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prepared by the Bordeaux Working Group

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Number of citations selected for this issue: **24**

Citation format (by alphabetical order of the authors): Author(s). **Title**. Source. **Abstr**. (Authors' text) or **Introduction** (Authors' text) or **Selection** (Selected sections of the paper) or **Notes** (Written by the Bordeaux Working Group). **Author address**, if available, **Free full text**, if available

Balkus J, Bosire R, John Stewart G, Mbori Ngacha D, Schiff MA, Wamalwa D, Gichuhi C, Obimbo E, Wariua G, Farquhar C. **High uptake of postpartum hormonal contraception among HIV-1-seropositive women in Kenya**. Sexually Transmitted Diseases 2007;34(1):25-29.

Abstr. Objectives: The objectives of this study were to determine patterns of contraceptive utilization among sexually active HIV-1-seropositive women postpartum and to identify correlates of hormonal contraception uptake. Goal: The goal of this study was to improve delivery of family planning services to HIV-1-infected women in resource-limited settings. Study Design: HIV-1-infected pregnant women were followed prospectively in a perinatal HIV-1 transmission study. Participants were referred to local clinics for contraceptive counseling and management. Results: Among 319 HIV-1-infected women, median time to sexual activity postpartum was 2 months and 231 (72%) women used hormonal contraception for at least 2 months during follow-up, initiating use at approximately 3 months postpartum (range, 1-11 months). Overall, 101 (44%) used DMPA, 71 (31%) oral contraception, and 59 (25%) switched methods during follow-up. Partner notification, infant mortality, and condom use were similar between those using and not using contraception. Conclusions: Using existing the healthcare infrastructure, it is possible to achieve high levels of postpartum hormonal contraceptive utilization among HIV-1-seropositive women.

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Becquet R, Bequet L, Ekouevi DK, Viho I, Sakarovitch C, Fassinou P, Bedikou G, Timite Konan M, Dabis F, Leroy V. **Two-year morbidity-mortality and alternatives to prolonged breast-feeding among children born to HIV-infected mothers in Cote d'Ivoire**. Plos Medicine 2007;4(1):139-151.

Notes. In the issue of PLos Medecine of January 2007, Becquet and colleagues have published an original study looking at two year morbidity and mortality data in the context of alternative infant feeding interventions aimed at reducing mother to child transmission (MTCT) in an urban setting in Africa.

In the midst of the continuing debate over infant feeding practices2 for children born to HIV-infected mothers in resource constrained settings, this article brings important information on when replacement feeding might be safe for babies. The primary finding of this study provides the best reassurance to date that, when appropriate support is given, the long term morbidity and mortality outcomes among short-term breastfed and formula fed infants are comparatively similar as opposed to the standard more prolonged breastfeeding.

In the light of the UNAIDS guidelines3 which recommend that HIV-infected women should use replacement feeding only when it is AFASS (acceptable, feasible, affordable, sustainable and safe) or otherwise practice exclusive breast-feeding for the first six months or until AFASS criteria are met, this study provides information on the safety of two alternative options.

Whereas new evidence has recently shown that early cessation of breastfeeding (BF) was associated with increased morbidity and mortality in infants in completed (Malawi, Botswana)[4] and ongoing studies (Kenya, Uganda and Zambia)[5], data on morbidity in an environment where women were asked to choose one of the two feeding options and offered support (free formula, transport and health care provision) and counselling for either one is here being shown.

