Pediatric HIV: Successes and Challenges

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Combination antiretroviral (ARV) therapy dramatically improves survival among children born with HIV infection in resource-poor areas, according to encouraging data presented by Thailand- and Cambodia-based researchers at the Fifth International AIDS Society (IAS) Conference on HIV Pathogenesis, Treatment and Prevention on Monday, July 20, in Cape Town. Troubling, however, was a South African study reporting significant delays in switching children to second-line ARV regimens after virologic failure on an initial drug combination.

Without ARV treatment, half of all children infected with HIV at birth die from AIDS before their second birthday. UNAIDS estimates that 370,000 children younger than 15 became infected in 2007 alone. Yet only 200,000 children across the world are receiving ARV therapy.

A study published in *The New England Journal of Medicine* in 2008 concluded that early HIV diagnosis and early ARV treatment lower infant mortality by 76 percent and the rate of progression to AIDS by 75 percent. Yet long-term outcomes of ARV therapy in children residing in resource-poor countries have not been well documented.

Two recent analyses were reported at IAS in Cape Town. The first study involved nearly 3,500 HIV-positive children in Thailand beginning ARV treatment for the first time between 2000 and 2005; it was presented by Michelle McConnell, MD, of the U.S. Centers Disease Conrol in concert with the Thai Ministry of Public Health. The second study focused on 670 HIV-positive Cambodian children who began ARV therapy between 2003 and 2007; it was presented by Petros Isaakidis, MD, PhD, of Médecins Sans Frontieres (Doctors Without Borders) in Phnom Penh.

McConnell's Thai team calculated a 93 percent survival rate after one year of treatment and 88 percent survival after five years. Of 305 (9 percent) of children who died, 274 (90 percent) died of AIDS and most died in the first months of treatment because of advanced HIV disease. Higher pretreatment weight for age, higher CD4 percentage and less advanced clinical stage significantly bettered the odds of survival.

In the Cambodian study, Isaakidis reported survival rates of 95 percent after the first year of ARV treatment, 93 percent after two years and 91 percent after three years. CD4 counts among older children increased, on average, by 304 cells during the first six months, 704 cells after two years and 737 cells after three years. Among children younger than 5—typically monitored using the

CD4 percentage as opposed to the absolute CD4 cell count—gains averaged 10 percent during the first six months, 15.2 percent after two years and 15 percent after three years.

Two hundred-seventy Cambodian children included in the analysis also received viral load monitoring. After three years, an encouraging 93.5 percent had undetectable HIV levels. Twenty-two children had viral loads in excess of 1,000 copies after three years of treatment, but only two met the World Health Organization's criteria for immunologic failure.

More sobering news was reported by Mary-Ann Davies, MBChB, of the University of Cape Town. A 16-month study conducted by Davies and her colleagues, involving 5,484 children starting ARV therapy in South Africa, found that only 146 of 310 (47 percent) whose treatment failed got switched to a new ARV combination. Among those who were switched, the average time between treatment failure and the start of a new regimen was 4.8 months.

Delays in switching after virologic failure can greatly jeopardize long-term survival benefits because it significantly increases the risk of drug resistance to available HIV medications. But such delays can be expected in poor clinics because most do not have viral load tests to detect failure and because drugs for second-line regimens can be scarce. The good news reported by Davies: a 97 percent survival rate one year after switching, and an 89 percent retention-in-care rate.
