HIV Care & PMTCT in Resource-Limited Settings

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Back Issues on Line

prepared by the Bordeaux Working Group

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**Abstr.** Objectives. We investigated whether the prevalence of contraceptive use among women who are HIV positive varied according to use of highly active antiretroviral therapy (HAART) in Mbarara, Uganda. Methods. We used data from a cross-sectional survey of 484 women who were HIV positive (18-50 years) and were attending Mbarara University’s HIV clinic, 45% of whom were receiving HAART. Multivariate logistic regression was used to investigate the association between HAART use and contraceptive use. Data were collected between November 2005 and June 2006. Results. Overall, 45% of the women were sexually active in the previous 3 months. Of these, 85% reported using contraceptive methods, with 84% reporting use of barrier contraceptive methods. Women receiving HAART were more than twice as likely to use contraceptive methods (adjusted odds ratio [AOR]=2.64; 95% confidence interval [CI] = 1.07, 6.49) and more than 3 times as likely to use barrier contraceptive methods (AOR=3.62; 95% CI=11.54, 8.55) than were women not receiving HAART. Conclusions. Our findings support the need for increased attention to better integration of reproductive health and HIV and AIDS services for women who are HIV positive.

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**Abstr.** Background: Despite the 15 million children orphaned by AIDS, and fears of sexual vulnerability, little is known about the link between orphanhood and HIV risk. Methods: A random sample of 1283 15 to 19-year-old girls in a high-density suburb of Harare was identified in a cross-sectional survey in 2004. A total of 863 agreed to be interviewed and 839 provided a specimen for HIV and herpes simplex virus type-2 (HSV-2) testing. Sexual health outcomes, sexual behaviours and marriage were assessed by type and timing of orphanhood. Results: Half of the participants were single or double orphans. Prevalence of HIV and/or HSV-2 was higher among orphans than non-orphans [17 versus 12%; age-adjusted odds ratio (aOR)=1.5; 95% confidence interval (CI) 1.0-2.3]. Associations with orphan status were only significant among the 743 never-married participants. In comparison with non-orphaned peers, increased sexual risk (defined as HSV2-positive, HIV-positive or ever pregnant) was seen among maternal orphans (aOR = 3.6; 95% CI, 1.7-7.8), double orphans (aOR = 2.4; 95% CI, 1.2-4.9), and girls who lost their father before age 12 (aOR = 2.1; 95% CI, 0.9-4.8) but not later (aOR = 0.8; 95% CI, 0.3-2.2). Maternal and double orphans were most likely to initiate sex early and to have had multiple partners. Maternal orphans were least likely to have used a condom at first sex, and to have a regular sexual partner. Experience of forced sex was high in all groups. Conclusions: In urban Zimbabwe, female adolescent orphans are at increased risk of HIV and HSV-2 infection. Infection rates vary by type and age of orphanhood, and marital status, and are associated with high-risk sexual behaviours.

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Abstr. Objectives: Successful antiretroviral therapy (ART) is largely attributed to the type of third drug. Guidelines recommend regimens without systematic review of all factors that might affect treatment Success, such as study design, eligibility criteria and participant characteristics. Why patients cease ART has not been systematically studied. Design and setting: Systematic review of initial ART studies (64 randomized, 15 cohort). Group-based analysis was by weighted, forward, stepwise, linear regression. Main outcome measures: Treatment efficacy (undetectable plasma HIV viral load by intention-to-treat) and cessation for adverse events. Results: Seven variables were independently associated with study groups reporting higher treatment Success (mean 59%, r(2)=0.79): nonwhite race (P=0.002), exclusion for low haemoglobin (P=0.0006), lower CD4 cell count (P=0.014), closing relative to food (P=0.001), dual-nucleoside backbone (favouring didanosine or tenofovir with emtricitabine or lamivudine; P=0.002), nonnucleoside analogue or ritonavir-boosted protease inhibitor as the third drug (P<0.0001), and shorter follow-up (P=0.0004). Although the most common cause of treatment cessation (9.0%), adverse events were reported in only half of studies and were significantly more likely in studies that were phase 2 or 3, academia-sponsored and less than 36 months duration, and in older participants. Nausea was the. only adverse event significantly associated with treatment Success (r=0.277). Conclusion: Multiple reasons influence initial ART success beyond the type of third drug and should be considered when designing and comparing studies. Most studies are too short and report insufficient adverse event data. Didanosine is an effective option for initial ART, with particular relevance to resource-limited settings. ART guideline development might benefit from systematic review.