The authors compared formula-fed (FF) to BF-mothers (early cessation of BF from 4 months) in Abidjan, Côte d'Ivoire and found that severe adverse events amongst infants were similar in both groups. Of the 557 live born children, 47% were BF for a median of 4 months whereas 295 were FF. The 2 year probability of presenting with a severe adverse event (hospitalization or death) was the same among FF (14%) and short term BF children (15%) (Adjusted HR: 1.19, CI: 0.75-1.91 p=0, 44). Even though FF infants had a slightly higher increased risk of diarrhoea (27 versus 22 cases per 100 persons year) and acute respiratory disease (9 versus 6 person-year) and BF children higher rates of malnutrition (14 versus 10 per 100 person-year), this did not however translate over the 2 year period in higher incidence rates of hospitalisation or mortality. The authors also compared the mortality with a historical trial[6] done in the same area with no specific infant feeding counselling; infants were long-term BF in this trial, and the MTCT rate was therefore much higher. Compared to HIV-negative children, there was no difference in risk of death among

the FF and short term BF babies from this new cohort.
These modified feeding practices were proposed with appropriate conditions (provision of nutritional counselling for all women, free provision of breast milk substitutes, and assurance of access to clean water) in association with frequent follow-up, infant growth assessment as well as morbidity assessment. This translated into a high rate of retention into care with 88% of expected follow up completed. These conditions do not always apply to other settings in Africa and therefore the authors have only pointed out that replacement feeding or short term BF is safe within a specific package of interventions. These data help pave the way to more individual-oriented recommendations helping to promote informed and free choice of infants feeding methods for HIV-infected mothers. The authors believe that HIV-infected women should be given specific guidance in selecting the option most likely to be suitable for their individual situation in PMTCT programs even in resource-constrained settings.
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Boer K, Nellen JF, Patel D, Timmermans S, Tempelman C, Wibaut M, Sluman MA, van der Ende ME, Godfried MH. **The AmRo study: pregnancy outcome in HIV-1-infected women under effective highly active antiretroviral therapy and a policy of vaginal delivery**. International Journal of Obstetrics and Gynaecology 2007;114(2):148-155.

Abstr. Objective To explore pregnancy outcome in HIV-1-positive and HIV-negative women, and mother-to-child transmission (MTCT) according to mode of delivery under effective highly active antiretroviral therapy (HAART). Design Cohort of 143 pregnant HIV-1-infected women including a matched case-control study in a 2:1 ratio of controls to cases (n = 98). Setting Academic Medical Center in Amsterdam and Erasmus Medical Center in Rotterdam, the Netherlands. Population Consecutive referred HIV-1 infected pregnant women treated with HAART and matched control not infected pregnant women. Main outcome measures MTCT, preterm delivery, low birthweight, pre-eclampsia. Results MTCT was 0% (95% CI 0-2.1%). Seventy-eight percent of HIV-1-infected women commenced and 62% completed vaginal delivery. The calculated number of caesarean sections needed to prevent a single MTCT was 131 or more. Preterm delivery rates were 18% (95% CI 11-27) in women infected with HIV-1 and 9% (95% CI 5-13) in controls (P = 0.03). HAART used at < 13 weeks of gestation was associated with a 44% preterm delivery rate compared with 21% when HAART was started at or after 13 weeks and 14% in controls. (Very) low birthweight and incidence of pre-eclampsia were not different between HIV-1 and controls. Conclusions We have not demonstrated any MTCT after vaginal delivery in women effectively treated by HAART. The HAART-associated increase in preterm delivery rate is mainly seen after first trimester HAART use.

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Duran AS, Losso MH, Salomon H, Harris DR, Pampuro S, Soto Ramirez LE, Duarte G, de Souza RS, Read JS. **Drug resistance among HIV-infected pregnant women receiving antiretrovirals for prophylaxis**. AIDS 2007;21(2):199-205.

