (one elective at 37 1/7 weeks and one unscheduled at 32 6/7 weeks). The prematurity rate (< 37 weeks' gestation) was 22.0% (95% CI, 16.9%-28.0%) including 3 twin and 1 triplet pregnancies. In multiple regression analysis no association was noted for individual PIs or the week of gestation that PIs were initiated. Adverse maternal, obstetric, and infant events possibly related to PIs were uncommon. Conclusions: In this series, PIs during pregnancy appeared generally safe for mothers and infants. Perinatal transmission was low and the prematurity rate is similar to prior data in HIV positive women not on PIs.

**Address:** Morris, AB; Community Res Initiat New England; 780 Chestnut St, Suite 30; Springfield; MA 01107; USA. [amorris@crine.org](mailto:amorris@crine.org)

**HAART, Industrialized countries, PMTCT / ARV**

Muro E, Droste JAH, ter Hofstede H, Bosch M, Dolmans W, Burger DM. **Nevirapine plasma concentrations are still detectable after more than 2 weeks in the majority of women receiving single-dose nevirapine - Implications for intervention studies.** Journal of Acquired Immune Deficiency Syndromes 2005;39(4):419-421.

**Abstr.** Background: Single-dose nevirapine is a highly cost-effective strategy to reduce perinatal HIV-1 transmission. Its major disadvantage is the selection of nevirapine resistance in 20% to 30% of women, probably attributable to the long elimination half-life of nevirapine. To develop intervention strategies, it is important to know the interpatient variability in nevirapine half-life in women receiving a single dose of nevirapine. Methods: HIV-negative, healthy, nonpregnant Dutch women were eligible for this study After administration of a single 200-mg dose of nevirapine to the subjects, blood was sampled for measurement of nevirapine twice a week for a total of 21 days. Nevirapine plasma levels were determined by a validated high-performance liquid chromatography method with a lower limit of quantification of 0.15 mg/L. The primary end point was the first sample with an undetectable nevirapine concentration. Results: Forty-four subjects participated. The median age, height, and body weight (interquartile range) were 26 (21-33) years, 1.72 (1.68-1.75) m, and 64 (59-75) kg, respectively. The median elimination half-life of nevirapine was 56.7 hours, with a range of 25.6 to 164 hours. The time to the first undetectable nevirapine plasma concentration was 10 days in 4 subjects, 14 days in 12 subjects, 17 days in 12 subjects, and 21 days in 9 subjects. In the remaining 7 subjects, nevirapine was still detectable on day 21, the last day of sampling. Time to an undetectable nevirapine plasma concentration was influenced by oral contraceptive use but not by age, height, body weight, body surface area, alcohol use, or smoking. Conclusions: Most women who received a single 200-mg nevirapine dose still had detectable plasma concentrations of nevirapine after more than 2 weeks. This information is valuable for designing intervention studies to prevent the development of nevirapine resistance.

**Address:** Burger, DM; Radboud Univ; Med Ctr; 533 Radboud, Geert Grootpl 8; NL-6525 GA Nijmegen; Netherlands. [D.Burger@akf.umcn.nl](mailto:D.Burger@akf.umcn.nl)

**PMTCT / ARV**

Nsubuga FM, Jaakkola MS. **Needle stick injuries among nurses in sub-Saharan Africa.** Tropical Medicine and International Health 2005;10(8):773-781.