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Abstr. Antiretroviral treatment roll-out programmes in Africa often have difficulties to cope with the increasing number of clients. Based on the findings of a survey carried out in 2005 that showed long waiting times, innovative organizational changes (nurse visits and pharmacy-only refill visits) were introduced in our clinic. In August 2007, the survey was repeated to evaluate the impact of these changes. During both surveys we used the same standardized questionnaire. In 2007, 400 patients visited the clinic on the study day compared to 250 in 2005. The median time spent at the clinic decreased from 157 minutes in 2005 (range 22-426) to 124 minutes (15-314). All the waiting times for different services decreased except the time between the visit to the triage nurse and the doctors' visit. A similar methodology could be used by other health services to evaluate and compare different models of care.

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**Abstr.** To assess the availability of equipment and the staff's knowledge to prevent Mother-To-Child Transmission (PMTCT) in rural healthcare facilities recently covered by the national PMTCT programme in Cameroon. In eight districts inventories of antiviral drugs and HIV test kits were made on site, using a standardised check-list. Knowledge of HIV and PMTCT was evaluated with a multiple-choice (MC) questionnaire based on typical clinical PMTCT cases. Staff participated subsequently in a 2-day training on HIV/AIDS and the Cameroon PMTCT guidelines. Immediately after training and after 7 months, retention of knowledge was tested with the same questions but in different order and layout. Sixty two peripheral nurse-led clinics and the eight district hospitals were assessed. Whereas all district hospitals presented complete equipment, only six of the peripheral clinics (10%) were equipped with both complete testing materials and a full set of drugs to provide PMTCT. Thirty six peripheral facilities (58%) possessed full equipment for HIV-testing and 8 (13%) stocked all PMTCT drugs. Of 137 nurses, 102 (74%) agreed to the two knowledge tests. Fewer than 66% knew that HIV-diagnosis requires positive results in two different types of rapid tests and only 19% chose the right recommendation on infant-feeding for HIV-positive mothers. Correct answers on drug regimens in different PMTCT settings varied from 25% to 56%. All percentages of correct answers improved greatly with training (P < 0.001) and retention remained high 7 months after training (P < 0.001). Prevent Mother-To-Child Transmission programmes in settings such as rural Cameroon need to be adapted to the special needs of peripheral nurse-led clinics. Appropriate short training may considerably improve nurses' competence in PMTCT. Other important components are regular supervision and measures to guarantee supply of equipment in rural areas.

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**Abstr.** Objective: To determine the relationship between mortality risk and the CD4 cell response to antiretroviral therapy (ART). Design: Observational community-based ART cohort in South Africa. Methods: CD4 cell counts were measured 4 monthly, and deaths were prospectively ascertained. Cumulative person-time accrued within a range of updated CD4 cell count strata (CD4 cell-strata) was Calculated and used to derive CD4 cell-stratified mortality rates. Results: Patients (2423) (median baseline CD4 cell count of 105 cells/mu l) were observed for up to 5 years of ART. One hundred and ninety-seven patients died during 3155 person-years of observation. In multivariate analysis, mortality rate ratios associated with 0-49, 50-99, 100-199, 200-299, 300-399, 400-499 and at least 500 cells/mu l updated CD4 cell-strata were 11.6, 4.9, 2.6, 1.7, 1.5, 1.4 and 1.0, respectively. Analysis of CD4 cell count recovery permitted calculations of person-time accrued within these CD4 cell-strata. Despite rapid immune recovery, high mortality in the first year of ART was related to the large proportion of person-time accrued within CD4 cell-strata less than 200 cells/mu l. Moreover, patients with baseline CD4 cell counts less than 100 cells/mu l had Much higher cumulative mortality estimates at 1 and 4 years (11.6 and 16.7%) compared with those of patients with baseline counts of at least 100 cells/mu l (5.2 and 9.5%) largely because of greater cumulative person-time at CD4 cell counts less than 200 cells/mu l. Conclusion: Updated CD4 cell Counts are the variable most strongly associated with mortality risk during ART. High cumulative mortality risk is associated with person-time accrued at low CD4 cell counts. National HIV programmes in
resource-limited settings should be designed to minimize the time patients spend with CD4 cell counts less than 200 cells/μl both before and during ART. (c) 2009 Wolters Kluwer Health vertical bar Lippincott Williams and Wilkins.