Abstr. Objective: To quantify primary resistance mutations (PRMs) among HIV-1-infected women receiving antiretroviral therapy (ART) for prevention of mother-to-child transmission (MTCT). Methods: Peripheral blood mononuclear cell samples from HIV-1-infected women enrolled in a prospective cohort study in Argentina, the Bahamas, Brazil, and Mexico (NISDI Perinatal Study) were assayed for PRMs. Eligible women were those enrolled by March 2005 and diagnosed with HIV-1 infection during the current pregnancy, and who received ART for MTCT prophylaxis and were followed for 6-12 weeks postpartum. Results: Of 819 women, 198 met the eligibility criteria. At enrollment, 98% were asymptomatic, 62% had plasma viral load < 1000copies/ml, 53% had CD4+ cell count >= 500 cells/mu l, and 78% were ART-exposed (mean duration, 8.0 weeks; 95% confidence interval, 7.1-8.9). The most complex ART regimen during pregnancy was usually (81%) a three-drug regimen [two nucleoside reverse transcriptase inhibitors (NRTIs) + one protease inhibitor or two NRTIs + one non-nucleoside reverse transcriptase inhibitor). PRMs were observed in samples from 19 (16%) of 118 women that were amplifiable at one or both time points [11/76 (14%) at enrollment; 14/97 (14%) at 6-12 weeks]. The occurrence of PRMs was not associated with clinical, immunological, or virological disease stage at either time point, whether ART-naive versus exposed at enrollment, or the most complex or number of antiretroviral drug regimens received during pregnancy (P > 0.1). Of 55 women with amplifiable samples at both time points, PRMs were detected in I I samples (20%). Conclusions: PRMs occurred among 16.1% of relatively healthy HIV-1-infected mothers from Latin American and Caribbean countries receiving MTCT prophylaxis.

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Floridia M, Tamburrini E, Ravizza M, Anzidei G, Tibaldi C, Bucceri A, Maccabruni A, Guaraldi G, Meloni A, Probizer MFR, Guerra B, Martinelli P. **Antiretroviral therapy at conception in pregnant women with HIV in Italy: Wide range of variability and frequent exposure to contraindicated drugs**. Antiviral Therapy 2006;11 (7):941-946.

Abstr. Methods: Data from a large national surveillance study was used to describe antiretroviral regimens in pregnant women with HIV, with particular reference to the presence at conception of antiretroviral treatments contraindicated in pregnancy. Therapeutic changes during pregnancy were also analysed. Results: Among 334 women on antiretroviral treatment at conception, less than half (42.4%) reported current pregnancy as planned. A large number of different regimens (80) was observed. All the regimens included at least one nucleoside or nucleotide reverse transcriptase inhibitor. Non-nucleoside reverse transcriptase inhibitors and protease inhibitors were present in similar proportions (39.2% and 40.7%, respectively). The most commonly used drugs were lamivudine (83.2% of regimens), zidovudine (50.0%), stavudine (d4T; 38.0%), nevirapine (25.7%), didanosine (ddI; 17.7%) and nelfinavir (17.7%). Treament with efavirenz (13.5% of regimens) and ddI+d4T (9.6%) was markedly frequent. Use of efavirenz at conception was associated with a subsequent treatment change during pregnancy (odds ratio [OR]: 13.2.; 95% confidence interval [CI]: 3.2-53.8, P < 0.001). A similar but less strong association was found for ddI (OR: 1.8; 95% CI: 1.03-3.25, P=0.033), whereas being on nevirapine was associated with a lower risk (OR: 0.58; 95% CI: 0.38-0.81, P=0.013). Conclusions: Our data show that treatment at conception frequently represents the regimen previously selected for the treatment of the non-pregnant woman. The observed rates of exposure to contraindicated treatment should lead prescribing physicians to consider in HIV-positive women therapeutic choices that take into account the likelihood of an unplanned pregnancy. Such an approach is likely to reduce not only unintended exposures to contraindicated drugs, but also therapeutic changes during pregnancy.

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Hosseinipour MC, Corbett AH, Kanyama C, Mshali I, Phakati S, Rezk NL, van der Horst C, Kashuba ADM. **Pharmacokinetic comparison of generic and trade formulations of lamivudine, stavudine and nevirapine in HIV-infected Malawian adults**. AIDS 2007;21(1):59-64.

