HIV Care & PMTCT in Resource-Limited Settings

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Back Issues on Line

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**Abstr.** Background Single-dose nevirapine (NVP) is the main option for the prevention of mother-to-child transmission (PMTCT) of HIV-1 in countries with limited resources. However, the use of single-dose NVP results in HIV-1 viral resistance which could compromise the success of subsequent treatment of mother and child with antiretroviral combinations that include non-nucleosidic-reverse-transcriptase inhibitors. This systematic review and meta-analysis of summarized data aimed to estimate the proportion of mothers and children with NVP resistance mutations detected in plasma samples 4-8 weeks postpartum after single-dose NVP use for PMTCT. Methods Systematic search of electronic databases (MEDLINE, PASCAL) and conference proceedings (1997 to February 2006). Inclusion of all studies, without design, place or language restrictions, meeting the following criteria: use of single-dose NVP; viral genotyping performed with standard sequence analyses, between 4 and 8 weeks postpartum, in plasma samples; available public report; report of mothers median baseline plasma HIV-1 RNA levels. Data extraction by two independent reviewers using a standardized form created for this purpose. Logistic random effect models to obtain pooled estimates. Univariable and multivariable meta-regression to explore sources of heterogeneity. Results The pooled estimate of NVP resistance prevalence was 35.7% [95 confidence interval (CI) 23.0-50.6] in women in 10 study arms using single-dose NVP other antepartum antiretrovirals and 4.5% (CI 2.1-9.4) in three study arms providing also postpartum antiretrovirals (adjusted odds ratio 0.08; CI 0.04-0.16). The corresponding estimates in children were 52.6% (CI 37.7-67.0) in seven study arms using single-dose NVP and 16.5% (CI 8.9-28.3) in eight study arms combining single-dose NVP with other antiretrovirals. Conclusions Single-dose NVP is widely used for PMTCT in resource-poor settings, but the burden of viral resistance is high in both women and children. It is substantially lower in studies providing additional postpartum antiretrovirals. The clinical implications of these findings should be further investigated.

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Bland RM, Becquet R, Rollins NC, Coutsoudis A, Coovadia HM, Newell ML. **Breast health problems are rare in both HIV-infected and HIV-uninfected women who receive Counseling and support for breast-feeding in South Africa.** Clinical Infectious Diseases 2007;45(11):1502-1510.

**Abstr. Edited.** Background. Breast problems, including mastitis, can interfere with the duration and exclusivity of breast-feeding. However, there are no large prospective studies documenting the prevalence, duration, and timing of such problems in breast-feeding women, particularly those who are infected with human immunodeficiency virus (HIV). Methods. Women enrolled prenatally in rural South Africa underwent a breast-feeding counseling intervention until 6 months after delivery. Breast health problems were documented per breast for 180 days after delivery, with 14-day recall histories. Results. Breast health problems were rare, and there were no significant differences between 1119 HIV-infected and 1207 HIV-uninfected women for any of the following conditions: engorgement, 39 HIV-infected women (3.5%) versus 33 HIV-uninfected women (2.7% P = .30); breast thrush, 17 (1.5%) versus 12 (1.0% P = .25); bleeding nipple, 6 (0.5%) versus 4 (0.3% P = .45); and mastitis/abscess, 11 (1.0%) versus 6 (0.5%). Most problems occurred during the first month after birth, with few additional mothers experiencing problems after this point: at 1 and 6 months, 13% and 17% of all mothers, respectively, had experienced a minor or major breast health problem, including sore nipples. Women who had not exclusively breast-fed their infants were
more likely to experience any of the breast health problems than were women who had exclusively breast-fed their infants (time-dependent variable; adjusted odds ratio, 1.46; 95% confidence interval, 1.13-1.87 P = .003). HIV-infected women who experienced (P = .003) any serious breast health problem (i.e., bleeding nipple, pus oozing from a nipple or breast, or mastitis/abscess) were 3.55 times (95% confidence interval, 0.86-14.78 times;) more likely to transmit HIV postnatally to their infant. Conclusions. With encouragement to exclusively breast-feed, women experienced few breast health problems. When those problems did occur, HIV-infected women with bleeding nipple, pus oozing from a nipple or breast, or mastitis/abscess were more likely to transmit HIV to their infants.

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Abstr. Edited. We examined the incidence of and risk factors for tuberculosis during the first year of highly active antiretroviral therapy in low-income (4540 patients) and high-income (22,217 patients) countries. Although incidence was much higher in low-income countries (7.4 per 100 persons-years in the first year versus 1.0) , the reduction in the incidence of tuberculosis associated with highly active antiretroviral therapy was similar: the rate ratio for months 7-12 versus months 1-3 was 0.48 (95% confidence interval, 0.36-0.64) in low-income countries and 0.36 (95% confidence interval, 0.26-0.50) in high-income countries. A low CD4 cell count at the start of therapy was the most important risk factor in both settings.

