



HIV Care & PMTCT in Resource-Limited Settings

Monthly Intelligence Report

2005, Vol 1, Issue 2

prepared by the Bordeaux Working Group

Members: Elise Arrivé, Renaud Becquet, François Dabis (Coordinator), Valérie Leroy, Dominique Marchand, Evelyne Mouillet (Coordinator), Joanna Orne-Gliemann, Freddy Perez, Charlotte Sakarovitch, Catherine Seyler, Besigin Tonwe-Gold.

Number of citations selected for this issue: 20

Subject headings / Subheadings indexing the selected references (by alphabetical order)

Adults / Women	Eastern Europe	Infant feeding / Breastfeeding	Prevention of Mother-To-Child Transmission (PMTCT) / AntiRetroViral (ARV)	Treatment impact and response
Children	Gynæcology	Infections (Others) / Prophylaxis	Prevention of sexual transmission	Treatment monitoring
Clinical manifestations (Others)	Hepatitis B infection (HBV)	Low Income Countries (LICs) / Africa, Asia, Carribean, South America	Randomized Controlled Trial (RCT)	Treatment programme
Comprehensive care	Hepatitis C infection (HCV)	Mother-To-Child Transmission (MTCT)	Termination of pregnancy / Abortion	Tuberculosis (TB) / Prophylaxis
Conference summary	Highly Active AntiRetroviral Treatment (HAART)	Natural history	Treatment adherence	Viral resistance
Contraception	Industrialized countries	Obstetrics	Treatment complications	Voluntary Counselling and Testing (VCT)

Citation format (by alphabetical order of the authors): Author(s). **Title**. Source. **Abstr.** (Authors' abstract) or **Notes** (prepared by the Bordeaux Working Group) **Author address**, if available, **Subject Headings**

Bi XQ, Gatanaga H, Tanaka M, Honda M, Ida S, Kimura S, Oka S. **Modified Dynabeads method for enumerating CD4(+) T-lymphocyte count for widespread use in resource-limited situations.** Journal of Acquired Immune Deficiency Syndromes 2005;38(1):1-4.

Abstr. The Dynabeads method showed the potential for enumerating CD4(+) T lymphocytes (CD4 count) in HIV-1-infected individuals. The large volume of Dynabeads required for 1 sample and complex procedure made the method expensive and not easy for use, however. To decrease the cost and simplify the procedure, we reduced the volume of the Dynabeads, added wash times, and skipped over the staining step so as to count the CD4 cells directly under an optical microscope. The CD4 count of 246 blood samples using our modified Dynabeads method (DynabeadsCD4) showed a significant correlation with that obtained by flow cytometry (FlowcytoCD4) ($r = 0.91$ [$P < 0.0001$]; slope = 1.03, intercept = -16). The sensitivity and specificity for a CD4 count less than 200 cells/ μL were 79% and 94%, and for a CD4 count less than 350 cells/ μL , the sensitivity and specificity were 95% and 88%, respectively. The positive and negative predictive values for a CD4 count less than 350 cells/ μL were 97% and 83%, respectively. The systematic error was 8 cells/ μL (95% confidence interval [CI]: 0.4-16). The cost of Dynabeads for 1 sample was less than \$1.00; thus, the estimated cost per DynabeadsCD4 test is less than \$3.00, including the cost of other disposable materials. Our modified method is simple, economic, and accurate enough to monitor antiretroviral therapy in resource-limited situations.

Address: Oka, S; Int Med Ctr Japan; AIDS Clin Ctr; 1-21-1 Toyama; Tokyo 1628655; Japan.
oka@imcj.hosp.go.jp

HAART, LICs, Treatment monitoring

Blower S, Bodine E, Kahn J, McFarland W. **The antiretroviral rollout and drug-resistant HIV in Africa: insights from empirical data and theoretical models.** AIDS 2005;19(1):1-14.

Abstr. The U.S. Government has pledged to spend \$15 billion in Africa and the Caribbean on AIDS. A central focus of this plan is to provide antiretroviral treatment (ART) to millions. Here, we evaluate whether the plan to rollout ART in Africa is likely to generate an epidemic of drug-resistant strains of HIV. We review what has occurred as a result of high usage of ART in developed countries in terms of changes in risky behavior, and the emergence and transmission of drug-resistant HIV. We also review how mathematical models have been used to predict the evolution of drug-resistant HIV epidemics. We then show how models can be used to predict the likely impact of the ART rollout on the evolution of drug-resistant HIV in Africa. At currently planned levels of treatment coverage, we predict that (over the next decade) in Africa: (i) the impact of ART on reducing HIV transmission (and prevalence) is likely to be undetectable (unless accompanied by substantial changes in behavior), (ii) the transmission rate of drug-resistant HIV will be below the WHO surveillance threshold of 5%, and (iii) the majority of cases of drug-resistant HIV that will occur will be due to acquired (and not transmitted) resistance. For the next decade, large-scale surveillance for detecting transmitted resistance in Africa is unnecessary. Instead, we recommend that patients should be closely monitored for acquired resistance, and sentinel surveillance (in a few urban centers) should be used to monitor transmitted resistance. (C) 2005 Lippincott Williams Wilkins.