Abstr. Background: The Malawian antiretroviral program uses generic Triomune (stavudine, lamivudine, and nevirapine). Objective: To determine the pharmacokinetics and bioequivalence of generic and trade formulations of stavudine, lamivudine, and nevirapine in HIV-infected Malawians. Methods: This randomized, open label, cross-over study comprised six men and six women currently receiving Triomune-40 TM who were randomized to the generic or trade formulation of stavudine (40 mg twice daily), lamivudine (150 mg twice daily) and nevirapine (200 mg twice daily). After at least 21 days, the alternate formulation was administered. At the end of each period, six blood samples were collected over 8h. Bioequivalence was achieved if the 90% confidence interval (CI) for the geometric mean ratio (GMR) of generic:trade formulations for maximum plasma concentration (C-max) and the area under the concentration-time curve (AUC) was within 0.8-1.25. Results: Mean patient age, weight, and height were 38.4 years (SD, 7.7), 71.2 kg (SD, 7.0), and 164.8cm (SD, 6.3), respectively. The GMR for stavudine, lamivudine, and nevirapine were 1.4 (90% C1,1.2-1.7), 1.1 (90%,CI, 0.8-1.6), and 0.9 (90% CI, 0.7-1.2), respectively, for C-max; and 1.1 (90% CI, 1.0 1.2), 1.0 (90% CI, 0.7-1.3), and 0.9 (90 % CI, 0.7-1.1), respectively, for AUC(0-8h). Regardless of formulation, Malawians had higher nevirapine exposures compared with historical reports of Western HIV-infected patients. Conclusions: Although exposures were similar, Triomune did not meet the strict definition of bioequivalence for these drugs. Patients taking Triomune had notably higher stavudine C-max values. Antiretroviral pharmacokinetics and bioequivalence of generic formulations should be evaluated in the populations in which they are being used.

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Hulgan T, Shepherd BE, Raffanti SP, Fusco JS, Beckerman R, Barkanic G, Sterling TR. **Absolute count and percentage of CD4(+) lymphocytes are independent predictors of disease progression in HIV-infected persons initiating highly active antiretroviral therapy**. Journal of Infectious Diseases 2007;195(3):425-431.

Abstr. Background. Highly active antiretroviral therapy (HAART) is recommended when the absolute CD4(+) T lymphocyte count is < 200 cells/mm(3), and it should be considered when that count is >= 200, although the optimal timing when it is >= 200 is unclear. Because preliminary data had suggested that a low CD4+ T lymphocyte percentage (% CD4) is associated with disease progression in persons initiating HAART who have a higher absolute CD4, we sought to further characterize the predictive utility of % CD4. Methods. We conducted an observational study of persons in Collaborations in HIV Outcomes Research/ US cohort who initiated their first HAART regimen between 1997 and 2004, received >= 30 days of therapy, and had baseline values of absolute CD4, %CD4, and HIV-1 RNA. Cox proportional-hazards models determined associations between % CD4 and disease progression (to either a new AIDS-defining event [ADE] or death). Results. Of 1891 persons, 11% were female and 18% were African American; the median age was 38 years. Median follow-up was 55 months (interquartile range, 23 - 83 months), and 468 (25%) had disease progression. Multivariable analysis including age, race, sex, HIV-1 RNA, prior antiretroviral therapy, probable route of infection, prior ADE, absolute CD4, and % CD4 was performed; prior ART (P <.0001), injection-drug use (P =.04), lower absolute CD4 (P <.002) and lower % CD4 (P =.002) predicted disease progression. Conclusions. % CD4 at initiation of the first HAART regimen predicted disease progression independent of absolute CD4; % CD4 may be used to determine the timing of HAART.

