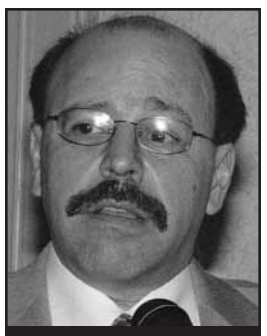

BY STEPHEN I. PELTON, M.D.

ID CONSULT

Pediatric HIV Still a Problem

We've made great strides in combating pediatric HIV/AIDS in the last few years, but children living with HIV still face enormous difficulties.

Indeed, the number of new cases of vertical transmission has dropped to an all-time low, from about 1,000 in the early 1990's to less than 50 in 2003. The obstetric community is now doing a far better job of identifying women with HIV; delivering medical care to them; and, thereby, reducing the rate of vertical transmission to just 1%-2%, from 25%-30% in the 1990's.

Unfortunately, this great success in reducing vertical transmission and the effectiveness of highly active antiretroviral treatment (HAART) in maintaining immune function in HIV-infected children has created a public perception that pediatric HIV/AIDS is no longer an issue.

In fact, there are approximately 5,000 children currently living with HIV/AIDS in the United States, with 250 of them here in Massachusetts. These children have substantial, ongoing problems that place them at increasing risk as they get older. Ongoing services will be required to meet their needs, as will innovative research to ensure that our current approach is safe and effective over a prolonged time period.

Yet, as a result of a shift in public focus to HIV in Africa, there has been a dramatic decrease in both federal and private funds for HIV here in the United States. In Massachusetts, for example, money for HIV programs has declined about 40% in the last 5 years, from about $50 million to about $30 million, without any decline in the number of patients needing services.

Although the numbers of vertically infected newborns have dropped dramatically in the United States, a small number of cases still occur when a woman is tested early in pregnancy and is found to be uninfected, but then acquires the infection later during pregnancy, prior to delivery. We've had a couple of cases in the last year or 2, in which the infant has presented with advanced HIV in the first 6 months of life.

Moreover, increasing numbers of HIV-infected pregnant women and children are coming to the United States from other countries. We currently have two new patients—one is an HIV-infected child from Haiti who was adopted by a New Hampshire couple, the other the child of a mother who had recently come from Cape Verde.

But by far, the greatest number of new cases of pediatric HIV in the United States is now among adolescents who acquire the infection through risky behavior. We see a newly infected adolescent every few months.

The greatest number of new cases of pediatric HIV in the United States is now among adolescents who acquire the infection through risky behavior.

Once adolescents become infected with HIV, it can be a challenge to engage them, to convince them that they must take their medications regularly even though they're feeling fine, and to be responsible with regard to their sexual behavior. We've had several of our teenage HIV-infected girls become pregnant, and some of our boys have fathered babies.

Regardless of how children acquire HIV, they face significant health challenges despite the dramatic increase in lifespan that has come with the success of HAART.

Resistance is a major problem. About 50% of all HIV-infected children have some degree of resistance to at least one of the currently licensed antiretroviral agents, while about 10%-15% are completely out of treatment options. The latter scenario, which arises after long-term treatment with multiple agents from multiple classes, will likely only get worse with time.

Unfortunately, there have been no major breakthroughs in terms of new drug classes introduced for the treatment of pediatric HIV in the last 3-4 years. The problem is particularly bad for younger children who can't take large capsules and are relegated to taking liquids or suspensions. The best of these are poor tasting, and the worst ones are foul tasting. Many children simply refuse to take them and end up with inadequate dosing, which increases their risk for developing resistance.

Among the 10%-15% of children whose viruses have mutated to the point that they are 100-fold less susceptible than are wild-type viruses, the only options are to try using five or six different medications, often in combination with a relatively new agent called T20. But T20 can only be given by injection, which is a problem in children. We have one patient on the drug, a very slender boy who now has exquisitely sensitive nodules all over his arms.

The metabolic and cardiovascular changes we're seeing in adults on long-term HAART therapy are also a major cause for concern among children. Although we haven't seen coronary artery disease yet in children, some do have quite high cholesterol and triglyceride levels. I have one child right now with a cholesterol level of more than 700 mg/dL, with visible deposits in his elbows and knees.