Address: Blower, S; Univ Calif Los Angeles; David Geffen Sch Med; 1100 Glendon Ave PH2; Los Angeles, CA 90024; USA. sblower@mednet.ucla.edu

HAART, LICs / Africa, Treatment impact and response, Viral resistance

Boschi A, Tinelli C, Ortolani P, Moscatelli G, Morigi G, Arlotti M. **CD4+cell-count-guided treatment interruptions in chronic HIV-infected patients with good response to highly active antiretroviral therapy.** AIDS 2004;18(18):2381-2389.

Abstr. Objective: To evaluate the safety of treatment interruption guided by CD4+ cell count in HIV-infected patients followed up prospectively. Methods: Patients on highly active antiretroviral therapy with CD4+ cell counts $> 500 \times 10^6$ cells/I discontinued therapy with instructions to start therapy again before their CD4+ count dropped below 200×10^6 cells/I. Any patients who resumed therapy would be eligible to interrupt treatment again once their CD4+ cell count increased above 500×10^6 cells/I. Results: Data on 71 HIV infected patients is reported. Their median nadir CD4+ cell count before antiretroviral treatment was 352×10^6 cells/I [interquartile range (IQR), $294-445 \times 10^6$ cells/I]. The median CD4+ cell count at the time of first interruption was 790×10^6 cells/I (IQR, $657-1041 \times 10^6$ cells/I). The median follow-up after starting the first treatment interruption was 28.3 months (IQR, 21.4-37.0 months). During the follow-up 49 patients restarted therapy and 22 patients remain off therapy; 24 patients have interrupted therapy twice, nine patients have interrupted therapy three times and six patients four times. No AIDS-defining illnesses occurred during the follow-up. The median duration of the first interruption was 15 months (IQR, 6-26 months). The overall reduction of time on therapy was 71.1%. The duration of the first interruption and the reduction of time on therapy were related to nadir CD4+ cell count. The patients who resumed HAART rapidly regained CD4+ cells and achieved viral suppression. Conclusion: If carefully monitored, treatment interruptions guided by CD4+ cell count in patients

with an initially high CD4+ cell counts are clinically safe, decrease exposure to the drugs and do not reduce the efficacy of therapy when this is re-started. (C) 2004 Lippincott Williams Wilkins.

Address: Boschi, A; AUSL Rimini; Div Infect Dis; Via Settembrini 2; I-49300 Rimini; RN; Italy.
boschia@libero.it

Adults, HAART, Industrialized countries, Treatment impact and response,

Calmy A, Klement E, Teck R, Berman D, Pecoul B, Ferradini L, Ford N. **Simplifying and adapting antiretroviral treatment in resource-poor settings: a necessary step to scaling-up [Editorial]**. AIDS 2004;18(18):2353-2360.

Introduction: Access to antiretroviral (ARV) therapy for patients in developing countries has become an increasing global public health and political concern in recent years. Both donor governments and those of high-burden countries agree that treating AIDS is a major priority. Efforts are underway in many countries to increase the numbers receiving ARV treatment, and the level of international funds committed to assist this effort has increased significantly, albeit insufficiently. In 2002, this led the World Health Organization (WHO) to launch an ambitious '3x5' plan to place three million people on ARV by 2005. While numbers benefiting from ARV therapy in the developing world have increased over the last few years, the need for scaling-up is as urgent as ever: over two-thirds of the six million people in the developing world who are in urgent need of ARV therapy live in sub-Saharan Africa, but less than 2% of these have access to this treatment. It is estimated that around 6500 people are dying of AIDS each day in this region. Treating AIDS in the developing world means working in a context of poor health-care infrastructure and limited financial and human resources, most of which are concentrated in capital cities. Health-care providers in the developing world are faced with patients who have different characteristics to those seen in clinics in Western countries: half of all cases in developing countries are among women of childbearing age; there are much higher proportions of children affected; patients tend to be in a more critical condition as they are diagnosed late in the course of the disease; and they are commonly afflicted with one or more complex comorbidities, such as tuberculosis, malaria and malnutrition. In moving towards providing sustainable access to treatment for the majority in the developing world, models of care must be adapted to the realities of these regions. Current treatment models have been developed in Europe and North America, are based on the availability of more than 20 ARV drugs, assume the routine use of sophisticated laboratory tools by specialists, and address viral strains that predominate in wealthy countries. Simplification and decentralization of treatment are therefore essential components of a successful strategy to extend ARV therapy. The concept of simplification covers the whole process of providing ARV drugs: inclusion criteria, management of side effects, choice of a drug regimen (first line, alternative first line and salvage therapy), when to switch, and so on. Simplification of the drug regimen is a crucial strategy in facilitating adherence, which is a key condition to optimize the chances of long-term success for the therapy. Clearly, this is not just important for resource-poor settings: for example US guidelines state that 'regimens should be simplified as much as possible by reducing the number of pills and therapy frequency'. Simplification of the first-line regimen has been the cornerstone of the treatment strategy in developing countries since triple therapy started to become available in 2001. While treatment cannot rely on one single combination alone, the availability of an affordable and easy-to-use first-line regimen is the starting point from which other strategies can be usefully explored. This editorial draws on the experience within Médecins sans Frontières (MSF) to date, based on treating 21,000 people in 27 countries worldwide, together with information gathered through a series of expert consultations. It is intended to provide a brief overview of priorities in adaptation and simplification in developing-country settings.

