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.** Background: The pregnancy-related adverse effects of antiretroviral therapy (ART) have yielded discordant results, which could be explained in part by the heterogeneity of ART protocols. The objective of our study was to explore whether lopinavir/ritonavir (LPV/r) exposure during pregnancy is associated with adverse outcomes. Methods: Data on 100 consecutive HIV type-1 (HIV-1)-infected women receiving LPV/r during pregnancy and who delivered after 15 weeks gestational age (GA) between January 2003 and June 2007 in a single centre were analysed. For each HIV-1-infected woman, two uninfected women matched by age, parity and geographical origin were selected among patients delivering during the same period. Preterm delivery (PTD), vasculoplacental complications, gestational glucose intolerance and post-partum complication rates were compared between cases and controls. Factors associated with PTD and post-partum complications were assessed in HIV-1-infected women by a logistic regression model. Results: Rates of vasculoplacental complication and gestational glucose intolerance were not higher among HIV-1-infected women than in controls. PTD was higher in HIV-1-infected women (21%) than in controls (10%; P<0.01). In HIV-1-infected women, PTD was associated with HIV-1 RNA level >= 50 copies/ml at delivery (adjusted odds ratio 6.15, 95% confidence interval 1.83-20.63; P=0.003). No association was found between occurrence of PTD and LPV/r exposure before 14 weeks GA. Conclusions: In this population of HIV-1-infected pregnant women receiving LPV/r, the risk of PTD was higher than in HIV-1-uninfected controls. As PTD risk was not associated with early exposure to LPV/r, these data support current guidelines to initiate ART earlier in pregnancy.

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**Abstr.** Background: Since 2003, the President's Emergency Plan for AIDS Relief (PEPFAR) has been the most ambitious initiative to address the global HIV epidemic. However, the effect of PEPFAR on HIV-related outcomes is unknown. Objective: To assess the effect of PEPFAR on HIV-related deaths, the number of people living with HIV, and HIV prevalence in sub-Saharan Africa. Design: Comparison of trends before and after the initiation of PEPFAR's activities. Setting: 12 African focus countries and 29 control countries with a generalized HIV epidemic from 1997 to 2007 (451 country-year observations). Intervention: A 5-year, $15 billion program for HIV treatment, prevention, and care that started in late 2003. Measurements: HIV-related deaths, the number of people living with HIV, and HIV prevalence. Results: Between 2004 and 2007, the difference in the annual change in the number of HIV-related deaths was 10.5% lower in the focus countries than in the control countries (P = 0.001). The difference in trends between the groups before 2003 was not significant. The annual growth in the number of people living with HIV was 3.7% slower in the focus countries than in the control countries from 1997 to 2002 (P = 0.05), but during PEPFAR's activities, the difference was no longer significant. The difference in the change in HIV prevalence did not significantly differ throughout the study period. These estimates were stable after sensitivity analysis. Limitation: The selection of the focus countries was not random, which limits the generalizability of the results. Conclusion: After 4 years of PEPFAR activity, HIV-related deaths decreased in sub-Saharan African focus countries compared with control countries, but trends in adult prevalence did not differ. Assessment of

**Abstr.** Co-infection with malaria and HIV in pregnant women is particularly common in sub-Saharan Africa and has serious consequences for both mother and newborn child. Numerous studies have been published on the effects in pregnancy of HIV on malaria infection and on the effects of malaria on HIV infection. The increased prevalence and intensity of parasitaemia (placental and peripheral infection and parasite density) in HIV-infected women is well established. Similarly, malaria infection seems to be associated with higher viral loads. However, there is still uncertainty as to the influence of malaria on the clinical course of HIV infection, mother-to-child transmission of HIV, and the consequences of co-infection on post-neonatal infant morbidity and mortality. These questions require further investigation. In terms of prevention, intermittent preventive treatment with two doses of sulfadoxine-pyrimethamine (SP) has been found less effective in preventing malaria in HIV-infected than uninfected women, and a higher dosage (such as monthly (SP) has been recommended. Regarding malaria, there is also a lack of clear recommendations for women taking daily cotrimoxazole prophylaxis, and anti-malarial-antiretroviral interactions are not well understood. Multi-centre clinical trials should be undertaken to investigate effective, coherent and well-tolerated strategies to prevent malaria in HIV-infected women. Safe alternatives to SP should be identified and evaluated rapidly. Finally, a central pharmaco-vigilance network should be instituted to report adverse effects.