**Abstr.** Despite a heavy burden of HIV/AIDS and other blood borne infections, few studies have investigated needle stick injuries in sub-Saharan Africa. We conducted a cross-sectional study at Mulago national referral hospital in Kampala, Uganda, to assess the occurrence and risk factors of needle stick injuries among nurses and midwives. A total of 526 nurses and midwives involved in the direct day-to-day management of patients answered a questionnaire inquiring about occurrence of needle stick injuries and about potential predictors, including work experience, work load, working habits, training, and risk behaviour. A 57% of the nurses and midwives had experienced at least one needle stick injury in the last year. Only 18% had not experienced any such injury in their entire career. The rate of needle stick injuries was 4.2 per person-year. Multiple logistic regression analysis showed that the most important risk factor for needle stick injuries was lack of training on such injuries (OR 5.72, 95% CI 3.41-9.62). Other important risk factors included working for more than 40 h/week (OR 1.90, 95% CI 1.20-3.31), recapping needles most of the time (OR 1.78, 95% CI 1.11-2.86), and not using gloves when handling needles (OR 1.91, 95% CI 1.10-3.32). The study showed a high rate of needle stick injuries among nurses and midwives working in Uganda. The strongest predictor for needle stick injuries was lack of training. Other important risk factors were related to long working hours, working habits, and experience.

**Address:** Jaakkola, MS; Univ Birmingham; Inst Occupat & Environm Med; Birmingham B15 2TT; W Midlands; England. [m.jaakkola@bham.ac.uk](mailto:m.jaakkola@bham.ac.uk)

**Treatment programme**

Patel D, Thorne C, Fiore S, Newell ML. **Does highly active antiretroviral therapy increase the risk of congenital abnormalities in HIV-infected women?** Journal of Acquired Immune Deficiency Syndromes 2005;40(1):116-118.

**Conclusion.** In our study we found a similar pattern and prevalence of congenital abnormalities among infants exposed to antenatal ART and those who were not, and this was also true for exposure to HAART. Furthermore, there was no evidence to suggest that exposure to first-trimester ART increases the risk of congenital abnormalities. As such, our findings are consistent with those of the Antiretroviral Pregnancy Registry.<sup>5,6</sup> As a long-running birth-cohort study, however, we benefit from a large number of mother-child pairs (exposed and nonexposed) and are not subject to the potential for ascertainment and reporting bias that may limit interpretation of registry data. Although a small risk cannot be excluded, such data should reassure the increasing number of HIV-infected women becoming pregnant while taking HAART. Further monitoring and research are necessary,

however, particularly to assess the teratogenic risk of use of combinations of antiretroviral and other drugs at the time of conception or in early pregnancy.

**Address:** NA

**HAART, Industrialized countries, Obstetrics, PMTCT / ARV**

Pau AK, Moodley NK, Holland DT, Fomundam H, Matchaba GU, Capparelli EV. **Instability of lopinavir/ritonavir capsules at ambient temperatures in sub-Saharan Africa: relevance to WHO antiretroviral guidelines.** AIDS 2005;19(11):1233-1234.

**Abstr.** WHO recommends lopinavir/ritonavir as an antiretroviral option in resource-limited countries. Lopinavir/ritonavir is recommended to be stored at 2-8 degrees C until dispensing, and afterwards, may be kept at  $\leq 25$  degrees C for  $\leq 2$  months. Anticipating lopinavir/ritonavir use in countries lacking adequate cold-chains, we assessed its physical and chemical stability at 35 and 45 degrees C. Although maintaining chemical stability for 4 weeks at 35 degrees C, at 45 degrees C the capsules clumped after 7 days, supporting a need for more temperature-stable formulations for hotter climates.

**Address:** Pau, AK; NIAID; NIH; 9000 Rockville Pike; Bethesda; MD 20892; USA

**HAART, LICs / Africa**

Rodriguez WR, Christodoulides N, Floriano PN, Graham S, Mohanty S, Dixon M, Hsiang M, Peter T, Zavahir S, Thior I, Romanovicz D, Bernard B, Goodey AP, Walker BD, McDevitt JT. **A microchip CD4 counting method for HIV monitoring in resource-poor settings.** Plos Medicine 2005;2(7):663-672.

