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Barin F, Jourdain G, Brunet S, Ngo Giang Huong N, Weerawatgoompa S, Karnchanamayul W, Ariyadej S, Hansudewechakul R, Achalapong J, Yuthavisuthi P, Ngampiyaskul C, Bhakeecheep S, Hemwutthiphon C, Lallemand M. **Revisiting the role of neutralizing antibodies in mother-to-child transmission of HIV-1.** *Journal of Infectious Diseases* 2006;193(11):1504-1511.

Abstr. We analyzed the association between mother-to-child transmission (MTCT) of human immunodeficiency virus type 1 (HIV-1) and maternal neutralizing antibodies to heterologous primary isolates of various HIV-1 clades, to test the hypothesis that protective antibodies are those with broad neutralizing activity. Our study sample included 90 Thai women for whom the timing of HIV-1 transmission (in utero or intrapartum) was known. The statistical analysis included a conditional logistic-regression model to control for both plasma viral load and duration of zidovudine prophylaxis. The higher the titer of neutralizing antibodies to a heterologous strain of the same clade, the lower the rate of MTCT of HIV-1. More specifically, high levels of neutralizing antibodies to the MBA (CRF01_AE) strain were associated with low intrapartum transmission of HIV-1. This suggested that such heterologous neutralizing antibodies may be involved in the natural prevention of late perinatal HIV transmission. These data are consistent with the hypothesis that the use of some antibodies might help to prevent perinatal HIV transmission, through passive immunoprophylaxis. Moreover, the study of humoral factors associated with MTCT of HIV-1 may identify correlates of protection that should help in the design of efficient HIV/acquired immunodeficiency syndrome vaccines.

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Breen RAM, Miller RF, Gorsuch T, Smith CJ, Ainsworth J, Ballinger J, Swaden L, Cropley I, Johnson MA, Lipman MCI. **Virological response to highly active antiretroviral therapy is unaffected by antituberculosis therapy.** *Journal of Infectious Diseases* 2006;193(10):1437-1440.

Abstr. We compared 156 human immunodeficiency virus (HIV) infected patients who had tuberculosis with control populations of similar size. Of 111 patients with HIV infection and tuberculosis who received highly active antiretroviral therapy (HAART) and therapy for tuberculosis concurrently, 92 (83%) achieved or maintained virus loads of < 50 copies/mL, and 99 (89%) achieved or maintained a ≥ 2 log₁₀ reduction in virus load after 6 months. Virological response and changes in CD4 cell count were equivalent to those in 111 matched HIV-infected subjects without tuberculosis starting HAART. Tuberculosis recurrence rates were similar to those found in an HIV-uninfected population of 156 subjects (3% and 1%, respectively). Treatment for HIV and tuberculosis does not compromise outcomes for either disease.

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Cotter AM, Garcia AG, Duthely ML, Luke B, MJ OS. **Is antiretroviral therapy during pregnancy associated with an increased risk of preterm delivery, low birth weight, or stillbirth?** *Journal of Infectious Diseases* 2006;193(9):1195-1201.

Abstr. Background. Data on complications of pregnancy associated with antiretroviral therapy are limited. Some small studies have demonstrated an increased preterm delivery rate, but a recent retrospective United States multisite study did not concur with these findings. Our objective was to investigate whether antiretroviral therapy was associated with adverse pregnancy outcome at a single site. Methods. Using prospectively gathered data, women were identified who were determined to be human immunodeficiency virus positive before or during pregnancy who sought care at our prenatal clinic and who gave birth at the University of Miami/ Jackson Memorial Medical Center from 1990 through 2002. The outcome measures were preterm delivery, low birth weight, and stillbirth. Results. The cohort included 999 women who received antiretroviral therapy during pregnancy (monotherapy in 492, combination therapy without a protease inhibitor [PI] in 373, and combination therapy with a PI in 134) and 338 women who did not receive therapy. After adjustment for possible confounders, only combination therapy with a PI was associated with an increased risk of preterm delivery, compared with any other combination (odds ratio, 1.8 [95% confidence interval, 1.1-3.0]). There were no differences in rates of low birth weight and stillbirth, regardless of therapy. Conclusion. Compared with monotherapy and combination therapy without a PI, only combination therapy with a PI was associated with an increased risk of preterm delivery.

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Domek GJ. **Social consequences of antiretroviral therapy: preparing for the unexpected futures of HIV-positive children** [Editorial]. *Lancet* 2006;367(9519):1367-1369.

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Ferradini L, Jeannin A, Pinoges L, Izopet J, Odhiambo D, Mankhambo L, Karungi G, Szumilin E, Balandine S, Fedida G, Carrieri MP, Spire B, Ford N, Tassie JM, Guerin PI, Brasher C. **Scaling up of highly active antiretroviral therapy in a rural district of Malawi: an effectiveness assessment.** *Lancet* 2006;367(9519):1335-1342.

