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ICAP
Columbia University
MAILMAN SCHOOL
OF PUBLIC HEALTH

HIV Care & PMTCT in Resource-Limited Settings

Monthly Intelligence Report

2006, Vol 2, Issue 4

[Available on line](#)

prepared by the Bordeaux Working Group

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Number of citations selected for this issue: 10

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, **Free full text**, if available

Becquet R, Leroy V, Ekouevi DK, Viho I, Castetbon K, Fassinou P, Dabis F, Timité Konan M. **Complementary feeding adequacy in relation to nutritional status among early weaned breastfed children who are born to HIV-infected mothers: ANRS 1201/1202 Ditrane Plus, Abidjan, Cote d'Ivoire.** *Pediatrics* 2006;117(4):E701-E710.

Abstr. OBJECTIVE. In high HIV prevalence resource-constrained settings, exclusive breastfeeding with early cessation is one of the conceivable interventions aimed at the prevention of HIV through breast milk. Nevertheless, this intervention has potential adverse effects, such as the inappropriateness of complementary feeding to take over breast milk. The purpose of our study first was to describe the nature and the ages of introduction of complementary feeding among early weaned breastfed infants up to their first birthday and second was to assess the nutritional adequacy of these complementary foods by creating a child feeding index and to investigate its association with child nutritional status. METHODS. A prospective cohort study in Abidjan, Cote d'Ivoire, was conducted in HIV-infected pregnant women who were willing to breastfeed and had received a perinatal antiretroviral prophylaxis. They were requested to practice exclusive breastfeeding and initiate early cessation of breastfeeding from the fourth month to reduce breast milk HIV transmission. Nature and ages of introductory complementary feeding were described in infants up to their first birthday by longitudinal compilation of 24-hour and 7-day recall histories. These recalls were done weekly until 6 weeks of age, monthly until 9 months of age, and then quarterly. We created an index to synthesize the nutritional adequacy of infant feeding practices (in terms of quality of the source of milk, dietary diversity, food, and meal frequencies) ranging from 0 to 12. The association of this feeding index with growth outcomes in children was investigated. RESULTS. Among the 262 breastfed children included, complete cessation of breastfeeding occurred in 77% by their first birthday, with a median duration of 4 months. Most of the complementary foods were introduced within the seventh month of life, except for infant food and infant formula that were introduced at age 4 months. The feeding index was relatively low (5 of 12) at age 6 months, mainly as a result of insufficient dietary diversity, but was improved in the next 6 months (8.5 of 12 at 12 months of age). Inadequate complementary feeding at age 6 months was associated with impaired growth during the next 12 months, with a 37% increased probability of stunting. CONCLUSION. Adequate feeding practices around the weaning period are crucial to achieving optimal child growth. HIV-infected women should turn to early cessation of breastfeeding only when they are counseled properly to provide adequate complementary feeding to take over breast milk. Our child feeding index could contribute to the assessment of the nutritional adequacy of complementary feeding around the weaning period and therefore help to detect children who are at risk for malnutrition.

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Brahmbhatt H, Kigozi G, Wabwire Mangen F, Serwadda D, Lutalo T, Nalugoda F, Sewankambo N, Kiduggavu M, Wawer M, Gray R. **Mortality in HIV-infected and uninfected children of HIV-infected and uninfected mothers in rural Uganda.** *J AIDS Journal of Acquired Immune Deficiency Syndromes* 2006;41(4):504-508.

