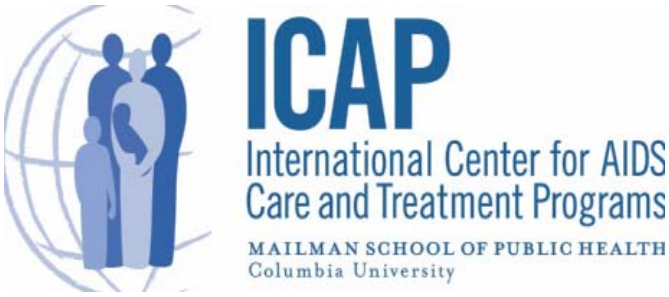

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Back Issues on Line

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

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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

Adams LV, Palumbo P. **The time to treat the children is now** [editorial commentary]. Journal of Infectious Diseases 2007;195(10):1396-1398. (**See the article by George et al.**)
Address: Palumbo, P; Dartmouth Hitchcock Med Ctr; Sect Infect Dis & Int Hlth; 1 Med Ctr Dr; Lebanon; NH 03756; USA. Paul.E.Palumbo@Dartmouth.edu

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George E, Noel F, Bois G, Cassagnol R, Estavien L, Rouzier PD, Verdier RI, Johnson WD, Pape JW, Fitzgerald DW, Wright PF. **Antiretroviral therapy for HIV-1-infected children in Haiti**. Journal of Infectious Diseases 2007;195(10):1411-1418. (**See the editorial commentary by Adams et al.**)

Abstr. Background. Data are limited about the effectiveness of pediatric antiretroviral therapy (ART) in low-income countries. Methods. We report the outcomes of consecutively treating 236 human immunodeficiency virus type 1 (HIV-1)-infected treatment-naive children with triple ART in Port-au-Prince, Haiti, between 1 May 2003 and 30 April 2006. Results. Kaplan-Meier survival analysis at follow-up demonstrated that 191 children (81%) remained in care, 21 (9%) were dead, and 24 (10%) were lost to follow-up. Independent baseline predictors of mortality were age <18 months, CD4(+) T cell percentage <= 5%, and weight-for-age Z score (WAZ) less than -3. Twelve months into ART, 56% of tested subjects had undetectable HIV-1 RNA loads. Median CD4(+) T cell percentages at 12 months increased by 15%, 11%, and 5% in children with baseline percentages of <= 5%, 6%-24%, and >= 25%, respectively (P<.01). The median WAZ at 12 months increased by 1.0, 0.6, and 0.2 in children with baseline WAZ less than -2, -2 to 1.1, and -1 or more, respectively (P<0.1). Conclusion. With continuous donor support, trained providers, and the availability of pediatric antiretroviral drug formulations, it proved feasible to deliver pediatric ART in Haiti. The effectiveness of this program should encourage efforts to make ART available for HIV-infected children in poor countries.

Address: George, E; Cornell Univ; Weill Med Coll; 1300 York Ave; New York; NY 10021; USA. erikgeorge@yepmail.net

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Bland RM, Rollins NC, Coovadia HM, Coutsoudis A, Newell ML. **Infant feeding counselling for HIV-infected and uninfected women: appropriateness of choice and practice**. Bulletin of the World Health Organization 2007;85(4):289-296.
Abstr. Objective To examine infant feeding intentions of HIV-infected and uninfected women and the appropriateness of their choices according to their home resources; and to determine their adherence to their intentions in the first postnatal week. Methods Feeding intentions of pregnant women were compared against four resources that facilitate replacement feeding: clean water, adequate fuel, access to a refrigerator and regular maternal income. First-week feeding practices were documented. Findings The antenatal feeding intentions of 1253 HIV-infected women were: exclusive breastfeeding 73%; replacement feeding 9%; undecided 18%. Three percent had access to all four resources, of whom 23% chose replacement feeding. Of those choosing replacement feeding, 8% had access to all four resources. A clean water supply and regular maternal income were independently associated with intention to replacement feed (adjusted odds ratio (AOR) 1,94, 95% confidence interval (0) 1.2-3.2; AOR 2.1, 95% CI: 1.2-3.5, respectively). Significantly more HIV-infected women intending to exclusively breastfeed, rather than replacement feed, adhered to their intention in week one (exclusive breastfeeding 78%; replacement feeding 42%; P < 0.001). Of 1238 HIV-uninfected women, 82% intended to exclusively breastfeed; 2% to replacement feed; and 16%