Abstr. Background The recording of outcomes from large-scale, simplified HAART (highly active antiretroviral therapy) programmes in sub-Saharan Africa is critical. We aimed to assess the effectiveness of such a programme held by Medecins Sans Frontieres (MSF) in the Chiradzulu district, Malawi. Methods We scaled up and simplified HAART in this programme since August, 2002. We analysed survival indicators, CD4 count evolution, virological response, and adherence to treatment. We included adults who all started HAART 6 months or more before the analysis. HIV-1 RNA plasma viral load and self-reported adherence were assessed on a subsample of patients, and antiretroviral resistance mutations were analysed in plasma with viral loads greater than 1000 copies per mL. Analysis was by intention to treat. Findings Of the 1308 patients who were eligible, 827 (64%) were female, the median age was 34.9 years (IQR 29.9-41.0), and 1023 (78%) received d4T/3TC/NVP (stavudine, lamivudine, and nevirapine) as a fixed-dose combination. At baseline, 1266 individuals (97%) were HAART-naive, 357 (27%) were at WHO stage IV, 311 (33%) had a body-mass index of less than 18.5 kg/m², and 208 (21%) had a CD4 count lower than 50 cells per mu L. At follow-up (median 8.3 months, IQR 5.5-13.1), 967 (74%) were still on HAART, 243 (19%) had died, 91 (7%) were lost to follow-up, and seven (0.5%) discontinued treatment. Low body-mass index, WHO stage IV, male sex, and baseline CD4 count lower than 50 cells per mu L were independent determinants of death in the first 6 months. At 12 months, the probability of individuals still in care was 0.76 (95% CI 0.73-0.78) and the median CD4 gain was 165 (IQR 67-259) cells per mu L. In the cross-sectional survey (n = 398), 334 (84%) had a viral load of less than 400 copies per mL. Of several indicators measuring adherence, self-reported poor adherence (<80%) in the past 4 days was the best predictor of detectable viral load (odds ratio 5.4, 95% CI 1.9-15.6). Interpretation These data show that large numbers of people can rapidly benefit from antiretroviral therapy in rural resource-poor settings and strongly supports the implementation of such large-scale simplified programmes in Africa.

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Robertson J, Meier M, Wall J, Ying J, Fichtenbaum CJ. **Immune reconstitution syndrome in HIV: Validating a case definition and identifying clinical predictors in persons initiating Antiretroviral therapy.** *Clinical Infectious Diseases* 2006;42(11):1639-1646.

Abstr. Background. Clinical deterioration after initiation of antiretroviral therapy may result from restored immunity. There is no standard clinical definition for immune reconstitution syndrome. The objectives of this study were to validate a proposed definition and to identify factors predictive of immune reconstitution syndrome. Methods. This was a retrospective case-control study from an academic university medical practice. Cases were matched to ≥ 2 control subjects by CD4(+) cell count at the time of initiation of antiretroviral therapy. Cases and "mock cases" were blindly reviewed by 2 human immunodeficiency virus (HIV) experts. Results. Twenty possible cases of immune reconstitution syndrome were identified; HIV experts excluded all cases of herpes zoster (shingles), with agreement on real and mock cases of 92%. For 14 confirmed case patients (compared with 40 control subjects), immune reconstitution syndrome was associated with a higher number of prior opportunistic infections (P = .003) and higher CD8(+) cell counts at baseline (P = .05) and at week 12 (P = .02). Immune reconstitution syndrome was associated with lower baseline levels of alanine aminotransferase (P = .05) and hemoglobin (P = .02). On multivariate analysis, the number of prior opportunistic infections (odds ratio, 2.7; P = .007) and lower hemoglobin level at baseline (odds ratio, 0.8; P = .003) were independently associated with development of immune reconstitution syndrome. A predictive model was defined by classification and regression tree analysis with a sensitivity and specificity of 78.57% and 87.50%, respectively, for an importance score of ≥ 4 (on a scale of 0.0 to 100.0), and 92.86% and 80.00%, respectively, for a score of ≥ 2 , using the number of prior opportunistic infections, CD8(+) cell count, and hemoglobin level. Conclusions. A standard definition for immune reconstitution syndrome is possible. Patients with a greater severity of illness at initiation of antiretroviral therapy are at risk for immune reconstitution syndrome. The model defined by classification and regression tree analysis may provide a basis for risk stratification before initiation of antiretroviral therapy.

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Tuomala RE, Yawetz S. **Protease inhibitor use during pregnancy: Is there an obstetrical risk?** [Editorial].
Journal of Infectious Diseases 2006;193(9):1191-1194.
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