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Abstr. Background. Tuberculosis (TB) immune reconstitution inflammatory syndrome (IRIS) is emerging as an important early complication of combination antiretroviral therapy in patients with TB in developing countries. The differential diagnosis of TB IRIS includes deterioration caused by other human immunodeficiency virus related morbidities and drug-resistant TB. Methods. We prospectively evaluated consecutive patients with suspected TB IRIS from February 2005 through July 2006 at a community-based secondary hospital in Cape Town, South Africa, by means of clinical case definitions for TB IRIS. Specimens were sent for TB culture and susceptibility testing, and a rapid test (FASTplaque-Response) was performed to expedite determination of rifampin susceptibility. Results. One hundred patients with suspected TB IRIS were evaluated, 26 of whom were being retreated for TB. IRIS symptoms developed a median of 14 days (interquartile range, 7-25 days) after the initiation of combination antiretroviral therapy. In 7 patients, an alternative opportunistic disease was diagnosed. Rifampin-resistant TB was present in 13 patients, 9 of whom received a diagnosis after study entry (7 of 9 had multidrug-resistant TB). Undiagnosed rifampin-resistant TB was thus present in 10.1% of patients (95% confidence interval, 3.9% 16.4%) who presented with TB IRIS, once those with alternative diagnoses and TB with known rifampin resistance were excluded. In the remaining 80 patients, TB IRIS without rifampin resistance was the final diagnosis. Conclusions. TB IRIS that is clinically indistinguishable from TB IRIS that occurs in the context of drug-susceptible disease may occur in patients with undiagnosed multidrug-resistant TB. Antitubercular drug resistance should be excluded in all cases of suspected TB IRIS, and corticosteroids should be used with caution for patients with presumed TB IRIS until the result of drug-susceptibility testing is known.

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Abstr. There are limited data describing the concentrations of zidovudine, lamivudine, and nevirapine in nursing infants as a result of transfer via breast milk. The Kisumu Breastfeeding Study is a phase IIb open-label trial of prenatal, intrapartum, and postpartum maternal treatment with zidovudine, lamivudine, and nevirapine from 34 weeks of gestation to 6 months postpartum. In a pharmacokinetic substudy, maternal plasma, breast milk, and infant dried blood spots were collected for drug assay on the day of delivery and at 2, 6, 14, and 24 weeks after delivery. Sixty-seven mother-infant pairs were enrolled. The median concentrations in breast milk of zidovudine, lamivudine, and nevirapine during the study period were 14 ng/ml, 1,214 ng/ml, and 4,546 ng/ml, respectively. Zidovudine was not detectable in any infant plasma samples obtained after the day of delivery, while the median concentrations in infant plasma samples from postpartum weeks 2, 6, and 14 were 67 ng/ml, 32 ng/ml, and 24 ng/ml for lamivudine and 987 ng/ml, 1,032 ng/ml, and 734 ng/ml for nevirapine, respectively. Therefore,
lamivudine and nevirapine, but not zidovudine, are transferred to infants via breast milk in biologically significant concentrations. The extent and effect of infant drug exposure via breast milk must be well understood in order to evaluate the benefits and risks of maternal antiretroviral use during lactation.

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Abstr. Background Maternal mortality is a major public-health problem in developing countries. Extreme differences in maternal mortality rates between developed and developing countries indicate that most of these deaths are preventable. Most information on the causes of maternal death in these areas is based on clinical records and verbal autopsies. Clinical diagnostic errors may play a significant role in this problem and might also have major implications for the evaluation of current estimations of causes of maternal death. Methods and Findings A retrospective analysis of clinico-pathologic correlation was carried out, using necropsy as the gold standard for diagnosis. All maternal autopsies (n = 139) during the period from October 2002 to December 2004 at the Maputo Central Hospital, Mozambique were included and major diagnostic discrepancies were analyzed (i.e., those involving the cause of death). Major diagnostic errors were detected in 56 (40.3%) maternal deaths. A high rate of false negative diagnoses was observed for infectious diseases, which showed sensitivities under 50%: HIV/AIDS-related conditions (33.3%), pyogenic bronchopneumonia (35.3%), pyogenic meningitis (40.0%), and puerperal septicemia (50.0%). Eclampsia, was the main source of false positive diagnoses, showing a low predictive positive value (42.9%). Conclusions Clinico-pathological discrepancies may have a significant impact on maternal mortality in sub-Saharan Africa and question the validity of reports based on clinical data or verbal autopsies. Increasing clinical awareness of the impact of obstetric and nonobstetric infections with their inclusion in the differential diagnosis, together with a thorough evaluation of cases clinically thought to be eclampsia, could have a significant impact on the reduction of maternal mortality.

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Palacios R, Senise JF, Vaz MJR, Diaz RS, Castelo A. **Short-term antiretroviral therapy to prevent mother-to-child transmission is safe and results in a sustained increase in CD4 T-cell counts in HIV-1-infected mothers.** *HIV Medicine* 2009;10(3):157-162.