Address: Calmy, A; Med Sans Frontieres; 78 Rue Lausanne, Case Postale 116; CH-1211 Geneva; Switzerland.
alexandra.calmy@geneva.msf.org

Comprehensive care, HAART, LICs, Treatment programme

Cassol E, Page T, Mosam A, Friedland G, Jack C, Lalloo U, Kopetka J, Patterson B, Esterhuizen T, Coovadia HM. **Therapeutic response of HIV-1 subtype C in African patients coinfecting with either Mycobacterium tuberculosis or human herpesvirus-8**. Journal of Infectious Diseases 2005;191(3):324-332.

Abstr. Background. A potential confounding factor in the treatment of human immunodeficiency virus (HIV) infection in Africa is the frequent occurrence of opportunistic infections (OIs). OI-induced immune activation can interfere with HIV-1 clearance by increasing viral replication and target cell availability. Study design. Treatment outcomes for patients dually infected with HIV-1 and Mycobacterium tuberculosis or HIV-1 and human herpesvirus (HHV)-8 were assessed by measuring changes in viral load and CD4(+) cell counts and by determining the time taken to reach undetectable HIV-1 RNA levels, assessed by means of Kaplan-Meier survival analysis. Patients with HIV-1 and Kaposi sarcoma (KS) received generic nevirapine, stavudine, and lamivudine (3TC); patients with HIV-1 and tuberculosis (TB) received standard commercial didanosine, 3TC, and efavirenz. Results. Both cohorts exhibited a rapid, near-exponential phase I decline in viral load. Patients with TB and late-stage KS had the steepest decay kinetics. These same patients had the greatest initial increase in CD4(+) cell counts. Phase II clearance was slower and more variable. The proportions of patients reaching

undetectable plasma HIV-1 levels at days 7, 14, 28, 60, and 90 were, respectively, 15.8%, 30.0%, 52.6%, 78.9%, and 93.8% (Pearson's $\chi^2 = 50.5$; $P < .001$) for patients with TB and 0.0%, 5.0%, 22.2%, 64.7%, and 80.0% (Pearson's $\chi^2 = 63.6$; $P < .001$) for patients with KS. Conclusions. Nucleoside reverse-transcriptase inhibitor/nonnucleoside reverse-transcriptase inhibitor-based treatment regimens are highly effective in clearing rapidly replicating (phase I) virus in African patients dually infected with HIV-1 and either TB or KS.

Address: Cassol, E; Univ KwaZulu Natal; Nelson R Mandela Sch Med; Durban; South Africa.
ecassol@mrc.ac.za

Adults, HAART, Infections (Others), LICs / Africa, TB, Treatment impact and response,

Castro A, Farmer P. **Understanding and addressing AIDS-related stigma: From anthropological theory to clinical practice in Haiti.** American Journal of Public Health 2005;95(1):53-59.

Abstr. For the past several years, diverse and often confused concepts of stigma have been invoked in discussions on AIDS. Many have argued compellingly that AIDS-related stigma acts as a barrier to voluntary counselling and testing. Less compelling are observations regarding the source of stigma or its role in decreasing interest in HIV care. We reviewed these claims as well as literature from anthropology, sociology, and public health. Preliminary data from research in rural Haiti suggest that the introduction of quality HIV care can lead to a rapid reduction in stigma, with resulting increased uptake of testing. Rather than stigma, logistic and economic barriers determine who will access such services. Implications for scale-up of integrated AIDS prevention and care are explored.

Address: Castro, A; Harvard Univ; Sch Med; 641 Huntington Ave; Boston; MA 02115; USA.
arachu_castro@hms.harvard.edu

HAART, LICs / Caribbean, PMTCT / ARV, Treatment programme, VCT

Fawzi WW, Villamor E, Msamanga GI, Antelman G, Aboud S, Urassa W, Hunter D. **Trial of zinc supplements in relation to pregnancy outcomes, hematologic indicators, and T cell counts among HIV-1-infected women in Tanzania.** American Journal of Clinical Nutrition 2005;81(1):161-167.