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**Abstr.** Background. We explored the association between antituberculosis drug pharmacokinetics and treatment outcomes among patients with pulmonary tuberculosis in Botswana. Methods. Consenting outpatients with tuberculosis had blood samples collected 1, 2, and 6 h after simultaneous isoniazid, rifampin, ethambutol, and pyrazinamide ingestion. Maximum serum concentrations (C-max) and areas under the serum concentration time curve were determined. Clinical status was monitored throughout treatment. Results. Of the 225 participants, 36 (16%) experienced poor treatment outcome (treatment failure or death); 155 (69%) were infected with human immunodeficiency virus (HIV). Compared with published standards, low isoniazid C-max occurred in 84 patients (37%), low rifampin C-max in 188 (84%), low ethambutol C-max in 87 (39%), and low pyrazinamide C-max in 11 (5%). Median rifampin and pyrazinamide levels differed significantly by HIV status and CD4 cell count category. Only pyrazinamide pharmacokinetics were significantly associated with treatment outcome; low pyrazinamide C-max was associated with a higher risk of documented poor treatment outcome, compared with normal C-max (50% vs. 16%; P < .01). HIV-infected patients with a CD4 cell count <200 cells/mu L had a higher risk of poor treatment outcome (27%) than did HIV-uninfected patients (11%) or HIV-infected patients with a CD4 cell count >= 200 cells/mu L (12%; P = .01). After adjustment for HIV infection and CD4 cell count, patients with low pyrazinamide C-max were 3 times more likely than patients with...
normal pyrazinamide C-max to have poor outcomes (adjusted risk ratio, 3.38; 95% confidence interval, 1.84-6.22). Conclusions. Lower than expected antituberculosis drug C-max occurred frequently, and low pyrazinamide C-max was associated with poor treatment outcome. Exploring the global prevalence and significance of these findings may suggest modifications in treatment regimens that could improve tuberculosis cure rates.

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Abstr. Objective: To evaluate a simplification strategy for HIV-1-infected patients virologically suppressed on antiretroviral therapy (ART) by switching to a single-tablet regimen consisting of efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/FTC/TDF). Design: Prospective, randomized, controlled, open-label, multicenter study. Methods: Patients on stable ART with HIV-1 RNA <200 copies per milliliter for >= 3 months were stratified by prior nonnucleoside reverse transcriptase inhibitor-based or protease inhibitor-based therapy and randomized (2:1) to simplify treatment to EFV/FTC/TDF or to stay on their baseline regimen (SBR). Efficacy and safety assessments were performed at baseline and at weeks 4, 12, 24, 36, and 48. Additional patient-reported outcomes included the following: adherence by visual analog scale, quality of life by SF-36 (v2) survey, HIV Symptom Index, and the Preference of Medication and Perceived Ease of the Regimen for Condition questionnaires. Results: Three hundred patients (EFV/FTC/TDF 203, SBR 97) were evaluated (prior protease inhibitor-based ART, 53%; nonnucleoside reverse transcriptase inhibitor-based ART, 47%). The arms were well balanced at baseline with 88% males, 29% blacks, and a mean age of 43 years; CD4 was 540 cells per cubic millimeter, 96% had HIV-1 RNA <50 copies per milliliter, and 88% were on their first ART regimen. Through 48 weeks, 89% vs. 88% in the EFV/FTC/TDF vs. SBR arms, respectively, maintained HIV-1 RNA <200 copies per milliliter by time to loss of virologic response algorithm (intent to treat, noncompleters = failures) with the difference (95% confidence interval) between arms of 1.1% (-6.7% to 8.8%), indicating noninferiority of EFV/FTC/TDF vs. SBR. Similarly, maintenance of HIV-1 RNA <50 copies per milliliter by time to loss of virologic response algorithm was 87% vs. 85% for EFV/FTC/TDF vs. SBR, respectively [difference (95% confidence interval) 2.6% (-5.9% to 11.1%)]. Discontinuation rates were similar (EFV/FTC/TDF 11%, SBR 12%); more discontinuations for adverse events occurred in the EFV/FTC/TDF arm vs. SBA (5% vs. 1%), most commonly for nervous system symptoms. More patients withdrew consent in the SBR arm vs. EFV/FTC/TDF (7% vs. 2%). Estimated glomerular filtration rate (by Modification of Diet in Renal Disease) remained unchanged over 48 weeks in both arms (median change < 1 mL/min(-1).1.73 m(-2)). A decrease in fasting triglycerides was observed at 48 weeks in the EFV/FTC/TDF vs. SBR arm (-20 vs. -3.0 mg/dL; P = 0.035). Adherence of >= 96% was reported by visual analog scale in both arms at baseline and at all study visits. Conclusion: Simplification to EFV/FTC/TDF maintained high and comparable rates of virologic suppression vs. SBR through 48 weeks.