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John Stewart GC. **When is replacement feeding safe for infants of HIV-infected women? - art. no. e30**. Plos Medicine 2007;4(1):11-12.
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Martinson NA, Morris L, Gray G, Moodley D, Pillay V, Cohen S, Dhlamini P, Puren A, Bhayroo S, Steyn J, McIntyre JA. **Selection and persistence of viral resistance in HIV-infected children after exposure to single-dose nevirapine**. Journal of Acquired Immune Deficiency Syndromes 2007;44(2):148-153.
Abstr. Background: Single-dose nevirapine (sd-NVP) is the mainstay of prevention of mother-to-child transmission programs in developing countries. Exposure to sd-NVP selects for resistance mutations, however. We longitudinally assessed these mutations in HIV-1-infected infants from Soweto and Durban, South Africa. Methods: We prospectively followed 465 infants who received sd-NVP after enrolling their mothers when pregnant. If HIV infected, their virus was genotyped, using the ViroSeq HIV-1 Genotyping System, to detect resistant mutations. Those with resistance were genotyped at 6 months and then every 6 months out to 18 months if resistance was detected at the previous visit. Results: Of 53 HIV-infected infants, 24 (45.3%) had detectable resistance at their first visit, when the most frequent mutations were Y181C (75%), K103N (25%), and Y188C (12%). Of those whose visit was before 12 weeks of age, 2 of 24 infants shared identical resistance mutations with their mothers. By 18 months of age, 11 of 24 infants with resistance had died and 1 still had the Y181C mutation. Conclusions: Resistant mutations were selected in half of the infants exposed to sd-NVP, but fewer were detected over time and, unlike the case in their mothers, Y181C dominated initially and persists. Transient resistance mutations may have a negative impact on highly active antiretroviral therapy in infants and children.
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Moore RD, Keruly JC. **CD4(+) cell count 6 years after commencement of highly active antiretroviral therapy in persons with sustained virologic suppression**. Clinical Infectious Diseases 2007;44(3):441-446.
Abstr. Background. Sustained suppression of the human immunodeficiency virus (HIV) type 1 RNA load with the use of highly active antiretroviral therapy (HAART) results in immunologic improvement, but it is not clear whether the CD4(+) cell count increases to normal levels or whether it reaches a less- than- normal plateau. We characterized the increase in the CD4(+) cell count in patients in clinical practice who maintained sustained viral suppression for up to 6 years. Methods. All patients were from the Johns Hopkins HIV Clinical Cohort, a longitudinal observational study of patients receiving primary HIV care in Baltimore, Maryland, who were observed for > 1 year while receiving HAART and who had sustained suppression of the HIV RNA load at < 400 copies/ mL. We analyzed annual change in the CD4(+) cell count for up to 6 years after the start of HAART, stratified by baseline CD4(+) cell counts of <= 200, 201 - 350, >350 cells/ mL, and we assessed the development of clinical events (death and new acquired immunodeficiency syndrome - defining illness) by Kaplan- Meier analysis. Results. A total of 655 patients were observed for a median of 46 months (range, 13 - 72 months). The median change from baseline to most recent CD4(+) cell count was + 274 cells/mu L, with 92% of patients having an increase in CD4(+) cell count. By 6 years, the median CD4(+) cell count was 493 cells/mu L among patients with baseline CD4(+) cell counts <= 200 cells/mu L, 508 cells/ mL among those with baseline CD4(+) cell counts of 201 - 350 cells/mu L, and 829 cells/mu L among those with baseline CD4(+) cell counts >350 cells/ mL. In addition to baseline CD4(+) cell count, injection drug use and older age were associated with a lesser CD4(+) cell count response, and duration of therapy was associated with a greater CD4(+) cell count response. Conclusion. Only patients with baseline CD4(+) cell counts >350 cells/ mL returned to nearly normal CD4(+) cell counts after 6 years of follow- up. Significant increases were observed in all CD4(+) cell count strata during the first year, but there was a lower