Abstr. Background: In observational studies, the zinc status of HIV-infected persons has been associated with both positive and adverse clinical outcomes. Such endpoints may affect the risk of adverse birth outcomes among HIV-infected women. Objective: We examined the effects of zinc Supplements on birth outcomes, hematologic indicators, and counts of T lymphocyte subsets among 400 HIV-infected pregnant women. Design: Eligible women between 12 and 27 wk of gestation were randomly assigned to daily oral supplementation with either 25 in 9 Zn or placebo between recruitment and 6 wk after delivery. All women received iron, folic acid, and multivitamin supplements irrespective of the experimental assignment. Results: We observed no significant differences in birth weight, duration of gestation, or fetal and neonatal mortality between women in the zinc and placebo groups. Hemoglobin concentrations increased between baseline and 6 wk postpartum in both groups. However, the rise in hemoglobin over this period was significantly lower ($P = 0.03$) in the zinc group ($x \pm$ SD: 11.5 \pm 17.9 g/L) than in the placebo group (15.2 \pm 18.6 g/L). Similarly, the changes in red blood cell count and in packed cell volume over the same period were significantly lower in the zinc group ($P < 0.01$ and $P = 0.01$, respectively). Zinc had no effect on CD4(+), CD8(+), or CD3(+) cell counts during the follow-up period. Conclusion: Because of the lack of beneficial effects of zinc on adverse pregnancy outcomes and the likelihood of negative effects on hemoglobin concentrations, no compelling evidence exists to support the addition of zinc to prenatal supplements intended for pregnant HIV-infected women.

Address: Fawzi, WW; Harvard Univ; Sch Publ Hlth; 665 Huntington Ave; Boston; MA 02115; USA.
mina@hsph.harvard.edu

Adults / Women, Clinical manifestations (Others), LICs / Africa, Obstetrics, RCT

Kublin JG, Patnaik P, Jere CS, Miller WC, Hoffman IF, Chimbiya N, Pendame R, Taylor TE, Molyneux ME. **Effect of Plasmodium falciparum malaria on concentration of HIV-1-RNA in the blood of adults in rural Malawi: a prospective cohort study.** Lancet 2004;365(9455):233-240.

Abstr. Background Raised HIV viral load in blood has been associated with accelerated disease progression and increased transmission of infection. To assess the effect of Plasmodium falciparum malaria on concentrations of HIV in blood, we did a prospective cohort study in Malawi. Methods We recruited 367 HIV-1-infected adults. Among 334 people aparasitaemic at baseline, 148 had at least one malaria episode during follow-up and received antimalarial treatment. Of these, 77 had HIV-1-RNA measurements at baseline, during malaria, and post-malaria. We used linear regression with generalised estimating equations to assess effect of four definitions of malaria (any parasitaemia, parasite density greater than or equal to 2000/ μ L, febrile parasitaemia, and febrile parasitaemia with parasite density greater than or equal to 2000/ μ L) on changes in log HIV-1 RNA, overall and by baseline CD4 count. Findings With malaria defined as any parasitaemia, HIV-1-RNA concentration almost doubled between baseline (median 96 215 copies per mL) and malaria (168 901 copies per mL), a 0.25 (95% CI 0.11-0.39) log increase in mean RNA concentration. HIV-1-RNA concentration fell to median 82 058 copies per

mL by about 8-9 weeks postmalaria. Increases in HIV-1-RNA were greatest for people with fever, parasite density 2000/μL or greater, and CD4 count more than 300 cells per μL, in whom concentrations rose from median 38 483 copies per mL at baseline to 196 098 copies per mL during malaria, a mean log increase of 0.82 (95% CI 0.55-1.10, p<0.0001), and fell to median 75 331 copies per mL post-malaria. People who remained aparasitaemic showed no changes in HIV-1-RNA concentration. Interpretation HIV-infected individuals with malaria have a significantly increased viral load, which might enhance HIV transmission and accelerate disease progression.

Address: Kublin, JG; Fred Hutchinson Canc Res Ctr; 1100 Fairview Ave N, EL-500; Seattle; WA 98109; USA. jkublin@fhcrc.com

Adults, Infections (Others), LICs / Africa, Natural history

Laurent C, Gueye NFN, Ndour CT, Gueye PM, Diouf M, Diakhate N, Kane NCT, Laniece I, Ndir A, Vergne L, Ndoye I, Mboup S, Sow PS, Delaporte E. **Long-term benefits of highly active antiretroviral therapy in Senegalese HIV-1-infected adults.** *Journal of Acquired Immune Deficiency Syndromes* 2005;38(1):14-17.

Abstr. Objectives: To assess the long-term survival, as well as the immunologic and virologic effectiveness, adherence, and drug resistance, in HIV-infected patients receiving highly active antiretroviral therapy (HAART) in one of the oldest and best-documented African cohorts. Methods: A prospective observational cohort study included the first 176 HIV-1-infected adults followed in the Senegalese government-sponsored antiretroviral therapy initiative launched in August 1998. Patients were followed for a median of 30 months (interquartile range, 21-36 months). HAART comprised 2 nucleoside reverse transcriptase inhibitors and either 1 protease inhibitor or 1 nonnucleoside reverse transcriptase inhibitor. Results: At baseline, 92% of patients were antiretroviral naive and 82% had AIDS; the median CD4 count was 144 cells/mm³, and median viral load was 202,368 copies/mL. The survival probability was high (0.81 at 3 years; 95% CI, 0.74-0.86) and was independently related to a baseline hemoglobin level <10 g/dL and a Kamofsky score <90%. Antiviral efficacy was consistently observed during the 3 years of treatment (-2.5 to -3.0 log₁₀ copies/mL; 60-80% of patients with viral load <500 copies/mL) and the CD4 count increase reached a median of 225 cells/mm³. Most patients reported good adherence (80-90%). The emergence of drug resistance was relatively rare (12.5%). Conclusion: This study shows that clinical and biologic results similar to those seen in Western countries can be achieved and sustained during the long term in Africa.