were undecided. Seventy-five percent who intended to exclusively breastfeed adhered to this intention postnatally, and only 11 infants (< 1%) received no breast milk. The number of antenatal home visits significantly influenced adherence to feeding intention. Conclusion Most HIV-infected women did not have the resources for safe replacement feeding, instead choosing appropriately to exclusively breastfeed. Adherence to feeding intention among HIV-infected women was higher in those who chose to exclusively breastfeed than to replacement feed. With appropriate counselling and support, spillover of suboptimal feeding practices to HIV-negative women is minimal.
Address: Bland, RM; Univ KwaZulu Natal; Africa Ctr Hlth & Populat Sci; ZA-3935 Kwa Zulu; South Africa. rbland@africacentre.ac.za

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Global HIV PreventIon Working Group. **Bringing HIV Prevention to Scale: an Urgent Global Priority** ; 2007.

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Myer L, Morroni C, Rebe K. **Prevalence and determinants of fertility intentions of HIV-infected women and men receiving antiretroviral therapy in South Africa**. AIDS Patient Care and STDs 2007;21(4):278-285.
Abstr. Despite the increased emphasis on antiretroviral therapy (ART) and other health care services for HIV-infected individuals in sub-Saharan Africa, issues of fertility and childbearing have received relatively little attention. In particular, little is known about the prevalence and determinants of fertility intentions among HIV-infected women and men who are receiving ART. We conducted a cross-sectional study from August to November 2005 investigating these issues among patients attending a public sector ART service who had been receiving ART for at least one month. Overall, 311 individuals were interviewed (median age, 33 years) and 29% (n = 89) stated that they wanted to have children in the future. This proportion was slightly higher among males than females (36% versus 26%, p = 0.09). In a multivariate model predicting fertility desire among all participants, fertility desire was associated with male gender (odds ratio (OR): 2.58; 95% confidence interval [CI]: 1.29-5.08), younger age (OR: 0.92; 95% CI: 0.87-0.97), decreased number of children (OR: 0.32; 95% CI: 0.15-0.69), and being in a relationship of less than 5 years (OR: 3.93; 95% CI: 1.91-8.08). In addition, fertility desire was associated with increasing duration of ART among female participants, but not among males. These results suggest that a substantial proportion of HIV-infected women and men receiving ART in this setting would like to have children in the future. This highlights the importance of incorporating fertility-related counseling, as well as contraception and advice regarding safe conception and childbirth, as appropriate, into HIV treatment services. These findings also suggest that fertility desires may change through time and thus require ongoing attention as part of long-term care.
Address: Myer, L; Univ Cape Town; Infect Dis Epidemiol Unit; ZA-7700 Rondebosch; South Africa. landon.myer@uct.ac.za

Nachega JB, Hislop M, Dowdy DW, Chaisson RE, Regensberg L, Maartens G. **Adherence to nonnucleoside reverse transcriptase inhibitor-based HIV therapy and virologic outcomes**. Annals of Internal Medicine 2007;146(8):564-NIL_16.
Abstr. Background: Adherence of 95% or more to unboosted protease regimens is required for optimal virologic suppression in HIV-1 infected patients. Whether the same is true for nonnucleoside reverse transcriptase inhibitor (NNRTI)-based therapy is unclear. Objective: To assess the relationship between adherence to NNRTI-based therapy and viral load in treatment-naive patients. Design: Observational cohort study. Setting:

Private-sector HIV and AIDS disease management program in South Africa. Patients: 2821 adults infected with HIV who began NNRTI-based therapy between January 1998 and March 2003 (2764 patients [98%] were enrolled after December 2000). Measurements: Adherence was assessed by monthly pharmacy claims. The primary end point was sustained viral load suppression (< 400 copies/mL) in 100% of recorded viral load measurements throughout follow-up. Secondary end points included time to initial viral load suppression and time to subsequent virologic failure (< 400 copies/mL). Results: The median follow-up period was 2.2 years (interquartile range, 1.7 to 2.7 years). The proportion of patients with sustained viral load suppression ranged from 13% (41 of 325 patients) in patients who filled less than 50% of antiretroviral drug prescriptions to 73% (725 of 997 patients) in those who filled 100% of antiretroviral drug prescriptions. Each 10% increase in pharmacy claim adherence greater than 50% was associated with a mean absolute increase of 0.10 in the proportion of patients with sustained virologic suppression (P < 0.001). Predictors for shorter time to virologic failure after initial suppression in multivariable Cox regression included CD4(+) T-cell counts of 0.50 x 10(9) cells/L or less (hazard ratio, 1.60 [95% CI, 1.22 to 2.10] vs. CD4(+) T-cell counts > 0.20 x 10(9) cells/L), baseline viral load greater than 10(5) copies/mL (hazard ratio, 1.39 [CI 1.14 to 1.70]), nevirapine-based regimen (hazard ratio, 1.43 [CI 1.16 to 1.75]), and low pharmacy claim adherence (hazard ratio, 1.58 [CI 1.48 to 1.69], per 10% decrease in adherence to 50%). Limitations: Observational study with adherence stratification at study end and lack of standardized timing for outcome measurement. Conclusion: Virologic outcomes improve in a linear dose-response manner as adherence to NNRTI-based regimens increases beyond 50%.

Address: Nachega, JB; Johns Hopkins Bloomberg Sch Publ Hlth; Dept Int Hlth; 615 N Wolfe St,Suite W5031; Baltimore; MD 21205; USA. jnachega@jhsph.edu

Reithinger R, Megazzini K, Durako SJ, Harris DR, Vermund SH. **Monitoring and evaluation of programmes to prevent mother to child transmission of HIV in Africa**. British Medical Journal 2007;334(7604):1143-1146.

Abstr. NA

Address: Reithinger, R; WESTAT Corp; Clin Trials Area; Rockville; MD 20850; USA. rreithinger@yahoo.co.uk

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Schechter M, Nunes EP. **Monotherapy with lopinavir/ritonavir**. Expert Opinion on Investigational Drugs 2007;16(5):735-741.

Abstr. Despite the unprecedented pace of development of drugs for the treatment of a viral disease and the unquestionable efficacy of antiretroviral therapy, there is a need for less toxic and cheaper regimens that could simplify the treatment of HIV infection without sacrificing efficacy. The favorable pharmacokinetic profile and the high genetic barrier of boosted protease inhibitors make them ideal candidates for use as monotherapy. Given the encouraging results of available studies on lopinavir/ritonavir monotherapy in patients with no prior failure with protease inhibitors, it may be warranted to conduct trials to investigate the cost-effectiveness of lopinavir/ritonavir monotherapy as second-line therapy in resource-constrained settings where virologic monitoring is not feasible. In addition, larger trials with longer follow up, with particular attention to the potential consequences of viral replication in sites where the penetration of protease inhibitors may be poor, are needed before this strategy can be considered for routine use.

Address: Schechter, M; Univ Fed Rio de Janeiro; Projeto Praca Onze; BR-21941 Rio De Janeiro; Brazil. maurosch@hucff.ufrj.br

Walker AS, Mulenga V, Ford D, Kabamba D, Sinyinza F, Kankasa C, Chintu C, Gibb DM. **The impact of daily cotrimoxazole prophylaxis and antiretroviral therapy on mortality and hospital admissions in HIV-infected Zambian children**. Clinical Infectious Diseases 2007;44(10):1361-1367.

Abstr. Background. Data on the population effectiveness of cotrimoxazole prophylaxis and antiretroviral therapy (ART) in human immunodeficiency virus (HIV)-infected African children are few Methods. A total of 534 Zambian children with HIV infection were randomized to receive daily cotrimoxazole prophylaxis or placebo in the Children with HIV Antibiotic Prophylaxis trial. Following trial closure, children who received the placebo initiated cotrimoxazole prophylaxis, and all children were observed in a closed cohort. Mortality and hospital admission rates were compared, over calendar time, in 9-month periods: trial recruitment (March 2001 to April 2002, May 2002 to January 2003), trial follow-up to closure (February 2003 to October 2003), initial follow-up posttrial (November 2003 to July 2004), and early and later ART availability (August 2004 to April 2005, and May 2005 to May 2006, respectively). Results. A total of 546 child-years of follow-up, 40 deaths, and 80 hospital admissions were observed between the time of trial closure and June 2006. A total of 117 of 283 children who were alive at trial closure received ART in the posttrial period (median child age at first use of ART, 8.8 years). Rates decreased in both groups during the trial period, suggesting a survivorship effect. Mortality and hospital admission rates before trial closure were 14 (95% confidence interval [CI], 9-21) deaths per 100 child-years and 24 (95% CI, 15-39) hospital admissions per 100 child-years, respectively, for children who were receiving cotrimoxazole, and were 23 (95% CI, 16-34) deaths per 100 child-years and 35 (95% CI, 23-53) hospital admissions per 100 child-years, respectively, for children who were receiving the placebo. After trial closure, rates remained stable in the cotrimoxazole group, but decreased to 15 (95% CI, 8-26) deaths per 100 child-years and 19 (95% CI, 10-41) hospital admissions per 100 child-years, respectively, for the group of children who received placebo and then initiated cotrimoxazole prophylaxis. In both groups combined, mortality rates decreased to 6 (95% CI, 3-11) deaths per 100 child-years and then 2 (95% CI,0.8-6) deaths per 100 child-years during periods of ART availability; hospital admission rates decreased to 17 (95% CI, 11-27) hospital admissions per 100 child-years and 8 (95% CI, 4-15) hospital admissions per 100 child-years, respectively. Conclusion. The benefits of once- daily cotrimoxazole prophylaxis continued throughout the trial and after trial closure. Mortality and hospital admissions decreased (by > 6-fold and similar to 3-fold, respectively) following ART availability, similar to findings observed in resource- rich countries.