Abstr. Objective: To estimate 2-year mortality rates in HIV-1-infected and uninfected infants born to HIV+ and HIV- mothers. Methods: Data are from a prospective study in rural Rakai District, Uganda. Infant HIV status (determined by polymerase chain reaction) was evaluated at 1 to 6 weeks postpartum and during breastfeeding, and maternal HIV viral load and CD4 levels were measured at the postpartum visit. Multivariate Cox proportional hazards models and Kaplan-Meier survival analysis were used to assess survival of infants by maternal and infant HIV status and by quartiles of viral load. Log-rank tests were used to test the equality of survival functions. Results: Of the 4604 pregnant women, 16.9% were HIV+, and the proportion of children infected was 20.9%. Median survival of HIV-infected infants was 23 months. Two-year child mortality rates were 128 of 1000 children born to HIV- mothers, 165.5 of 1000 uninfected children born to HIV+ mothers, and 540.1 of 1000 HIV-infected children ($P < 0.0001$). Compared with children of HIV- mothers, the hazard of child mortality was 2.04 ($P < 0.001$) if the mother was HIV+ and 3.78 ($P < 0.001$) if the infant was also infected. In the adjusted model, the highest quartiles of \log_{10} HIV viral load in infants and mothers were associated with significantly increased hazard of child mortality (hazard ratio [HR] = 8.54 and HR = 2.50, respectively). Maternal CD4 counts < 200 cells/mL were also significant predictors of child mortality (HR = 2.61). A total of 67.6% of HIV-infected children with viral loads above the median died by the age of 2 years and are in need of early antiretroviral therapy (ART). Conclusions: More than half of HIV-infected infants died at less than 2 years of age. Therefore, ART may need to be initiated earlier in HIV-infected African children.

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Corbett EL, Marston B, Churchyard GJ, De Cock KM. **Tuberculosis in sub-Saharan Africa: opportunities, challenges, and change in the era of antiretroviral treatment.** *Lancet* 2006;367(9514):926-937.

Abstr. Rapid scale-up of antiretroviral treatment programmes is happening in Africa, driven by international advocacy and policy directives and supported by unprecedented donor funding and technical assistance. This welcome development offers hope to millions of HIV-infected Africans, among whom tuberculosis is the major cause of serious illness and death. Little in the way of HIV diagnosis or care was previously offered to patients with tuberculosis, by either national tuberculosis or AIDS control programmes, with tuberculosis services focused exclusively on diagnosis and treatment of rising numbers of patients. Tuberculosis control in Africa has yet to adapt to the new climate of antiretroviral availability. Many barriers exist, from drug interactions to historic differences in the way that tuberculosis and HIV are perceived, but failure to successfully integrate HIV and tuberculosis control will threaten the viability of both programmes. Here, we review tuberculosis epidemiology in Africa and policy implications of HIV/AIDS treatment scale-up.

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Harries AD, Chimzizi R, Zachariah R. **Safety, effectiveness, and outcomes of concomitant use of highly active antiretroviral therapy with drugs for tuberculosis in resource-poor settings [Essay focus].** *Lancet* 2006;367(9514):944-945.

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Libamba E, Makombe S, Mhango E, Teck OD, Limbambala E, Schouten EJ, Harries AD. **Supervision, monitoring and evaluation of nationwide scale-up of antiretroviral therapy in Malawi.** *Bulletin of the World Health Organization* 2006;84(4):320-326.

Abstr. Objective To describe the supervision, monitoring and evaluation strategies used to assess the delivery of antiretroviral therapy during nationwide scale-up of treatment in Malawi. Methods In the first quarter of 2005, the HIV Unit of the Ministry of Health and its partners (the Lighthouse Clinic; Medecins Sans Frontieres-Belgium, Thyolo district; and WHO's Country Office) undertook structured supervision and monitoring of all public sector health facilities in Malawi delivering antiretroviral therapy. Findings Data monitoring showed that by the end of 2004, there were 13 183 patients (5274 (40%) male, 12 527 (95%) adults) who had ever started antiretroviral therapy. Of patients who had ever started, 82% (10 761/13 183) were alive and taking antiretrovirals; 8% (1026/13 183) were dead; 8% (1039/13 183) had been lost to follow up; < 1% (106/13 183) had stopped treatment; and 2% (251/13 183) had transferred to another facility. Of those alive and on antiretrovirals, 98% (7098/7258) were ambulatory; 85% (6174/7258) were fit to work; 10% (456/4687) had significant side effects; and, based on pill counts, 96% (6824/7114) had taken their treatment correctly. Mistakes in the registration and monitoring of patients were identified and corrected. Drug stocks were checked, and one potential drug stock-out was averted. As a result of the supervisory visits, by the end of March 2005 recruitment of patients to facilities scheduled to start delivering antiretroviral therapy had increased. Conclusion This report demonstrates the importance of early supervision for sites that are starting to deliver antiretroviral therapy, and it shows the value of combining data collection with supervision. Making regular supervisory and monitoring visits to delivery sites are essential for tracking the national scale-up of delivery of antiretrovirals.