Address: Laurent, C; Univ Montpellier; Inst Rech Dev; 911 Ave Agropolis, BP 64501; F-34394 Montpellier; France. Christian.Laurent@mpl.ird.fr

Adults, HAART, LICs / Africa, Treatment impact and response, Viral resistance

Le Coeur S, Khlat M, Halembokaka G, Augereau Vacher C, Batala M' Pondo G, Baty G, Ronsmans C. **HIV and the magnitude of pregnancy-related mortality in Pointe Noire, Congo.** *AIDS* 2005;19(1):69-75.

Abstr. Objectives: The extent to which HIV affects pregnancy-related mortality in countries with high HIV/AIDS and maternal mortality is poorly understood. The objectives of this study were to investigate the mortality of women of reproductive age by both HIV and pregnancy status, and quantify the excess mortality attributable to HIV during pregnancy in Pointe Noire, Congo. Design: Prospective mortuary investigation of all deaths in women aged 15-44 years, during 112 consecutive days. Methods: Mortality rates by HIV and pregnancy were computed. During the study, period, 378 corpses were examined, blood was tested for HIV and pregnancy, relatives were interviewed and hospital files were reviewed. Denominators were obtained from a census with women-years assigned to pregnancy and/or HIV based on levels of fertility and HIV prevalence in the city. Results: The mortality rate was 32 times higher [95% confidence interval (CI), 25-39] among HIV-positive than among HIV-negative women. The relative increase in mortality associated with HIV was much higher in non-pregnant [rate ratio (RR), 41; 95% CI, 32-52] than in pregnant women (RR, 4; 95% CI, 2-9). Among HIV-positive women, pregnancy appeared to confer a survival benefit. Conclusion: These findings have important implications for the interpretation of trends in maternal mortality in the context of HIV. The apparent survival benefit of pregnant HIV-positive women is largely due to their low fertility in the latest stage of the disease. As the HIV epidemic matures and more women become severely ill, any potential adverse effects associated with HIV and pregnancy may be increasingly offset by selection effects, and maternal mortality may not increase further. (C) 2005 Lippincott Williams Wilkins.

Address: Le Coeur, S; INED; Unites Mortal Sante Epidemiol & Populat & Dev; 133 Blvd Davout; F-75980 Paris; France. lecoeur@ined.fr

Adults / Women, LICs / Africa, Natural history

Lyons FE, Coughlan S, Byrne CM, Hopkins SM, Hall WW, Mulcahy FM. **Emergence of antiretroviral resistance in HIV-positive women receiving combination antiretroviral therapy in pregnancy.** AIDS 2005;19(1):63-67.

Abstr. Background: Antenatal anti retroviral therapy is integral to preventing vertical transmission of HIV-1. The impact of temporary triple antiretroviral therapy in pregnancy on the emergence of antiretroviral resistance has not been studied. Objective: To determine the impact of temporary triple antiretroviral therapy in pregnancy on emergence of antiretroviral resistance. Methods: Pregnant HIV-1 infected women with a pre-treatment CD4 cell count >300 x 10(6)/l initiated triple antiretroviral therapy in the third trimester and discontinued postpartum. Genotypic resistance testing was performed after antiretroviral cessation and on pretreatment samples when postpartum samples showed primary mutations. Results: In a cohort of 50 women who initiated antiretroviral therapy in pregnancy, 39 (78%) had postpartum HIV-1 nucleotide sequences available for analysis: 35 of these (90%) were previously antiretroviral naive. Seven primary mutations, V106A (one), Y181C (two), G190A (one), K101E (one), M184V (one), T215S (one) were detected in five (13%) women. All five were on regimens that included nevirapine and all were antiretroviral therapy naive prior to the index pregnancy. Four had no mutations detected pretreatment (one did not have a pretreatment analysis available, viral load 83 copies/ml). The median duration of antiretroviral exposure was 70 days. Conclusion: Emergence of genotypic resistance is significant in this cohort of pregnant women. All mutations detected were in those that took nevirapine-containing regimens. The clinical implications of these mutations are unknown. (C) 2005 Lippincott Williams Wilkins.