**Abstr.** Background More than 35 million people in developing countries are living with HIV infection. An enormous global effort is now underway to bring antiretroviral treatment to at least 3 million of those infected. While drug prices have dropped considerably, the cost and technical complexity of laboratory tests essential for the management of HIV disease, such as CD4 cell counts, remain prohibitive. New, simple, and affordable methods for measuring CD4 cells that can be implemented in resource-scarce settings are urgently needed. Methods and Findings Here we describe the development of a prototype for a simple, rapid, and affordable method for counting CD4 lymphocytes. Microliter volumes of blood without further sample preparation are stained with fluorescent antibodies, captured on a membrane within a miniaturized flow cell and imaged through microscope optics with the type of charge-coupled device developed for digital camera technology. An associated computer algorithm converts the raw digital image into absolute CD4 counts and CD4 percentages in real time. The accuracy of this prototype system was validated through testing in the United States and Botswana, and showed close agreement with standard flow cytometry ( $r=0.95$ ) over a range of absolute CD4 counts, and the ability to discriminate clinically relevant CD4 count thresholds with high sensitivity and specificity. Conclusion Advances in the adaptation of new technologies to biomedical detection systems, such as the one described here, promise to make complex diagnostics for HIV and other infectious diseases a practical global reality.

**Address:** Rodriguez, WR; Massachusetts Gen Hosp; Partners AIDS Res Ctr; Charlestown; MA 02129; USA.

[wrodriguez@partners.org](mailto:wrodriguez@partners.org)

**Free full text :** [http://medicine.plosjournals.org/archive/1549-1676/2/7/pdf/10.1371\\_journal.pmed.0020182-L.pdf](http://medicine.plosjournals.org/archive/1549-1676/2/7/pdf/10.1371_journal.pmed.0020182-L.pdf)

**LICs, Treatment monitoring**

Sedgh G, Larsen U, Spiegelman D, Msamanga G, Fawzi WW. **HIV disease progression and fertility in Dar es Salaam, Tanzania.** Journal of Acquired Immune Deficiency Syndromes 2005;39(4):439-445.

**Abstr.** Objectives: To examine the association of HIV-1 disease progression with pregnancy and live birth incidence in a cohort of HIV-1-positive women in Dar es Salaam, Tanzania, and to identify other determinants of fertility in this population. Design and Methods: Clinic-based prospective cohort study of HIV-1-infected women followed for LIP to 6 years and Cox proportional hazards models. Results: The multivariate pregnancy rate ratio (RR) comparing women at clinical stage II with women at stage I was 0.56 (95% confidence interval [CI]: 0.39, 0.82), and the pregnancy RR for women at stage III or IV compared with women at stage I was 0.24 (95% CI: 0.16, 0.36), controlling for independent predictors of pregnancy incidence. Pregnancy rates were lower among older women, unmarried women, women who had revealed their HIV status to someone, and women who had living children from their most recent pregnancy. The association of HIV-1 clinical progression with a decline in pregnancy incidence was not explained by weight loss, menstrual dysfunction, or nutritional status. Conclusion: Pregnancy and live birth rates decline dramatically with progression of HIV-1 disease. This decline is not explained by observed social, behavioral, or biologic factors.

**Address:** Sedgh, G; Harvard Univ; Sch Publ Hlth; 655 Huntington Ave; Boston; MA 02115; USA.

[gsedgh@yahoo.com](mailto:gsedgh@yahoo.com)

**Gynaecology, LICs / Africa, Obstetrics**

Shapiro RL, Holland DT, Capparelli E, Lockman S, Thior I, Wester C, Stevens L, Peter T, Essex M, Connor JD, Mirochnick M. **Antiretroviral concentrations in breast-feeding infants of women in Botswana receiving antiretroviral treatment.** *Journal of Infectious Diseases* 2005;192(5):720-727.