Notes: A major article was published in the 15th of May 2007 edition of Clinical Infectious Diseases investigating the benefits of cotrimozaxole prophylaxis among HIV infected African children. Cotrimozaxole has been shown to substantially reduce deaths non related to pneumocystis carinii pneumonia and is currently recommended for primary prophylaxis in all infants born to HIV infected mothers in industrialized and resource poor settings, starting at 6 weeks of age and continuing until the HIV negative status has been confirmed. Its use is also recommended among HIV-infected children with CD4 count lower than 15% of the total lymphocyte count.

The CHAP1 trial in Zambia was the first randomized placebo-controlled trial assessing the efficacy of cotrimoxazole in children (median age at recruitment, 4.4 years) living in areas with high levels of bacterial resistance to this antibiotic. In 2004, this trial showed a 43% reduction in mortality and a 23% reduction in hospital admissions across all ages and levels of CD4 cell percentage, as well as a 2-year cumulative probability of dying in hospital from a serious bacterial infection (predominantly pneumonia) of 7% in the cotrimoxazole group and 12% in the placebo group (P=0.08). Then Walker et al2 analysed the determinants of survival, and described how malnutrition and hospitalizations for respiratory/bacterial infections predict mortality independently of immunosuppression, suggesting that these determinants capture HIV- and non-HIV related mortality, whereas oral candidiasis was a proxy for immunosuppression.

In this recent paper, Walker et al studied mortality and hospital admission rates during 3 periods over calendar time from March 2001 to June 2006: during the CHAP trial (comparing placebo versus cotrimozaxole prophylaxis), as well as after trial closure when all children received cotrimozaxole in a closed cohort and lastly during early and late antiretroviral therapy (ART) availability. This analysis allowed to address a major bias (e.g. confounding by indication) when directly comparing children who are initiating ART or cotrimozaxole prophylaxis with those who are not.

These results are interesting as data collected during these periods have provided original data on the natural history of HIV infection in older children and allowed comparison of various periods encompassing eras of absence of treatment, daily cotrimozaxole prophylaxis, and receipt of ART. After the trial, mortality rates decreased in the placebo group when children initiated cotrimozaxole prophylaxis until it matched rates observed in the group of children originally randomized to antibiotic prophylaxis during the trial. During the period of ART availability, mortality and hospital admission rates decreased even further by 6 and 3 fold respectively; this impact of ART being similar to what was observed in resource rich countries. This reduction in hospital admissions, as the authors point out, may result in important cost implications in the context of overburdened pediatric wards throughout sub-Saharan Africa and further cost effectiveness data are being analyzed.

The added impact of cotrimozaxole in those children on ART requires further investigation even though these data3 might suggest that there may be a role for continuing the relatively inexpensive cotrimoxazole prophylaxis alongside antiretroviral therapy, as it is currently recommended for children under 5 years of age in the WHO guidelines. The authors call for the urgent need of placebo-controlled randomized trials in order to answer the important question on when antibiotic prophylaxis could be stopped in children on ART.

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Address: Walker, AS; MRC; Clin Trials Unit; 222 Euston Rd; London NW1 2DA; England. asw@ctu.mrc.ac.uk

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