Address: Lyons, FE; St James Hosp; GUIDE Clin; Dublin 8; Ireland. fionalyons69@yahoo.co.uk

Adults / Women, HAART, Industrialized countries, PMTCT / ARV, Viral resistance

Magder LS, Mofenson L, Paul ME, Zorrilla CD, Blattner WA, Tuomala RE, LaRussa P, Landesman S, Rich KC. **Risk factors for in utero and intrapartum transmission of HIV.** Journal of Acquired Immune Deficiency Syndromes 2005;38(1):87-95.

Abstr. Objective: To identify predictors of in utero and intrapartum HIV-1 transmission in infants born in the Women and Infants Transmission Study between 1990 and 2000. Methods: In utero HIV-1 infection was defined as an infant with the first positive HIV-1 peripheral blood mononuclear cell culture and/or DNA polymerase chain reaction assay at 7 days of age or younger; intrapartum infection was defined as having a negative HIV-1 culture and/or DNA polymerase chain reaction assay at 7 days of age or younger and the first positive assay after 7 days of age. Results: Of 1709 first-born singleton children with defined HIV-1 infection status, 166 (9.7%) were found to be HIV-1 infected; transmission decreased from 18.1% in 1990-1992 to 1.6% in 1999-2000. Presumed in utero infection was observed in 34% of infected children, and presumed intrapartum infection, in 66%. Among infected children, the proportion with in utero infection increased over time from 27% in 1990-1992 to 80% (4 of 5) in 1999-2000 (P = 0.072). Maternal antenatal viral load and antiretroviral therapy were associated with risk of both in utero and intrapartum transmission. Controlling for maternal antenatal viral load and antiretroviral therapy, low birth weight was significantly associated with in utero transmission, while age, antenatal CD4(+) cell percentage, year, birth weight, and duration of membrane rupture were associated with intrapartum transmission. Conclusion: Although there have been significant declines in perinatal HIV-1 infection over time, there has been an increase in the proportion of infections transmitted in utero.

Address: Magder, LS; Univ Maryland; Dept Epidemiol & Prevent Med; Baltimore; MD 21201; USA. Lmagder@epi.umaryland.edu

Industrialized countries, MTCT, PMTCT / ARV

McCoy D, Chopra M, Loewenson R, Aitken JM, Ngulube T, Muula A, Ray S, Kureyi T, Ijumba P, Rowson M. **Expanding access to antiretroviral therapy in sub-Saharan Africa: Avoiding the pitfalls and dangers, capitalizing on the opportunities.** American Journal of Public Health 2005;95(1):18-22.

Abstr. We describe a number of pitfalls that may occur with the push to rapidly expand access to antiretroviral therapy in sub-Saharan Africa. These include undesirable opportunity costs, the fragmentation of health systems, worsening health care inequities, and poor and unsustainable treatment outcomes. On the other hand, AIDS "treatment activism" provides an opportunity to catalyze comprehensive health systems development and reduce health care inequities. However, these positive benefits will only happen if we explicitly set out to achieve them. We call for a greater commitment toward health activism that tackles the broader political and economic constraints to human and health systems development in Africa, as well as toward the resuscitation of inclusive and equitable public health systems.

Address: Ijumba, P; Hlth Syst Trust; POB 808; ZA-4000 Durban; South Africa. petrida@hst.org.za

HAART, LICs / Africa, Treatment programme

Mills E, Foster BC, van Heeswijk R, Phillips E, Wilson K, Leonard B, Kosuge K, Kanfer I. **Impact of African herbal medicines on antiretroviral metabolism.** AIDS 2005;19(1):95-97.

Abstr. We examined the effects of two African herbal medicines recommended for HIV/AIDS patients on antiretroviral metabolism. Extracts from Hypoxis and Sutherlandia showed significant effects on cytochrome P450 3A4 metabolism and activated the pregnane X receptor approximately twofold. P-glycoprotein expression was inhibited, with Hypoxis showing 42-51% and Sutherlandia showing 19-31% of activity compared with verapamil. Initiating policies to provide herbal medicines with antiretroviral agents may put patients at risk of treatment failure, viral resistance or drug toxicity.

Address: Mills, E; McMaster Univ; Dept Clin Epidemiol & Biostat; Hamilton; ON; Canada. millsej@mcmaster.ca.

Comprehensive care, HAART, LICs / Africa, Treatment impact and response,

Monpoux F, Tricoire J, Lalande M, Reliquet V, Bebin B, Thuret I. **Treatment interruption for virological failure or as sparing regimen in children with chronic HIV-1 infection.** AIDS 2004;18(18):2401-2409.