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Lyons F, Hopkins S, Kelleher B, McGeary A, Sheehan G, Geoghegan J, Bergin C, Mulcahy FM, McCormick PA. **Maternal hepatotoxicity with nevirapine as part of combination antiretroviral therapy in pregnancy.** *Hiv Medicine* 2006;7(4):255-260.

Abstr. Objectives To describe the maternal tolerability of nevirapine as part of combination antiretroviral therapy in pregnancy at three HIV centres in Dublin, Ireland and to determine risk factors for development of significant hepatotoxicity. Methods A retrospective study was carried out of all women prescribed nevirapine as part of combination antiretroviral therapy in pregnancy at three HIV centres in Dublin, Ireland (October 2000 to February 2003). Toxicities experienced were graded according to the Division of AIDS toxicity guidelines for adults. Statistical analysis was performed to determine whether there were differences between those that did and those that did not experience significant hepatotoxicity. Results A total of 123 women initiated nevirapine as part of combination antiretroviral therapy in the study period. Eight women developed significant hepatotoxicity, including two women who died from fulminant hepatitis. Women who experienced more severe hepatotoxicity had higher pretreatment CD4 counts ($P=0.01$). Conclusions In this cohort, women who experienced more severe hepatotoxicity had higher pretreatment CD4 counts, lending additional weight to the need for caution in using nevirapine as part of combination antiretroviral therapy in women not requiring antiretroviral therapy for their own health.

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Mermin J, Ekwaru JP, Liechty CA, Were W, Downing R, Ransom R, Weidle P, Lule J, Coutinho A, Solberg P. **Effect of co-trimoxazole prophylaxis, antiretroviral therapy, and insecticide-treated bednets on the frequency of malaria in HIV-1-infected adults in Uganda: a prospective cohort study.** *Lancet* 2006;367(9518):1256-1261.

Abstr. Background HIV-1 and malaria are common infections in Africa, and cause substantial morbidity and mortality. HIV infection has been associated with an increased incidence of malaria, and more severe disease. Our aim was to assess the effect of antiretroviral treatment (ART) on the frequency of clinical malaria in people with HIV, and to measure the additive effects of co-trimoxazole (trimethoprim and sulfamethoxazole) prophylaxis, ART, and insecticide-treated bednets. Methods In 2001, we enrolled 466 HIV-infected individuals aged 18 years or older in Uganda in a prospective cohort study that provided co-trimoxazole prophylaxis to 399 participants after 5 months of no intervention. In 2003, we enrolled 138 survivors from the initial study, and 897 new participants from the same community, to take antiretroviral therapy (ART) in addition to co-trimoxazole prophylaxis. The ART was in most cases a combination of stavudine, lamivudine, and nevirapine or efavirenz. In 2004, we also gave participants insecticide-treated bednets. Households were visited weekly by study staff to record fever, illness, or death in the preceding 7 days. In cases of reported fever in the previous 2 days, we took blood to test for malaria parasites. We compared the frequency of clinical malaria, adjusting for CD4-cell count, age, sex, and season. Findings 1035 individuals were given co-trimoxazole and ART (median age 38 years, 74% female, and median CD4-cell count 124 cells/ μ L); 985 of these, plus four new participants, received co-trimoxazole, ART, and bednets. There were 166 cases of clinical malaria in the study. Compared with a baseline malaria incidence of 50.8 episodes per 100 person-years, co-trimoxazole prophylaxis was associated with 9.0 episodes per 100 person-years (adjusted incidence rate ratio [IRR] 0.24, 95% CI 0.15-0.38); ART and co-trimoxazole with 3.5 episodes per 100 person-years (0.08, 0.04-0.17); and co-trimoxazole, ART, and bednets with 2.1 episodes per 100 person-years (0.05, 0.03-0.08). Malaria incidence was significantly lower during ART and co-trimoxazole than during co-trimoxazole alone (IRR 0.36 [95% CI 0.18-0.74], $p=0.0056$). Interpretation A combination of co-trimoxazole, antiretroviral therapy, and insecticide-treated bednets substantially reduced the frequency of malaria in adults with HIV.