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Selection of the text. Recent research suggests earlier initiation of therapy may provide individual as well as public health benefits. Antiretroviral therapy (ART) can suppress the level of human immunodeficiency virus (HIV) viremia to undetectable levels in the plasma of a substantial proportion of individuals infected with HIV and has greatly reduced HIV-related morbidity and mortality. Given the dramatic effect of ART on viral load, it is reasonable to consider using treatment of individuals infected with HIV as a means of preventing HIV transmission. In this sense, a recent modeling study provides the theoretical basis for a new and potentially important public health policy strategy. There is little doubt that ART has preventive effects; what is uncertain is how best to apply it and combine it with other evidence-based prevention interventions. A number of important issues arise when a program of this potential magnitude and impact is considered: universal testing, relationship of the stage of infection to efficiency of transmission, efficacy of ART in preventing transmission of HIV, drug resistance, behavioral disinhibition, benefit to the individual and cost-effectiveness for society.

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Abstr. In HIV-1-infected individuals on currently recommended antiretroviral therapy (ART), viremia is reduced to <50 copies of HIV-1 RNA per milliliter, but low-level residual viremia appears to persist over the lifetimes of most infected individuals. There is controversy over whether the residual viremia results from ongoing cycles of viral replication. To address this question, we conducted 2 prospective studies to assess the effect of ART intensification with an additional potent drug on residual viremia in 9 HIV-1-infected individuals on successful ART. By using an HIV-1 RNA assay with single-copy sensitivity, we found that levels of viremia were not reduced by ART intensification with any of 3 different antiretroviral drugs (efavirenz, lopinavir/ritonavir, or atazanavir/ritonavir). The lack of response was not associated with the presence of drug-resistant virus or suboptimal drug concentrations. Our results suggest that residual viremia is not the product of ongoing, complete cycles of viral replication, but rather of virus output from stable reservoirs of infection.

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Abstr. Children living with HIV often display delayed motor performance owing to HIV infection of the central nervous system, the effects of opportunistic infections and, indirectly, owing to their social environments. Although these problems have been well documented, the impact of the virus on the development of South African children is less well known. The aim of this study was to document the motor performance of a group of HIV infected children in Cape Town, South Africa. The Bayley Scales of Infant Development Second Edition were administered to 51 HIV infected children [mean age
15.8 months (SD = 7.5, range 6.2-31.7 months)] of whom 34 were receiving antiretroviral therapy. Their performance was compared with an age-matched reference sample (n = 35), whose HIV status was unknown. The HIV infected sample and the age-matched sample were comparable with regard to caregiver's level of education (P = 0.42), employment status (P = 0.35) and income (P = 0.28). However, the HIV infected sample had significantly more hospital admissions (P < 0.01), their caregivers were mostly single (P = 0.04) and most lived in formal houses (P < 0.01). The prevalence of significant motor delay was 66.7% in the HIV infected sample compared with 5.7% in the age-matched sample. As expected, the performance of the HIV infected sample was significantly poorer than the age-matched sample. However, the extent of the delay is a cause of concern as so many children presented with significant motor delay. Unexpectedly, a significant number of healthy children also displayed delayed performance. It is recommended that the developmental performance of HIV infected children be monitored over an extended period to determine whether the developmental delay can be reduced with treatment. In the interim, there is a need to provide stimulation and treatment to the large number of children who are developmentally delayed as a result of HIV infection, including those uninfected children in the community who are at risk owing to their socio-economic status.