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Abstr. Objectives: African and Asian cohort studies have demonstrated the feasibility and efficacy of HAART in resource-poor settings. The long-term virological outcome and clinico-immunological criteria of success remain important questions. We report the outcomes at 24 months of antiretroviral therapy (ART) in patients treated in a Medecins Sans Frontieres/Ministry of Health programme in Cambodia. Methods: Adults who started HAART 24 2 months ago were included. Plasma HIV-RNA levels were assessed by real-time polymerase chain reaction. Factors associated with virological failure were analysed using logistic regression. Results: Of 416 patients, 59.2% were men; the median age was 33.6 years. At baseline, 95.2% were ART naive, 48.9% were at WHO stage IV, and 41.6% had a body mass index less than 18 kg/m(2). The median CD4 cell count was 11 cells/mu l. A stavudine-lamivudine-efavirenz-containing regimen was initiated predominantly (81.0%). At follow-up (median 23.8 months), 350 (84.1%) were still on HAART, 53 (12.7%) had died, six (1.4%) were transferred, and seven (1.7%) were lost to follow-up. Estimates of survival were 85.5% at 24 months. Of 346 tested patients, 259 (74.1 %) had CD4 cell counts greater than 200 cells/mu l and 306 (88.4%) had viral loads of less than 400 copies/ml. Factors associated with virological failure at 24 months were non-antiretroviral naive, an insufficient CD4 cell gain of less than 350 cells/mu l or
a low trough plasma ART concentration. In an intention-to-treat analysis, 73.6% of patients were successfully treated. Conclusion: Positive results after 2 years of advanced HIV further demonstrate the efficacy of HAART in the medium term in resource-limited settings.

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Abstr. OBJECTIVE. Increasing access to highly active antiretroviral therapy to reach all those in need in developing countries (scale up) is slowly expanding to HIV-positive children, but documented experience remains limited. We aimed to describe the clinical, immunologic, and virologic outcomes of pediatric patients with >12 months of highly active antiretroviral therapy in 2 routine programs in Cambodia. METHODS. Between June 2003 and March 2005, 212 children who were younger than 13 years started highly active antiretroviral therapy. Most patients started a standard first-line regimen of lamivudine, stavudine, and nevirapine, using split adult fixed-dosage combinations. CD4 percentage and body weight were monitored routinely. A cross-sectional virologic analysis was conducted in January 2006; genotype resistance testing was performed for patients with a detectable viral load. RESULTS. Mean age of the subjects was 6 years. Median CD4 percentage at baseline was 6. Survival was 92% at 12 months and 91% at 24 months; 13 patients died, and 4 were lost to follow-up. A total of 81% of all patients had an undetectable viral load. Among the patients with a detectable viral load, most mutations were associated with resistance to lamivudine and non-nucleoside reverse-transcriptase inhibitor drugs. Five patients had developed extensive antiretroviral resistance. Being an orphan was found to be a predictor of virologic failure. CONCLUSIONS. This study provides additional evidence of the effectiveness of integrating HIV/AIDS care with highly active antiretroviral therapy for children in a routine setting, with good virologic suppression and immunologic recovery achieved by using split adult fixed-dosage combinations. Viral load monitoring and HIV genotyping are valuable tools for the clinical follow-up of the patients. Orphans should receive careful follow-up and extra support.

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Abstr. Background: Single-dose nevirapine (SDNVP) is widely used to prevent mother-to-child HIV transmission in resource-limited settings. Given detection of resistant mutants among women who receive SDNVP, concerns have arisen over the efficacy of SDNVP in repeat pregnancies. Methods: Retrospective data were collected from SDNVP-exposed and -unexposed women from the HIV Network for Prevention 012 trial who subsequently received SDNVP in another pregnancy. Prospective data were collected from pregnant women who were SDNVP exposed or unexposed before delivery. Kaplan-Meier and Cox regression analyses were used to estimate rates of HIV infection and HIV-free survival among infants born to women with or without prior SDNVP exposure. Results: In the retrospective cohort, the infection rates were 11.3% and 16.7% for 104 infants of SDNVP-exposed and -unexposed mothers, respectively (P = 0.41). In the prospective cohort, among 103 infants of SDNVP-exposed and -unexposed mothers, the 12-month infant HIV infection rates were 20.5% and 18.7% (P = 0.81) and HIV-free survival rates were 74.4% and 78.1% (P = 0.66), respectively. Conclusions: There was no increased risk of infant HIV infection among SDNVP-exposed women compared with -unexposed women. These findings support current international guidelines to offer SDNVP to HIV-infected pregnant women, regardless of previous SDNVP exposure, when more complex prophylaxis regimens are not available.