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Perez F, Zvandaziva C, Engelsmann B, Dabis F. **Acceptability of routine HIV testing ("opt-out") in antenatal services in two rural districts of Zimbabwe.** *J AIDS Journal of Acquired Immune Deficiency Syndromes* 2006;41(4):514-520.

Abstr. Low uptake of prevention of mother-to-child transmission of HIV (PMTCT) services in resource-limited settings requires new approaches to prevent missed opportunities. Routine HIV testing ("opt-out" testing) in antenatal care (ANC) should be considered. An exploratory cross-sectional survey was conducted in 6 PMTCT sites in rural Zimbabwe. Women who had attended ANC in health centers where PMTCT was provided were surveyed in postnatal services. Of 520 women sampled, 285 (55%) had been HIV tested during their last pregnancy. Primary education or no education ($P = 0.02$), reporting receiving neither group education in the ANC clinic ($P < 0.001$) nor individual pretest counseling ($P < 0.001$), and having attended < 6 ANC visits ($P < 0.03$) were associated with not having been HIV tested. Among the 235 women not HIV tested in ANC, 79% would accept HIV testing if opt-out testing was introduced. Factors associated with accepting the opt-out approach were being < 20 years old ($P = 0.005$), having secondary education or more ($P = 0.03$), living with a partner ($P = 0.001$), and the existence of a PMTCT service where the untested women delivered. Thirty-seven women of 235 (16%) would decline routine HIV testing, mainly because of their fear of knowing their HIV status and the need to have their partner's consent. Among the women already tested in ANC ($n = 285$), 97% would accept the opt-out approach. In Zimbabwe, where 25% of pregnant women are HIV infected, introducing the opt-out strategy for HIV testing may have a far-reaching public health impact on PMTCT. Issues regarding stigma, quality of post-testing counseling and staffing must be considered, however.

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Rochat TJ, Richter LM, Doll HA, Buthelezi NP, Tomkins A, Stein A. **Depression among pregnant rural South African women undergoing HIV testing [Letter].** *Jama Journal of the American Medical Association* 2006;295(12):1376-1378.

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Sungkanuparph S, Manosuthi W, Kiertiburanakul S, Vibhagool A. **Initiation of antiretroviral therapy in advanced AIDS with active tuberculosis: clinical experiences from Thailand.** Journal of Infection 2006;52(3):188-194.

Abstr. Objectives: To study treatment outcomes of antiretroviral therapy (ART) initiated in advanced HIV-infected patients with active tuberculosis (TB). Methods: A retrospective cohort study was conducted in ART-naive HIV-infected patients who presented with active TB, CD4 < 200 cells/ μ l, and had been initiated ART. ART, TB treatment and treatment outcomes of both HIV and TB were studied. Results: There were 29 patients (19 males) with a median age of 37 (range 26-65) years. Site of TB were: lung (70%), lymph node (27.6%), and gastrointestinal tract (3.4%). At the time of TB diagnosis, median (range) CD4 cell count and HIV RNA were 74 (23-178) cells/ μ l and 229000 (26100-750000) copies/ml, respectively. All patients received isoniazid, rifampin, ethambutol, and pyrazinamide in the first 2 months of TB therapy but the continuation phase was different depending on whether efavirenz (EFV) or nevirapine (NVP) was used. ART was initiated at a median of 8 weeks of TB treatment. All patients received NNRTI-based regimens (EFV 62.1%, NVP 37.9%). Percentage of patients with HIV RNA < 50 copies/ml at 24 and 48 weeks of ART was 65.5 and 75.9%. Median CD4 cell count at 24, 48, and 72 weeks were 156, 186, and 227 cells/ μ l, respectively. Eighteen patients were cured; eight were treatment completed; two were treatment interrupted; and one died from CMV encephalitis. There was neither occurrence of new OI or relapse of TB in 26 patients who completed 72-week follow-up. Conclusions: Initiation of ART with NNRTI-based regimens at 4-12 weeks of TB treatment in advanced AIDS may be safe and effective, and may not be delayed. Further, prospective clinical, studies for the optimal timing of ART initiation and ART regimen are needed.

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