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Abstract edited. Objectives: The difficulties diagnosing infants and children with HIV infection have been cited as barriers to increasing the number of children receiving antiretroviral therapy worldwide. Because HIV-exposed and HIV-infected children are at high risk for infectious and nutritional complications, we hypothesized that routinely offering HIV antibody testing to all hospitalized children would identify large numbers of HIV-positive children. Design: We implemented routine HIV antibody counseling and testing for pediatric patients hospitalized at the University Teaching Hospital (UTH), a national reference center, in Lusaka, Zambia. We also introduced HIV DNA polymerase chain reaction (PCR) testing for early infant diagnosis. Methods: Caregivers/parents of children ≤ 15 years of age admitted to any of the hospital wards were routinely offered HIV counseling and testing for their children. Two counselors obtained a venous blood sample and ran HIV antibody testing once verbal permission was granted. The tests were performed using the Abbott Determine rapid test kit. Positives were confirmed with Genie II. HIV antibody positive (HIV+) children < 18 months of age were tested with HIV DNA polymerase chain reaction (PCR). We evaluate the influence of child’s sex, age, and ward on seropositive status and the proportion of children counselled and tested using Mantel-Haenzel Chi square tests of association and Wilcoxon rank sum tests, and logistic regression for multivariate modelling. Results: From January 1, 2006, to June 30, 2007, there were 21,000 admissions to UTH, including 3997 (19.5%) repeat readmissions for 17,003 children. Pediatric patients had a median age of 12 months (IQR: 0-24 months).
Among 15,670 children with unknown HIV status, 13,239 (84.5%) received counseling and 11,571 (87.4%) of those counseled were tested. Overall, 3,373 (29.2%) of those tested were seropositive. Seropositivity was associated with younger age: 69.6% of those testing HIV antibody positive were <18 months of age. The proportion of counselled children who were tested increased each quarter from 76.0% in January to March 2006 to 88.2% in April to June 2007 (P< 0.001). From April 2006 to June 2007, 1276 PCR tests were done; 806 (63.2%) were positive. The rate of PCR positivity increased with age from 22% in children < 6 weeks of age to 61% at 3–6 months and to 85% at 12–18 months (P< 0.001). Conclusions: Routine counseling and antibody testing of pediatric inpatients can identify large numbers of HIV-seropositive children in high prevalence settings. The high rate of HIV infection in hospitalized infants and young children also underscores the urgent need for early infant diagnostic capacity in high prevalence settings.

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Abstr. Objectives The aim of the study was to evaluate the impact of different patterns of nonadherence on treatment outcomes in patients with long-term follow-up. Methods This cohort study included patients who began highly active antiretroviral therapy during 1996-1999, with the last follow-up in 2007. Adherence was evaluated every 2 months by monitoring of pharmacy refills and by using self-reports. Patients were considered nonadherent at a specific visit when less than 90% of the prescribed drugs had been taken. Adherence was categorized as follows. (A) Continuous adherence: a patient had to be adherent in all of the evaluations throughout the period of follow-up. (B) Treatment interruption: drugs were not taken for more than 3 days, for any reason. Treatment failure was defined as viral load >500 HIV-1 RNA copies mL or death. Cox proportional risk models were used to calculate adjusted relative hazards (ARHs) of treatment failure. Results A total of 540 patients were included in the study, with a median follow-up of 8.3 years. Only 32.78% of patients achieved and maintained continuous adherence, and 42.78% of patients had treatment interruptions. Noncontinuous adherence [ARH 1.48; 95% confidence interval (CI) 1.02-2.14] and treatment interruptions (ARH 1.39; 95% CI 1.04-1.85) were associated with treatment failure for the overall cohort; however, for patients with more than 3 years of follow-up, only treatment interruptions were independently associated with treatment failure. Conclusions Only one-third of patients managed to achieve continuous adherence, and almost half of the patients had treatment interruptions, which have a particularly marked effect on treatment outcomes over the long term.