**Abstr.** Background. The magnitude of infant antiretroviral (ARV) exposure from breast milk is unknown. Methods. We measured concentrations of nevirapine, lamivudine, and zidovudine in serum and whole breast milk from human immunodeficiency virus type 1 (HIV-1)-infected women in Botswana receiving ARV treatment and serum from their uninfected, breast-feeding infants. Results. Twenty mother-infant pairs were enrolled. Maternal serum concentrations of nevirapine were high (median, 9534 ng/mL at a median of 4 h after nevirapine ingestion). Median breast-milk concentrations of nevirapine, lamivudine, and zidovudine were 0.67, 3.34, and 3.21 times, respectively, those in maternal serum. The median infant serum concentration of nevirapine was 971 ng/mL, at least 40 times the 50% inhibitory concentration and similar to peak concentrations after a single 2-mg/kg dose of nevirapine. The median infant serum concentration of lamivudine was 28 ng/mL, and the median infant serum concentration of zidovudine was 123 ng/mL, but infants were also receiving zidovudine prophylaxis. Conclusions. HIV-1 inhibitory concentrations of nevirapine are achieved in breast-feeding infants of mothers receiving these ARVs, exposing infants to the potential for beneficial and adverse effects of nevirapine ingestion. Further study is needed to understand the impact of maternal ARV treatment on breast-feeding HIV-1 transmission, infant toxicity, and HIV-1 resistance mutations among infected infants.

**Address:** Shapiro, RL; Beth Israel Deaconess Med Ctr; Div Infect Dis; 110 Francis St, Ste GB; Boston; MA 02215; USA. [rshapiro@bidmc.harvard.edu](mailto:rshapiro@bidmc.harvard.edu)

**Adults / Women, Children, HAART, Infant feeding / Breastfeeding, LICs / Africa, MTCT**

Shapiro RL, Ndung'u T, Lockman S, Smeaton LM, Thior I, Wester C, Stevens L, Sebetso G, Gaseitsiwe S, Peter T, Essex M. **Highly active antiretroviral therapy started during pregnancy or postpartum suppresses HIV-1 RNA, but not DNA, in breast milk.** *Journal of Infectious Diseases* 2005;192(5):713-719.

**Abstr.** Background. The ability of highly active antiretroviral therapy (HAART) to reduce human immunodeficiency virus type 1 (HIV-1) RNA and DNA in breast milk has not been described. Methods. We compared breast-milk HIV-1 RNA and DNA loads of women in Botswana who received HAART (nevirapine, lamivudine, and zidovudine) and women who did not receive HAART. Results. Women in the HAART group received treatment for a median of 98 days (range, 67 - 222 days) at the time of breast-milk sampling; 23 (88%) of 26 had whole breast-milk HIV-1 RNA loads < 50 copies/mL, compared with 9 (36%) of 25 women who did not receive HAART (P = .0001). This finding remained significant in a multivariate logistic-regression model (P = .0006). The whole-milk HIV-1 DNA load was unaffected by HAART. Of women who received HAART, 13 (50%) of 26 had HIV-1 DNA loads < 10 copies/10(6) cells, compared with 15 (65%) of 23 who did not receive HAART (P = .39). Conclusions. HAART suppressed cell-free HIV-1 RNA in breast milk and may therefore reduce mother-to-child transmission (MTCT) of HIV-1 via breast-feeding. However, HAART initiated during pregnancy or early after delivery had no apparent effect on cell-associated HIV-1 DNA loads in breast milk. Clinical trials to determine MTCT among breast-feeding women receiving HAART are needed.

**Address:** Shapiro, RL; Beth Israel Deaconess Med Ctr; Div Infect Dis; 110 Francis St, Suite GB; Boston; MA 02215; USA. [rshapiro@bidmc.harvard.edu](mailto:rshapiro@bidmc.harvard.edu)

**Adults / Women, Children, HAART, Infant feeding / Breastfeeding, LICs / Africa, MTCT**

Sivapalasingam S, Essajee S, Nyambi PN, Itri V, Hanna B, Holzman R, Valentine F. **Human immunodeficiency virus (HIV) reverse transcriptase activity correlates with HIV RNA load: Implications for resource-limited settings.** *Journal of Clinical Microbiology* 2005;43(8):3793-3796.

