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**Combination anti-retroviral therapies associated with reduced infections in HIV-infected children**

Since the introduction of highly active antiretroviral therapies, there has been a substantial reduction of opportunistic infections and other infections in HIV-infected children, such as pneumonia and tuberculosis, according to a study in the July 19 issue of JAMA.

The human immunodeficiency virus (HIV) epidemic has spurred the development of new antiretroviral, immune, and vaccine-based therapies geared to block transmission, prevent disease progression, and prolong the survival of individuals who are HIV positive, according to background information in the article. Highly active antiretroviral therapy (HAART) has dramatically decreased rates of AIDS-related opportunistic infections (infections caused by an organism capable of causing disease in a host whose resistance is lowered, e.g., by other diseases or by drugs) and deaths in adults. Although HAART has dramatically decreased illness and death in HIV-infected infants, children, and adolescents in the United States, no studies comparing the incidence of opportunistic and other related infections before and during the HAART era have been conducted.

Philimon Gona, Ph.D., of the Harvard School of Public Health and Boston University, Boston, and colleagues estimated the rates for the first occurrence of 29 targeted opportunistic and other related infections between Jan. 1, 2001, and Dec. 31, 2004, in HIV-infected infants, children, and adolescents to compare the rates in the HAART era to those of the pre-HAART era. The study included 2,767 children enrolled between Sept. 15, 2000, and Dec. 31, 2004, with information entered in the database up to August 1, 2005, when data analysis was conducted. The pre-HAART era comparison population included 3,331 children enrolled in 13 Pediatric AIDS Clinical Trials Group (PACTG) protocols from October 1988 to August 1998.

Seventy-five percent of the children were enrolled in 2000 and 2001. Overall, 553 first episodes of a specific infection occurred among 395 (14 percent) of the study participants. The incidence rates (IRs) per 100 person-years for the 4 most common first-time infections were bacterial pneumonia (IR, 2.15), herpes zoster (IR, 1.11), dermatophyte infections (IR, 0.88), and oral candidiasis (IR, 0.93). Infection rates were significantly lower than those reported in the PACTG in the pre-HAART era: bacterial pneumonia (IR, 11.1), bacteremia (IR, 3.3), herpes zoster (IR, 2.9), oral candidiasis (IR, 1.2) and tuberculosis (IR, 0.2).

"Despite these current advances due to HAART, some HIV-infected children continue to develop opportunistic infections. Some children fail to respond to antiretroviral therapy as a result of viral resistance, poor adherence, or inability to tolerate complex treatment regimens. Furthermore, prophylactic [preventive] therapies are not fully effective and poor adherence can further reduce their efficacy. Drug interactions, complex dosing schedules, adverse effects, and high costs can further limit the efficacy of these therapies. Although these issues do present challenges, our findings demonstrate a substantial reduction in the incidence of several opportunistic infections in HIV-infected children since the introduction of HAART therapy," the authors write. (JAMA. 2006;296:292-300. Available pre-embargo to the media at <http://www.jamamedia.org/>)

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Editor's Note: For funding/support information, please see the JAMA article.

Editorial: Antiretroviral Therapy for Children - Substantial Benefit But Limited Access

In an accompanying editorial, Joseph I. Harwell, M.D., of Brown Medical School, Providence, R.I., and Stephen K. Obaro, M.D., of Children's Hospital of Pittsburgh, discuss the findings of the study by Gona and colleagues.

"Although significant advances have been made in the improvement of the quality of life for patients with HIV/AIDS, several important challenges remain. A cure for HIV infection remains elusive and following infection, chronic suppression of viral replication with preservation of immune function remains the goal. If in the best case scenario, a combination of HAART and specific opportunistic infection prophylaxis continues to prolong survival, patients must contend with the adverse effects of

long-term treatment with these agents, most of which are new and have unknown long-term effects, particularly when administered to young children."

"In the past 5 years, the debate has begun to shift from whether these treatments can be provided in developing countries to how these treatments can be provided. Through [various] programs · the issues of 'how' to provide treatment are gradually being addressed, but these efforts need to be increased substantially. For 2.3 million children living with HIV infection worldwide, the question is not whether or how but when they will receive (and, like their counterparts in the study by Gona et al, benefit from) the therapy that will allow them to reach adulthood. (JAMA. 2006;296:330-331. Available pre-embargo to the media at <http://www.jamamedia.org>)

Editor's Note: Dr. Harwell reports that he is a consultant to the Clinton Foundation Pediatric HIV/AIDS Initiative. Dr. Obaro reports no financial disclosures.

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