Abstr. Objective: To assess both benefits and risks related to treatment interruption (TI) in children with chronic HIV-1 materno-fetal infection. Design: A multicentre, retrospective analysis in five university hospital pediatric departments in France. Methods: Clinical events, plasma HIV-1 RNA, CD4 cell counts, CD4 percentages (CD4%) and genotypes were recorded in 24 patients before and during TI. Patients were classified as sparing regimen or virological failure groups according to the main reason for treatment interruption. Clinical events, immuno-virological evolution and genotype reversions were monitored. Results: After a median of 40 weeks of TI, none of the patients presented with an AIDS-defining event. For the whole cohort, median viral load variation from baseline, measured during TI was +1.26 log(10) copies/ml (range, -0.22, +4.3 log(10)) with large inter-individual variability, median absolute CD4 cell loss was 32.5% (range, -82, +17%). These variations were not different in the two patient groups. The mean number of mutations conferring resistance to nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors and protease inhibitors at baseline and last evaluation did not differ significantly. Few mutation reversions to wild type were noted in our cohort. Conclusions: Treatment interruption in children with chronic HIV-1 infection is associated with higher viral load increases than observed in adult patients. The CD4 cell loss is comparable. Although no clinical AIDS-defining event was noted close monitoring is required when TI is proposed to HIV-infected children. Very few reversion mutations were observed during treatment interruption. (C) 2004 Lippincott Williams Wilkins.

Address: Monpoux, F; Hop Larchet II; Serv Pediat; 151,Route St Antoine Ginestiere,BP 3079; F-06202 Nice; France. monpoux.f@chu-nice.fr

Children, HAART, Industrialized countries, Treatment impact and response, Viral resistance

Negredo E, Molto J, Burger D, Cote H, Miro O, Ribalta J, Martinez E, Puig J, Ruiz L, Salazar J, Lopez S, Montaner J, Rey Joly C, Clotet B. **Lopinavir/ritonavir plus nevirapine as a nucleoside-sparing approach in antiretroviral-experienced patients (NEKA study).** Journal of Acquired Immune Deficiency Syndromes 2005;38(1):47-52.

Abstr. Objectives: To compare the efficacy and safety of a nucleoside-sparing approach with a conventional highly active antiretroviral therapy (HAART) regimen in antiretroviral-experienced patients with prolonged viral suppression. Methods: Pilot study including 31 antiretroviral-experienced patients with HIV RNA <80 copies/mL. Subjects were randomly assigned to lopinavir/ritonavir (LPV/rtv) 400/100 mg BID plus nevirapine (NVP) 200 mg BID (NVP group, n = 16) or LPV/rtv plus the 2 previous NRTIs (NRTI group, n = 15). The primary endpoint was the percentage of subjects who maintained viral suppression at week 48. Changes in lipid metabolism, mitochondrial parameters, and LPV trough levels were also assessed. Results: All patients maintained viral suppression after 48 weeks. No subject discontinued therapy because of adverse events. HDL cholesterol increased by 28% at week 24 (P < 0.0001) and 10% after 48 weeks of follow-up (P = 0.319) in the NVP group. In the NRTI group, LDL cholesterol increased by 14% at week 48 (P = 0.076). Mitochondrial DNA/nuclear DNA ratio and mitochondrial respiratory chain complex IV activity showed a trend toward increasing in the NVP group. Mean (SD) LPV trough levels were 6340 (2129) ng/mL in the NRTI group and 5161 (2703) ng/mL in the NVP group (P = 0.140). Conclusions: in antiretroviral-experienced subjects with sustained viral suppression, dual therapy with NVP plus LPV/rtv at standard dosage was as potent and safe as standard-of-care HAART at 48 weeks of follow-up. This approach may reduce mitochondrial toxicity and improve LPV/rtv-associated lipid abnormalities. The results of this pilot study support the study of this approach in a larger, randomized trial.

Address: Negredo, E; Hosp Univ Germans Trias & Pujol; Dept Internal Med; Ctra Canyet S-N; Badalona 08916; Barcelona; Spain. enegredo@ns.hugtip.scs.es

Adults, HAART, Industrialized countries, Treatment complications, Treatment impact and response

Respass RA, Cachafeiro A, Withum D, Fiscus SA, Newman D, Branson B, Varnier OE, Lewis K, Dondero TJ. **Evaluation of an ultrasensitive p24 antigen assay as a potential alternative to human immunodeficiency virus type 1 RNA viral load assay in resource-limited settings.** *Journal of Clinical Microbiology* 2005;43(1):506-508.

Abstr. An inexpensive enzyme-linked immunosorbent assay method for human immunodeficiency virus type I quantitation, ultrasensitive p24 antigen assay (Up24), was compared with RNA viral load assay (VL). Up24 had 100% sensitivity of detection at a viral load of greater than or equal to 30,000, with sensitivity of 46.4% at a viral load of <30,000 (232 specimens from 65 seropositive subjects). The assay was highly reproducible, with excellent correlation between duplicates and among three laboratories.

Address: Respass, RA; Ctr Dis Control & Prevent; Global AIDS Program; 1600 Clifton Rd, Mail Stop A-12; Atlanta; GA 30333; USA. respass@cdc.gov

Industrialized countries, LICs, Treatment monitoring

Rosen S, Sanne I, Collier A, Simon JL. **Hard choices: rationing antiretroviral therapy for HIV/AIDS in Africa [Discussion].** *Lancet* 2005;365(9456):354-356.