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Abstr. Background. To our knowledge, to date, no prospective, randomized, clinical trial has compared standard doses of efavirenz- and nevirapine-based antiretroviral therapy among patients with concurrent human immunodeficiency virus type 1 (HIV-1) infection

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and tuberculosis (TB) who are receiving rifampicin. Methods. Rifampicin recipients with concurrent HIV-1 infection and TB were randomized to receive antiretroviral therapy that included either efavirenz (600 mg per day) or nevirapine (400 mg per day). Efavirenz and nevirapine concentrations at 12 h after dosing (C12) were monitored at weeks 6 and 12. CD4(+) cell counts and HIV-1 RNA levels were assessed every 12 weeks. Results. One hundred forty-two patients were randomized into 2 groups equally. The mean body weight of patients was 53 kg, the mean CD4(+) cell count was 65 cells/mm(3), and the median HIV-1 RNA level was 5.8 log(10) copies/mL. At weeks 6 and 12, the mean C12 of efavirenz (+/- standard deviation) were 4.27 +/- 4.49 and 3.54 +/- 3.78 mg/L, respectively, and those for nevirapine were and 5.59 +/- 3.48 mg/L and 5.6 +/- 2.65 mg/L, respectively. Interpatient variability in the efavirenz group was 2.3-fold greater than that in the nevirapine group (coefficient of variation, 107% vs. 47%). At week 12, 3.1% of patients in the efavirenz group and 21.3% in the nevirapine group had C12 values that were less than the recommended minimum concentrations (odds ratio, 8.396; 95% confidence interval, 1.808-38.993; P = .002). Intention-to-treat analysis revealed that 73.2% and 71.8% of patients in the efavirenz and nevirapine groups, respectively, achieved HIV-1 RNA levels <50 copies/mL at week 48, with respective mean CD4(+) cell counts of 274 and 252 cells/mm(3) (P > .05). Multivariate analysis revealed that patients with low C12 values and those with a body weight <55 kg were 3.6 and 2.4 times more likely, respectively, to develop all-cause treatment failure (P < .05). Conclusions. Antiretroviral therapy regimens containing efavirenz (600 mg per day) were less compromised by concomitant use of rifampicin than were those that contained nevirapine (400 mg per day) in patients with concurrent HIV-1 infection and TB. Low drug exposure and low body weight are important predictive factors for treatment failure. Trial registration. ClinicalTrials.gov identifier:NCT00483054.

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Abstr. Background: Reduction of HIV-1 breast-feeding transmission remains a challenge for prevention of pediatric infections in Sub-Saharan Africa. Provision of formula decreases transmission but often increases child mortality in this setting. Methods: A prospective observational cohort study of HIV-1 exposed infants of mothers receiving pre and postnatal medical care at Drug Resource Enhancement Against AIDS and Malnutrition centers in Mozambique was conducted. Live-born infants of HIV-1-infected women receiving medical care were enrolled, HIV-1 testing was performed at 1, 6, and 12 months of age using branched DNA. Mothers were counseled to breast-feed exclusively for 6 months and were provided HAART antenatally mid postnatally for the first 6 months. Women with CD4 cell counts less than 350/cmm at baseline continued HAART indefinitely. Results: Of 341 infants followed from birth, 313 mother-infant pairs (92%) completed 6 months and 283 (83%) completed 12 months of follow-up. HIV-1 diagnosis was ascertained in 287 infants (84%) including 4 who died. There were 9 cases of HIV-1 transmission: 4 of 341 (1.2%) at 1 month, 2 of 313 (0.6%) at 6 months, and 2 of 276 (0.7%) at 12 months (cumulative rate: 2.8%). Two mothers (0.6%) and 11 infants (3.2%) died. Maternal and infant mortality rates were 587 of 100,000 and 33 of 1000, while country rates are 1000 of 100,000 and 101 of 1000. HIV risk reduction was 93% and HIV-free survival at 12 months was 94%. Conclusions: Late postnatal transmission of HIV-1 is significantly decreased by maternal use of HAART with high infant survival rates up to 12 months of age.