**Abstr.** Measurement of human immunodeficiency virus type 1 (HIV-1) plasma RNA levels using Roche AMPLICOR version 1.5 (HIV RNA) is an integral part of monitoring HIV-infected patients in industrialized countries. These assays are currently unaffordable in resource-limited settings. We investigated a reverse transcriptase (RT) assay as a less expensive alternative for measuring viral burden that quantifies RT enzyme activity in clinical plasma samples. A comparison of RT and HIV RNA assays was performed on 29 paired plasma samples from patients living in the United States and 21 paired plasma samples from patients living in Cameroon. RT levels correlated significantly with plasma HIV RNA viral loads in plasma from U.S. patients ( $r = 0.898$ ;  $P < 0.001$ ) and Cameroonian patients, a majority of whom were infected with HIV-1 clade type CRF02\_AG ( $r = 0.669$ ;  $P < 0.01$ ). Among 32 samples with HIV viral load of > 2,000 copies/ml, 97% had detectable RT activity. One Cameroon sample had undetectable RNA viral load but detectable RT activity of 3 fg/ml. The RT assay is a simple and less expensive alternative to the HIV RNA assay. Field studies comparing these assays in resource-limited settings are warranted to assess the practicality and usefulness of this assay for monitoring HIV-infected patients on antiretroviral therapy.

**Address:** Sivapalasingam, S; NYU; Med Ctr; 550 1st Ave, C&D Bldg, 5th Floor; New York; NY 10016; USA. [sumathi.sivapalasingam@med.nyu.edu](mailto:sumathi.sivapalasingam@med.nyu.edu)

**LICs, Treatment monitoring**

Sterne JAC, Hernan MA, Ledergerber B, Tilling K, Weber R, Sendi P, Rickenbach M, Robins JM, Egger M. **Long-term effectiveness of potent antiretroviral therapy in preventing AIDS and death: a prospective cohort study.** *Lancet* 2005;366(9483):378-384.

**Abstr.** Background Evidence on the effectiveness of highly active antiretroviral therapy (HAART) for HIV-infected individuals is limited. Most clinical trials examined surrogate endpoints over short periods of follow-up and there has been no placebo-controlled randomised trial of HAART. Estimation of treatment effects in observational studies is problematic, because of confounding by indication. We aimed to use novel methodology to overcome this problem in the Swiss HIV Cohort Study. Methods Patients were included if they had been examined after January 1996, when HAART became available in Switzerland, were not on HAART, and were free of AIDS at baseline. Cox regression models were weighted to create a statistical population in which the probability of being treated at each time point was unrelated to prognostic factors. Results Low CD4 counts and increasing HIV-1 viral load were associated with increased probability of starting HAART. Overall hazard ratios were 0.14 (95% CI 0.07-0.29) for HAART compared with no treatment, and 0.49 (0.31-0.79) compared with dual therapy. Compared with no treatment, HAART became more beneficial with increasing time since initiation but was less beneficial for patients whose presumed mode of transmission was via intravenous drug use (hazard ratio 0.27, 0.12-0.61) than for other patients (0.08, 0.03-0.19). Interpretation Our results, which are appropriately controlled for confounding by indication, are consistent with reported declines in rates of AIDS and death in developed countries, and provide a context in which to consider adverse effects of HAART.

**Address:** Sterne, JAC; Univ Bristol; Dept Social Med; Canynge Hall, Whiteladies Rd; Bristol BS8 2PR; Avon; England. [jonathan.sterne@bristol.ac.uk](mailto:jonathan.sterne@bristol.ac.uk)

**Adults, HAART, Industrialized countries, Treatment impact and response**

Stringer JSA, Sinkala M, Maclean CC, Levy J, Kankasa C, DeGroot A, Stringer EM, Acosta EP, Goldenberg RL, Vermund SH. **Effectiveness of a city-wide program to prevent mother-to-child HIV transmission in Lusaka, Zambia.** *AIDS* 2005;19(12):1309-1315.