plateau CD4(+) cell count at lower baseline CD4(+) cell strata. These data suggest that waiting to start HAART at lower CD4(+) cell counts will result in the CD4(+) cell count not returning to normal levels.
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Natarajan U, Pym A, McDonald C, Velisetty P, Edwards SG, Hay P, Welch J, de Ruiter A, Taylor GP, Anderson J. **Safety of nevirapine in pregnancy**. HIV Medicine 2007;8(1):64-69.
Abstr. Background Nevirapine has been widely used in pregnancy for its efficacy, low pill burden, bioavailability and rapid transplacental transfer. Concern about nevirapine toxicity during pregnancy has emerged over recent years. Objectives The aims of the study were to document the frequency of cutaneous and hepatic toxicity secondary to nevirapine use during pregnancy and to compare rates in women starting nevirapine during the current pregnancy with those in women who had commenced nevirapine prior to the current pregnancy. Design This was a retrospective, comparative, five-centre study carried out in London, UK, in 1997-2003. Methods All HIV-1-infected women who received nevirapine as part of combination antiretroviral therapy (ART) during pregnancy were included in the study. Data on demographics, HIV infection risk, Centers for Disease Control and Prevention (CDC) status, surrogate markers at initiation of therapy, other medications hepatitis B and C virus coinfection and clinical data relating to potential toxicity were collated and analysed. Results Fifteen of 235 eligible women (6.4%) developed rash and eight (3.4%) developed hepatotoxicity, including four with coexistent rash, giving a combined incidence of 19 potential cases of nevirapine toxicity during pregnancy (8.1%). Alternative causes of rash/hepatotoxicity were suspected in seven cases and only 10 mothers (5.8%) discontinued nevirapine. Of the 170 women who commenced nevirapine during this pregnancy, 13 (7.6%) developed rash and eight (4.7%) hepatotoxicity, a combined incidence of 10%. Only two of 65 women with nevirapine exposure prior to this pregnancy developed rash (3.1%). Conclusions Nevirapine-containing ART was well tolerated in this cohort of pregnant women. Although pregnancy did not appear to increase the risk of nevirapine-associated toxicity compared to published adult data, CD4 count may be less predictive of toxicity in pregnancy.
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Otieno PA, Brown ER, Mbori Ngacha DA, Nduati RW, Farquhar C, Obimbo EM, Bosire RK, Emery S, Overbaugh J, Richardson BA, John Stewart GC. **HIV-1 disease progression in breast-feeding and formula-feeding mothers: A prospective 2-year comparison of T cell subsets, HIV-1 RNA levels, and mortality**. Journal of Infectious Diseases 2007;195(2):220-229.

Notes. Othieno et al have published in the 15th of January issue of JID, a study regarding the association between breastfeeding and maternal disease progression and death, which is an issue with important implications for public health policy. As Wilfert and Fowler[1] point out in the editorial commentary in the same issue, it is of great importance to ascertain whether breastfeeding compromises maternal health in the presence of HIV infection. Two recent analyses in Kenya and South Africa regarding breast-feeding and mortality among women infected with HIV-1 have produced conflicting results and therefore Othieno *et al*'s results are reassuring as they found no association of breastfeeding with increased maternal mortality when appropriate care was available.

In a previous Kenyan clinical trial, Nduati *et al*[2] had found that breastfeeding by HIV-1 infected women resulted in adverse outcomes for both mother and infants. The authors found an attributable risk of maternal death due to breastfeeding of 69% with also an association between maternal death and subsequent infant death. They hypothesized that various factors such as higher viral replication during lactation and combined increased metabolic burdens of HIV-1 infection and breastfeeding could accelerate HIV-1 disease progression in postpartum mothers.