**Abstr.** Objective: To assess adverse effects of long-term highly active antiretroviral therapy (HAART), that is, lipodystrophy and metabolic disorders, in a cohort of African patients. Methods: One hundred eighty HIV-1-infected patients treated with HAART for 4-9 years in Dakar and 180 age-matched and sex-matched controls were enrolled. Regional subcutaneous fat changes were assessed by physicians, and fasting blood samples were drawn. Centralization of body fat was estimated using skinfold ratio, waist circumference, and waist to hip ratio (WHR). Results: Mean duration of HAART was 5.4 years. Main drugs received were zidovudine, stavudine, and protease inhibitors. The prevalence of moderate-severe lipodystrophy was 31.1% (95% confidence interval: 24.3 to 37.9), with 13.3%, 14.5%, and 3.3% for lipoatrophy, lipohypertrrophy, and mixed forms, respectively. Mild-severe lipodystrophy affected 65.0% (58.0; 72.0) of patients. Stavudine was the only independent risk factor (any vs. none: odds ratio = 2.8; 1.4 to 5.5). Patients had lower body mass index and skinfolds but greater centralization of body fat (WHR, P < 0.0001 and skinfold ratio, P < 0.001), fasting glucose (P < 0.0001), homeostasis model assessment insulin resistance, and triglyceride levels (P < 0.01 for both) than controls. Moderately-severely lipodystrophic patients had higher triglyceride and low-density lipoprotein cholesterol than other patients (P < 0.001 and P < 0.05, respectively). Conclusions: Moderate-severe lipodystrophy affected one third of West African patients on long-term HAART and was associated with a less favorable metabolic profile.

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**Abstr.** Background: There is limited information regarding the pattern and correlates of viral replication in vertically HIV-1-infected children and its role on their outcomes in resource-limited settings. Methods: HIV-1-infected infants were followed from birth to 24 months. Serial HIV-1 RNA levels were compared in infants infected in utero (< 48 hours), peripartum (48 hours-1 month), and late postnatal (after 1 month). Cofactors for viral peak [highest viral load (VL) within 6 months of infection] and set point and mortality were determined. Results: Among 85 HIV-1-infected infants, 24 were infected in utero, 41 peripartum, 13 late postnatal; 7 had no 48-hour assay. HIV-1 VL set point was significantly lower in infants infected > 1 month vs. <= 1 month (5.59 vs. 6.24 log(10) copies per milliliter, P = 0.01). Maternal VL correlated with peak infant VL (P < 0.001). Univariately, infant peak and set point VL and 6-month CD4% < 15% predicted mortality; and 6-month CD4% < 15% remained independently predictive in multivariate analyses (hazard ratio = 4.85, 95% confidence interval: 1.90 to 12.36). Conclusions: Infants infected after the age of 1 month contained virus better than infants infected before 1 month of age. Maternal VL predicted infant VL, which, in turn was associated with early mortality.

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**Abstr.** Background: Non-nucleoside reverse transcriptase inhibitor (NNRTI)-based highly active antiretroviral therapy (HAART) is the recommended first-line regimen for children in Thailand. This study was aimed to assess pattern and predictors of immune recovery in antiretroviral-naïve Thai children starting NNRTI-based HAART. Methods: Records were extracted from clinical databases of 2 treatment cohorts in Thailand. The inclusion criteria were HIV-infected naïve children who initiated NNRTI-based HAART when CD4 <25%. Immune recovery was defined as achieving a target CD4% of 25. The impact of age, gender, baseline clinical category, CD4 and HIV RNA titer, and regimen on immune recovery to weeks 96 was assessed using multiple logistic regression. Results: There were 274 patients (52% females) with a median baseline age of 7 (Interquartile range [IQR]: 4-9) years and a median CD4% of 5 (IQR: 1-12) who started treatment with nevirapine (66%) or efavirenz (34%) based HAART. Median duration of follow-up was 168 (IQR: 120-192) weeks. The median CD4% increase from baseline was 7% (IQR: 5-11) and 18% (IQR: 12-23) at weeks 24 and 96, respectively. The probability of reaching target CD4% was 51% (95% confidence interval: 45%-57%) by week 96. The predictors of immune recovery at week 96 were younger age, female gender, higher baseline CD4%, and sustained virologic suppression after week 24. Conclusion: In this cohort of children with low baseline CD4, half achieved immune recovery after 96 weeks of HAART. The predictors for immune recovery are younger children, female gender, high baseline CD4%, and long-term virologic suppression.