**Abstr.** Objective: To determine the population effectiveness of a city-wide perinatal HIV prevention program. Design: An anonymous surveillance of newborn cord blood for HIV serology and nevirapine (NVP). Methods: All 10 public-sector delivery centers in Lusaka, Zambia participated. All mother-infant pairs delivering during the 12-week surveillance period at the participating centers and who received antenatal care at a public-sector facility in Lusaka were included in the study. The main outcome measure was population NVP coverage, defined as the proportion of HIV-infected women and HIV-exposed infants in the population that ingested NVP. Results: Of 8787 women in the surveillance population, 7204 (82%) had been offered antenatal HIV testing, of which 5149 (71%) had accepted, and of which 5129 (99%) had received a result. Overall, 2257 of 8787 (26%) were cord seropositive. Of the 1246 (55%) cord blood seropositive women who received an antenatal HIV test result, 1112 (89%) received a positive result; the other 134 comprise seroconverters and clerical errors. Only 751 of 1112 (68%) women who received a positive antenatal test result and a NVP tablet for ingestion at labor onset had NVP detected in the cord blood (i.e., maternal non-adherence rate was 32%). A total of 675 infants born to 751 adherent mothers (90%) received NVP before discharge. Thus, only 675 of 2257 (30%) seropositive mother-infant pairs in the surveillance population received both a maternal and infant dose of NVP. Conclusions: Successful perinatal HIV prevention requires each mother-infant pair to negotiate a cascade of events that begins with offering HIV testing and continues through adherence to the prescribed regimen. This novel surveillance demonstrates that failures occur at each step, resulting in reduced coverage and diminished program effectiveness.

**Address:** Stringer, JSA; 1275 Lubutu Rd, POB 34681; Lusaka; Zambia. [stringer@cidrz.org](mailto:stringer@cidrz.org)

**LICs / Africa, PMTCT / ARV, Treatment programme**

Yazdanpanah Y, Losina E, Anglaret X, Goldie SJ, Walensky RP, Weinstein MC, Toure S, Smith HE, Kaplan JE, Freedberg KA. **Clinical impact and cost-effectiveness of co-trimoxazole prophylaxis in patients with HIV/AIDS in Cote d'Ivoire: a trial-based analysis.** *AIDS* 2005;19(12):1299-1308.

**Abstr.** Background: In 2000, WHO/UNAIDS recommended co-trimoxazole prophylaxis for persons at early stages of HIV infection (WHO stage > 2) in sub-Saharan Africa. Objective: To assess the cost-effectiveness of alternative strategies for initiation of cotrimoxazole in Cote d'Ivoire. Design: Cost-effectiveness analysis with an HIV simulation model using clinical and cost data from a randomized trial of co-trimoxazole in HIV-infected adults. Methods: The study included HIV-infected patients in Cote d'Ivoire, with median age 33 years. Thirty-four percent were classified as WHO stage 2, 59% as stage 3, and 7% as stage 4. The mean CD4 cell count was 331 X 10(6) cells/l. The interventions were no prophylaxis, clinical criteria-based co-trimoxazole initiation (early: WHO stage > 2; late: WHO stage >= 3), CD4-based co-trimoxazole initiation (< 500, < 200, < 50 x 10(6) CD4 cells/l). The outcome measures were life expectancy, lifetime costs, and incremental cost-effectiveness. Results: The most effective strategy, initiation of co-trimoxazole prophylaxis at WHO stage > 2, increased