**Abstr.** Short-term antiretroviral therapy (START) to prevent mother-to-child transmission (MTCT) is currently recommended for all HIV-1-infected pregnant women. The objective of this study was to assess the effect on CD4 cell counts and viral load dynamics the withdrawal of START after birth could generate. This was a 5-year cohort study involving HIV-1-infected pregnant women who presented with CD4 counts > 300 cells/mu L and had received START to prevent MTCT. Seventy-five pregnancies were assessed. In 24 cases, there was a history of antiretroviral therapy prior to prophylaxis. The median baseline CD4 count was 573 cells/mu L. In 75% of cases, prophylaxis was started after 26.6 weeks of gestation. The median CD4 cell count increase over baseline during prophylaxis was 24.5%. In only five cases did HIV-1 viral load remain detectable during prophylaxis. After START, CD4 cell counts did not drop significantly, and the HIV-1 viral load plateau was near the baseline level. The estimated mean time for CD4 count to fall below 300 cells/mu L was 3.5 years and was directly associated with high baseline CD4 cell count, as well as with CD4 increase after prophylaxis, whereas it was negatively correlated with previous use of antiretroviral (ARV) drugs and persistence of detectable HIV-1 viral load during prophylaxis. A potent, well-tolerated prophylactic ARV regimen can improve CD4 cell counts during and after START. In women receiving such prophylaxis, there is a remarkable time interval for CD4 cell counts to drop to levels that indicate treatment.

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**Abstr.** Objective: To assess the cost-effectiveness of cotrimoxazole prophylaxis in HIV-infected children in Zambia, as implementation at the local health centre level has yet to be undertaken in many resource-limited countries despite recommendations in recent updated World Health Organization (WHO) guidelines. Design: A probabilistic decision analytical model of HIV/AIDS progression in children based on the CD4 cell percentage (CD4%) was populated with data from the placebo-controlled Children with HIV Antibiotic Prophylaxis trial that had reported a 43% reduction in mortality with cotrimoxazole prophylaxis in HIV-infected children aged 1-14 years. Methods: Unit costs (US$ in 2006) were measured at University Teaching Hospital, Lusaka. Cost-effectiveness expressed as cost per life-year saved, cost per quality adjusted life-year (QALY) saved, cost per disability adjusted life-year (DALY) averted was calculated across a number of different scenarios at tertiary and primary healthcare centres. Results: Cotrimoxazole prophylaxis was associated with incremental cost-effectiveness ratios (ICERs) of US$72 per life-year saved, US$94 per QALY saved and US$53 per DALY averted, i.e. substantially less than a cost-effectiveness threshold of US$1019 per outcome (gross domestic product per capita, Zambia 2006). ICERs of US$5 or less per outcome demonstrate that cotrimoxazole prophylaxis is even more cost-effective at the local healthcare level. The intervention remained cost-effective in all sensitivity analyses including routine haematological and CD4% monitoring, varying starting age, AIDS status, cotrimoxazole formulation, efficacy duration and discount rates. Conclusion: Cotrimoxazole prophylaxis in HIV-infected children is an inexpensive low technology intervention that is highly cost-effective in Zambia, strongly supporting the adoption of WHO guidelines into essential healthcare packages in low-income countries.

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**Abstr.** Background: The President's Emergency Plan for AIDS Relief committed $15 billion to addressing HIV in resource-poor settings. Objective: To assess the impact of The President's Emergency Plan for AIDS Relief on the treatment services of an HIV care program. Design, setting, and patients: Cohort study utilizing computerized medical records of nonpregnant adults enrolled into the Academic Model for the Prevention and Treatment of HIV/AIDS system, in western Kenya between 27 November 2001 and 24 July 2006. Main outcomes measures: Number of clinics and patients enrolled in Academic Model for the Prevention and Treatment of HIV/AIDS, as well as patient demographics, immunologic, and clinical characteristics during three periods defined by the availability of combination antiretroviral therapy (cART). Results: Enrollment as of May 2006 was 23 539. Mean monthly enrollment increased from 64 to 815 between periods 1 and 3. The median CD4 cell count at enrollment during period 3 (172 cells/μl) was significantly higher than for period 2 (119 cells/μl; P<0.001). World Health Organization stage at enrollment differed significantly between periods with 6.7% having stage 4 disease in period 3 compared with 13.8% during period 1 (P<0.001). Significantly more patients had complete documentation of cART eligibility, during period 3 as compared with the previous periods. Time from enrollment to cART initiation decreased from a median of 64 weeks in period 1 to 12 weeks during period 3 (P < 0.001). Conclusion: The President's Emergency Plan for AIDS Relief funding has allowed Academic Model for the Prevention and Treatment of HIV/AIDS to significantly increase the number of individuals receiving HIV care and provided the ability to expand services allowing for identification of patients earlier in their disease process.  

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