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**Abstr.** Objectives: To determine the incidence, clinical manifestations and risk factors for immune reconstitution inflammatory syndrome (IRIS) in young children initiating highly active antiretroviral therapy (HAART). Design: A prospective cohort of anti retroviral-naïve HIV-infected children less than 24 months of age enrolled in a treatment strategies trial in Johannesburg, South Africa. Methods: Among 169 HIV-infected children initiating HAART, April 2005 to November 2006, the records of 83 children suspected to have IRIS within 6 months of starting treatment were reviewed to determine whether they met criteria for IRIS. Seven were excluded due to incomplete follow-up. Pretreatment and post-treatment characteristics of children with and without IRIS were compared. Results: Overall, 34/162 (21%) children developed IRIS at a median of 16 days (range 7-115 days) post-HAART initiation. Bacille Calmette-Guerin reaction was most common occurring in 24/34 (71%) children, primarily injection site lesions and/or ipsilateral axillary lymphadenitis with abscess. Other IRIS conditions (not mutually exclusive) included Mycobacterium tuberculosis (n=12), cytomegalovirus pneumonia (n=1), Streptococcus pneumonia sepsis (n=1), and severe seborrheic dermatitis (n=1). Children with IRIS were younger (median age 7 vs. 10 months, P=0.007) with a lower CD4 cell percentage (median 13.9 vs. 19.2, P=0.009) at HAART initiation than controls. After 24 weeks on HAART, 62% of IRIS cases vs. 28% of controls had HIV RNA more than 400copies/ml (P=0.001), odds ratio=2.88 (95% confidence interval=1.14-7.29) after adjusting for baseline factors. Conclusion: Infants and young children with advanced HIV disease initiating HAART are at high risk for developing IRIS, leading to additional
morbidity and possibly impairing virologic response to antiretroviral treatment. (C) 2009 Wolters Kluwer Health vertical bar Lippincott Williams & Wilkins.

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**Abstr.** Background: The incidence and risk factors for lipodystrophy and metabolic disorders among patients in Africa on first-line combined antiretroviral treatment (cART) mostly containing non-nucleoside reverse transcriptase inhibitors is poorly documented. Methods: This prospective cohort study recruited 88 HIV-infected patients initiating cART between October 2004 and June 2005 in Cotonou, Benin. Patients were followed for 24 months. The main outcomes were incidence of lipodystrophy and metabolic disorders. Multivariate Cox proportional hazards regression models were used to describe factors associated with progression to lipodystrophy. Results: After a median follow-up of 23.2 months (inter-quartile range 22.3-23.7), 24 (30%) patients developed lipodystrophy (lipoatrophy 9%, lipohypertrophy 24% and mixed pattern 2.5%). The incidence rate for lipodystrophy was estimated to 1.72 per person-month (95% confidence interval [CI] 1.15-2.56) occurring after a median time of 11 months on cART. Metabolic syndrome (International Diabetes Federation definition) appeared in 10 (13%) patients after a median of 15 months with an estimated incidence rate of 0.62 per person-month (95% CI 0.33-1.16). It was more common in women (19.2% versus 3.1% in men; P=0.043). Diabetes (8%) and hypercholesterolaemia (35%) were also observed. After adjustment, gender, young age (hazard ratio [HR] 0.45 [95% CI 0.22-0.90]; P=0.025), high BMI at inclusion (HR 1.53 [95% CI 1.28-1.83]; P<0.0001) and smoking (HR 28.0 [95% CI 2.5-307.4]; P=0.006) were significantly associated with lipohypertrophy. Conclusions: Lipodystrophy and metabolic syndrome were commonly and rapidly observed in this cohort of sub-Saharan patients initiating cART.

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