Introduction: As the world intensifies its fight against the global AIDS epidemic, African countries have begun to develop large-scale prevention and treatment programmes. A combination of funds from African governments and international donors are paying for drugs, diagnostics, clinic and laboratory infrastructure, and medical personnel. Although these funds, which reach into the billions of dollars, will pay for antiretroviral therapy for many thousands of HIV-positive Africans, there is almost no chance that African countries will have the human, infrastructural, or financial resources to treat everyone who is in need, at least in the early years. The numbers of patients targeted for treatment are ambitious, but they are only a small fraction of those who are eligible for antiretroviral drugs on even the most conservative medical grounds. In Zambia, for example, the first-year target for treatment is 10000 patients; 100000 Zambians have already reached the clinical threshold of fewer than 200 CD4 cells per L, and thousands more become eligible each year. Ghana is targeting 12000 patients for therapy in the first 2 years; 58000 are believed to be medically eligible now. Kenya's target is 50% coverage, as is the global target of WHO's 3x5 initiative. Economists call any policy or practice that restricts consumption of goods a rationing system. As used by economists, rationing is value-neutral, ie, it does not imply intent to deprive people of a good resource, but rather describes the allocation of a scarce resource. In the marketplace, rationing is based on price. Non-market goods, such as free medical care, are rationed in other ways. Ambitious targets for treatment of HIV/AIDS still represent only a few of those in need; therefore, the rationing of treatment services is inevitable. Rationing of antiretroviral therapy for HIV/AIDS will be necessary as long as demand exceeds supply.

Address: Rosen, S; Boston Univ; Sch Publ Hlth; Boston; MA 02118; USA. sbrosen@bu.edu

HAART, LICs / Africa, Treatment programme

Simpore J, Ilboudo D, Samandoulougou A, Guardo P, Castronovo P, Musumeci S. **HCV and HIV co-infection in pregnant women attending St. Camille Medical Centre in Ouagadougou (Burkina faso).** *Journal of Medical Virology* 2005;75(2):209-212.

Abstr. Five hundred and forty-seven pregnant women with less than 32 weeks of amenorrhoea, attending an antenatal clinic of St. Camille Medical Centre (SCMC) of Ouagadougou were enrolled for a hepatitis C virus (HCV) and HIV co-infection study. Fifty-eight (10.6%) were HIV positive and 18 (3.3%) were anti-HCV positive. Only seven pregnant women (i.e., 1.3%) had a documented HIV and HCV co-infection. HCV-RNA was found in 5 out of 18 (27.8%) patients, who had anti-HCV antibodies. The genotype analysis of these five patients showed that two were of 1b whereas three were of 2a genotype. Mother-to-infant transmission of the same HCV genotype (2a) was documented in only one case. High 1b prevalence has been reported in other parts of Africa, while 2a is the prevalent genotype (60%) in Burkina Faso. This genotype has a higher response rate to treatment. Serum transaminases were normal, also in presence of HCV-RNA. The higher than expected rate of co-infection in Burkina Faso seems to demonstrate a correlation between these two infections, which could influence the evolution of HIV and HCV diseases. (C) 2004 Wiley-Liss, Inc.

Address: Musumeci, S; Univ Sassari; Dept Pharmacol Gynecol Obstet; Viale San Pietro 43B; I-07100 Sassari; Italy. smusumeci@tiscalinet.it

Adults / Women, HVC, LICs / Africa, MTCT

Whitworth JAG, Hewitt KA. **Effect of malaria on HIV-1 progression and transmission [Discussion]**. *Lancet* 2004;365(9455):196-197.

Introduction: When two elephants collide beware, for the ground will shake. So it is with HIV-1 and malaria. Both infections are of such great public-health importance in tropical countries, particularly in sub-Saharan Africa, that any potential interaction should make us worry. In today's *Lancet*, James Kublin and colleagues report from a study in Malawi that acute malaria episodes are associated with transient increases of HIV-1 viral load in the blood, and they speculate that malaria episodes might accelerate HIV-1 disease progression and facilitate transmission. Evidence is now emerging of the deleterious effects of HIV-1 infection on malaria. In pregnant women HIV-1 is associated with more peripheral and placental malaria, higher parasite densities, more fever, and increased risks of adverse birth outcomes. Semi-immune non-pregnant adults infected by HIV-1 have higher rates of malaria infection and clinical disease, while adults without malaria immunity have higher rates of severe malaria and death. Less is known about the effects of malaria on HIV-1. Kublin and colleagues build on previous work from Malawi, which reported seven-fold higher HIV-1 viral loads in adults with acute malaria compared with those without, and that this increase resolved over a few weeks after antimalarial treatment.[4] By including a visit before the malaria episode as a reference, Kublin's study allows us to confidently blame the increase in viral load on the acute malaria episode.

Address: Whitworth, JAG; Univ London London Sch Hyg & Trop Med; Infect Dis Epidemiol Unit; Keppel St; London WC1E 7HT; England. j.whitworth@wellcome.ac.uk

Adults, Infections (Others), LICs / Africa, Natural history