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Abstr. Objective: This study measured the prevalence of lipodystrophy and the metabolic effects of highly active antiretroviral therapy (HAART) in HIV-infected African subjects. Methods: Prevalence was measured in 571 Rwandans receiving HAART for >= 6 months. Metabolic variables were measured in 100 HIV-positive adults with lipodystrophy, 50 HIV-positive nonlipodystrophic adults, and 50 HIV-negative controls. Results: A HAART regimen of stavudine, lamivudine, and nevirapine was used by 81.6% of subjects; none received protease inhibitors. Lipodystrophy was observed in 34% (48.5% in urban groups and 17.3% in rural groups) of subjects, with a prevalence of 69.6% in those receiving HAART for >72 weeks. Peripheral lipoatrophy combined with abdominal lipohypertrophy was observed in 72% of lipodystrophic subjects. HIV-positive adults with lipodystrophy had a significantly higher waist-to-hip ratio (WHR; 0.99 +/- 0.05 vs. 0.84 +/- 0.03: P < 0.0005) than HIV-positive nonlipodystrophic adults. Total cholesterol concentrations (median [interquartile range], mmol/L) were significantly higher in the HIV-positive adults with lipodystrophy (3.60 [1.38]) than in HIV-positive nonlipodystrophic adults (3.19 [0.65]; P < 0.005) and control (3.13 [0.70]; P < 0.0005) groups. Impaired fasting glucose was observed in 18% of HIV-positive adults with lipodystrophy, 16% of HIV-positive nonlipodystrophic adults, and 2% of controls, but insulin levels did not differ. Conclusions: African subjects with lipodystrophy have increased WHR, glucose, and cholesterol levels. Glucose concentrations are also elevated in nonlipodystrophic HIV-positive subjects. Therefore, factors other than body fat redistribution contribute to the glucose intolerance.

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Abstr. Background. Access to antiretroviral therapy is rapidly expanding in sub-Saharan Africa. Identifying the predictors of incomplete adherence, virologic failure, and antiviral drug resistance is essential to achieving long-term success. Methods. A total of 150 subjects who had received antiretroviral therapy for at least 6 months completed a structured questionnaire and adherence assessment, and plasma human immunodeficiency virus (HIV) RNA levels were measured. Virologic failure was defined as an HIV RNA level >400 copies/mL; for patients with an HIV RNA level >1000 copies/mL, genotypic antiviral drug resistance testing was performed. Predictors were analyzed using bivariable and multivariable logistic regression models. Results. A total of 23 (16%) of 150 subjects reported incomplete adherence. Sacrificing health care for other necessities (adjusted odds ratio [AOR], 19.8; P < .01) and the proportion of months receiving self-funded treatment (AOR, 23.5; P = .04) were associated with incomplete adherence. Virologic failure was identified in 48 (32%) of 150 subjects and was associated with incomplete adherence (AOR, 3.6; P = .03) and the proportion of months receiving self-funded antiretroviral therapy (AOR, 13.0; P = .02). Disclosure of HIV infection status to family members or others was protective against virologic failure (AOR, 0.10; P = .04). Conclusions. Self-funded treatment was associated with incomplete adherence and virologic failure, and disclosure of HIV infection status was protective against virologic failure. Efforts to provide free antiretroviral therapy and to promote social coping may enhance adherence and reduce rates of virologic failure.

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Abstr. Background: The ability of nucleoside reverse transcriptase inhibitors (NRTIs) to inhibit human mitochondrial polymerase-gamma results in impaired synthesis of mitochondrial enzymes that generate adenosine triphosphate (ATP) by oxidative phosphorylation. This has been associated with several long-term mitochondrial toxicities, which include lactic acidosis and pancreatitis, peripheral neuropathy, and lipoatrophy. Methods: Enrolled highly active antiretroviral therapy (HAART)-treated adults have completed nearly 2 years of follow-up as part of the ongoing randomized clinical trial Adult Antiretroviral Treatment and Drug Resistance (Tshepo) study. All patients were intensively screened for the presence of ARV-related toxicities. Results: Six hundred fifty adults (69% female) were initiated on NRTI-based HAART. Overall, 2.0% of patients developed moderate to severe symptomatic hyperlactatemia, with 7 (1.0%), all female, diagnosed with lactic acidosis. Female gender (P = 0.008) and being overweight, namely having a body mass index (BMI) of greater than 25 (P = 0.001), were predictive for the development of moderate to severe symptomatic hyperlactatemia or lactic acidosis. Older age (age > 40 years) showed a statistical trend (P = 0.053) as a predictor for the development of toxicity, whereas exposure to d4T and/or ddI for 6 or more months was not predictive (P = 0.102). Those diagnosed with lactic acidosis had a mean BMI of 32.38 (interquartile range [IQR] = 29.4 to 35) at the time of toxicity and had
been receiving HAART for a mean of 12.1 months (IQR = 7 to 20.8). Four of the 7 (57%)
died of lactic acidosis and/or hemorrhagic pancreatitis; these 4 patients also had a
comorbid diagnosis of severe clinical pancreatitis with grade 3/4 lipase elevations and
abdominal symptoms at the time of their demise. Conclusions: Rates of lactic acidosis
appear to be higher in southern Africa when compared with rates previously described
elsewhere. Risk factors for the development of moderate to severe symptomatic
hyperlactatemia or lactic acidosis appear to be multifactorial but include female gender
and having a BMI of greater than 25. Additional studies are ongoing to evaluate for other
possible risk factors, such as host genetic differences.

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