undiscounted life expectancy by 5.2 months, discounted life expectancy by 4.4 months, and lifetime costs by US\$ 60, compared with no prophylaxis. Delaying prophylaxis initiation until WHO stage > 3 was less costly and less effective. All CD4-based strategies were dominated. The incremental cost-effectiveness of early versus late co-trimoxazole prophylaxis initiation was US\$ 200/year of life gained. Results were stable despite wide variations in plausible assumptions about bacterial resistance and the prophylaxis efficacy on co-trimoxazole-resistant strains. Conclusions: For HIV-infected adults in Cote d'Ivoire, co-trimoxazole prophylaxis is reasonably cost-effective and most effective if initiated when WHO stage  $\geq$  2. Early co-trimoxazole prophylaxis will prevent complications prior to antiretroviral therapy initiation and should be considered an essential component of care for early HIV in sub-Saharan Africa.

**Address:** Yazdanpanah, Y; Ctr Hosp Tourcoing; Fac Med Lille; 135 Rue President Coty, BP 619; F-59208 Tourcoing; France. [yvazdan@yahoo.com](mailto:yvazdan@yahoo.com)

**Adults, LICs / Africa, Infections (Others) / Prophylaxis, Natural history**

Zijenah LS, Tobaiwa O, Rusakaniko S, Nathoo KJ, Nhembe M, Matibe P, Katzenstein DA. **Signal-boosted qualitative ultrasensitive p24 antigen assay for diagnosis of subtype C HIV-1 infection in infants under the age of 2 years.** Journal of Acquired Immune Deficiency Syndromes 2005;39(4):391-394.

**Abstr.** The gold standard for diagnosis of HIV-1 infection in infants under the age of 2 years is DNA or reverse transcriptase polymerase chain reaction. However, these tests are expensive and therefore not available in resource-limited countries. With the increasing availability of antiretroviral drugs for prevention of mother-to-child transmission of HIV and treatment of AIDS in resource-poor countries, there is an urgent need to develop cheaper, alternative, and cost-effective laboratory methods for early diagnosis of infant HIV-1 infection that will be useful in identifying infected infants who may benefit from early cotrimoxazole prophylaxis or commencement of antiretroviral therapy. We evaluated an alternative method, the enzyme-linked immunosorbent assay-based qualitative ultrasensitive p24 antigen assay for diagnosis of subtype C HIV-1 infection in infants under the age of 2 years using DNA polymerase chain reaction as the reference method. The assay showed a sensitivity of 96.7% (95% CI: 93.0-100) for detection of HIV-1 infection among infants 0-18 months of age with a specificity of 96.1% (95% CI: 91.7-100). These evaluated parameters were not statistically different between infants aged 0-6 and 7-18 months. The ultrasensitive p24 antigen assay is a useful diagnostic test for detection of HIV-1 infection among infants aged 0-18 months.

**Address:** Zijenah, LS; Univ Zimbabwe; Coll Hlth Sci; Mazoe St, POB A 178; Harare; Zimbabwe. [LZIJENAH@HEALTHNET.ZW](mailto:LZIJENAH@HEALTHNET.ZW)

**Children, LICs / Africa, PMTCT, Treatment monitoring**

3rd IAS conference on HIV Pathogenesis and treatment RdJ, Brazil, July, 24-27, 2005. **Highlights from the conference. Paediatric HIV/AIDS issues.**

Sub-Saharan countries can now report a much larger experience than in previous conferences on paediatric HIV care and use of HAART in particular, in the context of national roll-out programs. First line regimens combining two nucleosidic reverse transcriptase inhibitors (NRTIs) and one non-nucleosidic reverse transcriptase inhibitor (NNRTI) are now widely used, in agreement with WHO guidelines that have recently been updated [[http://www.who.int/3by5/Pediatricreport\\_June2005.pdf](http://www.who.int/3by5/Pediatricreport_June2005.pdf)].