However, data from a South African study[3] documented no difference in mortality of HIV-1-infected women according to their children's feeding modality (ever vs. never breast-fed). Over a mean follow-up period after delivery of 10 months, 0.49% (2 of 410) of women who ever breast-fed were

known to have died compared with 1.92% (3 of 156) of women who never breast-fed. In 2005, in a meta-analysis, the Breastfeeding and HIV International Transmission Study (BHITS study)[4], which used data regarding more than 4000 HIV-mothers in sub-Saharan Africa, found again no statistically significant differences in the risk of mortality during the 18-month period after delivery according to children's feeding modality (ever vs. never breast-fed).
Othieno *et al*, in this recent prospective study in Kenya designed primarily to assess maternal HIV-1 disease progression, document a significantly higher rate of decline in CD4 cell count and body mass index during prolonged breast-feeding among mothers which however does not translate in a difference in HIV-1 RNA levels or mortality over the 2 year postpartum period. Importantly they noted no difference in CD4 cell count decline among HIV-infected women who weaned at 6 months and those who never breastfed. This data suggest that breastfeeding may only have a minimal adverse effect on CD4 count during the recommended six-month period of exclusive breastfeeding recommended by WHO.
In the editorial commentary, Wilfert and Fowler ascertain that the current preponderance of evidence looking at the association of breastfeeding and maternal mortality indicates now that HIV-infected mothers are not compromised by breastfeeding their infants. New data regarding the use of highly active antiretroviral treatment (HAART) to protect both the breastfeeding mother and her HIV-exposed infant are currently being assessed and will hopefully provide information on the best strategy for reducing MTCT in order to promote maternal health and maximise HIV free infant survival.
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Plipat T, Naiwatanakul T, Rattanasuporn N, Sangwanloy O, Amornwichet P, Teeraratkul A, Ungchusak K, Mock P, Levine W, McConnell MS, Simonds RJ, Culnane M. **Reduction in mother-to-child transmission of HIV in Thailand, 2001-2003: results from population-based surveillance in six provinces**. AIDS 2007;21(2):145-151.

Abstr. Background: In 2000, Thailand implemented a national program to prevent mother-to-child HIV transmission (PMTCT). Objective: To describe the effectiveness of the prevention of mother-to-child HIV transmission program in Thailand. Design and methods: A register of HIV-exposed children at birth was created with follow-up of infection status. The register included children born to HIV-infected women between I January 2001 and 31 December 2003 at 84 public health hospitals in six provinces of Thailand. The main outcome measure was HIV infection in children. Results: A total of 2200 children born to HIV-infected mothers were registered. Of these mother-infant pairs, 2105 (95.7%) received some antiretroviral prophylaxis, including 1358 (61.7%) who received the complete short-course zidovudine regimen during pregnancy and labor for the mother and after birth for the infant, with or without other antiretrovirals. HIV infection outcome was determined for 1667 (75.8%) children, of whom 158 [9.5%, 95% confidence interval (0), 8.1-11.0%] were infected. Transmission risk was 6.8% (95% Cl 5.2-8.9%) among 761 mother-infant pairs that received the complete zidovudine regimen alone, and 3.9% (95% Cl, 2.2-6.6%) among 361 mother-infant pairs that received the complete zidovudine regimen combined with other anti retrovirals, usually nevirapine. The overall transmission risk from this cohort, including all antiretroviral prophylaxis combinations, is estimated to be 10.2%. Conclusions: The Thai national PMTCT program is effective in reducing mother-to-child transmission risk from the historical risk of 18.9-24.2%. The addition of nevirapine to short-course zidovudine beginning in 2004 may further