My expectation is that our adult medicine colleagues are the ones who will see serious heart disease in these patients, probably in their 20s or 30s, just as the adults are now getting coronary artery disease in their 30s, 40s, and 50s. Currently there is disagreement about how aggressively to treat cardiovascular risk factors in these children. Some argue that these kids have HIV and we should simply leave them alone. My attitude is that because these children have HIV and may live into their 50s, 60s, or 70s, we can't afford to leave them alone.

Body changes—typically increased weight and fat deposition in the trunk—are also a major problem, especially for the teenagers. Girls often have enlarged breasts, big abdomens, a "buffalo hump," and very large shoulders. Boys tend to develop barrel chests and gynecomastia. As you can imagine, these changes are quite disturbing to teenagers, and may lead them to stop taking their medications. While this syndrome, lipodystrophy, is being extensively studied in adults, little progress has been made in understanding its pathogenesis in children and adolescents.

Disclosure may be yet another problem for many HIV-infected teenagers. We've had several young adolescent patients who don't know their diagnosis. The parents often think they're protecting their kids by not telling them, but we believe that the more the children know, the more likely they are to take an active part in their own care as they mature. We begin discussing disclosure with families when their child reaches 8-10 years of age, depending on individual maturity and intellectual capacity.

A fourth cause for concern—and possibly the greatest—comes from a recent study published by the Pediatric AIDS Clinical Trials Group, in which I participate. We found that neuropsychological function was significantly poorer among HIV-infected children, and was worse with higher viral loads. Moreover, only one measure of neuropsychological functioning improved after effective viral suppression with combination protease inhibitor therapy, and that improvement was relatively minor (Pediatrics 2005;115:380-7).

While it had been previously recognized that HIV-infected children have cognitive and behavioral difficulties, this is the first time it has been looked at with regard to response to HAART therapy. Although the correlation with viral load suggests the problem is disease related, we have not yet determined the relative contributions of disease, treatment, and the often adverse socioeconomic environments these children live in.

We must continue to search for better and safer approaches to preventing vertical transmission. Currently, we give antiretrovirals as early as the second trimester, continue them through labor and delivery, and in the newborn for up to 6 weeks. With all the new drugs that are being introduced, we must be certain that the therapies we're delivering are safe. Now that 98%-99% of these children won't have HIV, we have to make sure they don't have toxicity from the medications, either.

We need to find safer regimens without losing what we've accomplished in preventing vertical transmission, which is in my mind the biggest accomplishment in the prevention of HIV to date. ■

DR. PELTON is chief of pediatric infectious disease at Boston Medical Center and coordinator for the Maternal-Child HIV Program at the center.

Single-Dose Azithromycin OK for Acute Otitis Media

BY MARK S. LESNEY
Associate Editor

Treatment of uncomplicated acute otitis media with single-dose azithromycin proved comparable in efficacy to the standard high-dose amoxicillin in an international trial of young children.

Azithromycin treatment for acute otitis media (AOM) also showed fewer adverse events and greater patient compliance in the randomized, double-blind, double-dummy trial, reported Adriano Arguedas, M.D., of the Instituto de Atención Pediátrica, San José, Costa Rica, and colleagues.

In a trial conducted at centers in Chile, Costa Rica, Finland, and the United States, 312 children 6-30 months of age with AOM were divided into two study populations (Pediatr. Infect. Dis. J. 2005;24:153-61).

The 158 patients in the azithromycin group received a single dose of the drug (30 mg/kg) plus 10 days of an amoxicillin placebo at 90 mg/kg per day, in two divided doses. The 154 patients in the amoxicillin group received an azithromycin placebo and 10 days of authentic amoxicillin. Clinical success was reported as cure or improvement at end of therapy and maintenance of cure at end of study. It was not significantly different between the treatments. Rates at end of therapy were 84% for each antibiotic for all patients and 82% for each antibiotic for children 2 years of age or younger. Rates at end of study for all patients were 77% for azithromycin and 78% for amoxicillin and 75% for both antibiotics for children aged 2 years and younger.

The rates of treatment-related adverse events for azithromycin and amoxicillin were 20% and 29%, respectively. Although adverse events rates were not significantly different overall, significant differences were seen in the incidence of diarrhea, which was greater with amoxicillin than with azithromycin (17.5% vs. 8.2%).

Compliance, defined as completion of at least 80% of the prescribed study medication, was significantly greater in the azithromycin group (100% vs. 90%).

The authors concluded single-dose azithromycin was noninferior to standard high-dose amoxicillin. The study was supported by a grant from Pfizer Inc., which makes azithromycin (Zithromax). ■