Data reported at the IAS Conference showed these regimens were effective in routine care, in term of viral load suppression (South Africa: Egbers et al. Abstract MoPe11.7C14 and Sarunchuk et al. MoPe9.2C19; Botswana : Yarosh et al. Abstract WePe4.4C05), lower mortality rate (Mozambique: Liotta et al. Abstract MoPe9.2C23) and tolerance (Benin: Azondekon et al. Abstract MoPe9.4C05). Fixed-dose combination of d4t/3TC/NVP was particularly studied in Uganda (Barlow-Mosha et al. Abstract WeOa0103 ; Mosam et al. Abstract MoPe11.7C01), reporting a significant increase in CD4 count and a decrease in plasma viral load after 48 weeks of therapy, while 65% of the children included in the Médecins Sans Frontières (MSF) programs already received this combination (MSF AIDS Working Group. Abstract WeOaLB0201), showing a good overall chance of survival (92% at one year and 91% at two years). These conference reports can be linked to a recent publication describing the response to non-paediatric and generic HAART used for treating HIV-infected children in Thailand's National access to ARV Program (Puthanakit et al. CID 2005;41:100-107, see IR 2005;1(7-8)). Alternative first line regimens including a protease inhibitor (PI) instead of the NNRTI are also used in children. For instance, in Côte d'Ivoire, the Projet Enfant Yopougon is an ANRS-sponsored observational cohort where 72% of the children were receiving Nelfinavir-based HAART (Msellati et al. Abstract WeOa0101). In this cohort of HAART-treated children, the overall probability of survival was 73% for those with CD4 percentage  $\leq$  5% and 98% if CD4 percentage  $>$  5%.

Beside the type of ARV regimen prescribed, age at HAART initiation is an important factor of therapeutic success under investigation. The MTCT-Plus initiative, providing HAART (2 NRTIs + 1 NRTI for 83% of them) to 217 children in nine countries in sub-Saharan Africa and in Thailand (Abrams et al. Abstract MoPe11.6C28) showed a greater CD4 reconstitution among children aged 12 months at HAART initiation. In another

collaborative study conducted in Europe, it is the cut-off age of 5 months that was found to discriminate the best the response to treatment in terms of CD4 z-score (Newell et al. MoPe9.2C14).

Orphanhood is a critical issue in the context of HAART use, especially for adherence. In Uganda, Biraro et al. (Abstract MoPe9.2C12) reported the experience of the pediatric HIV clinic at Mbarara University Teaching Hospital, where 41.7% of the children were paternally orphaned and 40% maternally orphaned. There were, however, no data on the effect of orphanhood on the response to treatment. In a study conducted in western Kenya where 40% of the children on HAART were orphans, being orphan did not seem to affect adherence, mortality rate and CD4 response (Nyandiko-Mokaya et al. Abstract MoPe9.2C11).

There is an increasing interest for the simplification of the ARV drug prescription for children in resource-limited settings. Weidle et al (Abstract MoPe9.2C04), addressed this issue in assessing an ARV dosing chart in weight ranges compared to dosing based on body-surface area, for the paediatric use of adult tablets of ZDV and DDI. They found a fairly good correspondence, which could be improved by the production of paediatric solid oral tabs. This finding corroborates those reported in a recent publication of the MSF group (Ponnet M, et al. Int J STD AIDS. 2005;16(6):420-6, see IR 2005;1(7-8)), showing a good acceptability of the use of a standardized drug dosage table among Thai doctors and the safety and the efficacy of such a tool, based on the measure of the incidence of adverse effects and of the virological response to treatment in 49 children.

Even if a lot of attention is paid to HAART, cotrimoxazole prophylaxis is also shown to reduce the overall HIV-related morbidity and mortality, especially when it is provided within a comprehensive follow-up plan including a nutritional package and social support, as reported in a study conducted in Uganda (Nannyonga-Musoke et al. Abstract MoPe9.2C06). In a recent publication from this country, this prophylaxis administered to HIV-infected adults and children was also reducing morbidity and mortality among HIV-uninfected family members (Mermin et al. AIDS 19(10):1035-1042, see IR 2005;1(7-8)).

**URL:** <http://www.ias-2005.org>