improve program effectiveness in Thailand.
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Sungkanuparph S, Manosuthi W, Kiertiburanakul S, Piyavong B, Chumpathat N, Chantratita W. **Options for a second-line antiretroviral regimen for HIV type 1-infected patients whose initial regimen of a fixed-dose combination of stavudine, lamivudine, and nevirapine fails**. Clinical Infectious Diseases 2007;44(3):447-452.
Abstr. Background. A fixed- dose combination of stavudine, lamivudine, and nevirapine is extensively used as an antiretroviral regimen in developing countries because of its affordability. Virological failure with this regimen has become more common, and a second- line regimen needs to be prepared in the national program. Methods. Genotypic resistance testing was conducted among human immunodeficiency virus type 1 (HIV1) - infected patients who experienced treatment failure with their first antiretroviral regimen (a fixed- dose combination of stavudine, lamivudine, and nevirapine) during 2003 - 2005. Patterns of resistance mutations and options for a second- line regimen were studied. Results. We studied 98 patients (mean age, 35.2 years), of whom, 63% were male. The median duration of antiretroviral therapy was 20 months. The median HIV- 1 RNA load at the time of virological failure detection was 4.1 log copies/ mL. The prevalences of patients with >= 1 major mutation conferring drug resistance to nucleoside reverse- transcriptase inhibitors and nonnucleoside reverse- transcriptase inhibitors were 95% and 92%, respectively. M184V was the most common nucleoside reverse- transcriptase inhibitor resistance mutation (observed in 89% of patients). Thymidine analogue mutations, K65R, and Q151M were observed in 37%, 6%, and 8% of patients, respectively. Patients with an HIV- 1 RNA load of 14 log copies/ mL at the time of treatment failure had higher prevalence of thymidine analogue mutations (P =.041), K65R (P =.031), and Q151M (P =.008) mutations. The second- line regimen was determined in a resource- limited setting where tenofovir and enfuvirtide are not available; the options were limited for 48% of patients. Conclusions. After experiencing treatment failure with a fixed- dose combination of stavudine, lamivudine, and nevirapine, almost all patients have lamivudine and nonnucleoside reverse- transcriptase inhibitor resistance. The options for a second-line regimen are limited for one- half of these patients. In resource- limited settings where availability of antiretroviral agents is limited, strategies for prevention of HIV- 1 resistance are crucial. Early detection of virological failure may provide more options and better treatment outcomes.
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Zhou J, Paton NI, Ditangco R, Chen YM, Kamarulzaman A, Kumarasamy N, Lee CKC, Li PCK, Merati TP, Phanuphak P, Pujari S, Vibhagool A, Zhang F, Chuah J, Frost KR, Cooper DA, Law MG. **Experience with the use of a first-line regimen of stavudine, lamivudine and nevirapine in patients in the TREAT Asia HIV Observational Database**. HIV Medicine 2007;8(1):8-16.
Abstr. Background The antiretroviral treatment (ART) combination of stavudine, lamivudine and nevirapine (d4T/3TC/NVP) is the most frequently used initial regimen in many Asian countries. There are few data on the outcome of this treatment in clinic cohorts in this region. Methods We selected patients from the TREAT Asia HIV Observational Database (TAHOD) who started their first ART regimen with d4T/3TC/NVP. Treatment change was defined as cessation of therapy or the

addition or change of one or more drugs. Clinical failure was defined as diagnosis with an AIDS-defining illness, or death while on d4T/3TC/NVP treatment. Results The rate of treatment change among TAHOD patients starting d4T/3TC/NVP as their first antiretroviral treatment was 22.3 per 100 person-years, with lower baseline haemoglobin (i.e. anaemia) associated with slower rate of treatment change. The rate of clinical failure while on d4T/3TC/NVP treatment was 7.3 per 100 person-years, with baseline CD4 cell count significantly associated with clinical failure. After d4T/3TC/NVP was stopped, nearly 40% of patients did not restart any treatment and, of those who changed to other treatment, the majority changed to zidovudine (ZDV)/3TC/NVP and less than 3% of patients changed to a protease inhibitor (PI)-containing regimen. The rates of disease progression on the second-line regimen were similar to those on the first-line regimen. Conclusion These real-life data provide an insight into clinical practice in Asia and the Pacific region. d4T/3TC/NVP is maintained longer than other first-line regimens and change is mainly as a result of adverse effects rather than clinical failure. There is a need to develop affordable second-line antiretroviral treatment options for patients with HIV infection in developing countries.
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Conference on Retroviruses and Opportunistic Infections. Los Angeles, 25-28 February 2007

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