



Breaking down barriers

At least 2.3 million children were living with perinatally acquired HIV infection at the end of 2005, most of them in sub-Saharan Africa. A new AAP policy statement, endorsed by organizations worldwide, offers solutions to providing antiretroviral access to children globally.

by **Sheryl Cash** • Correspondent

More readily available HIV tests and antiretrovirals (ARVs) in appropriate pediatric formulations are urgently needed to improve therapy for children with human immunodeficiency virus (HIV), especially in less-developed areas of the world, according to a new AAP policy statement.

Increasing Antiretroviral Drug Access for Children with HIV Infection (Pediatrics.2007;119:838-845) outlines solutions for overcoming barriers that prevent the quick diagnosis and treatment of young children with HIV. The statement was endorsed by an unprecedented 19 other international child and health care organizations, including the World Health Organization (WHO). (See sidebar.)

“The policy statement gives drug companies insight into what pediatricians think are appropriate approaches to making antiretrovirals available to children,” said Peter L. Havens, M.D., FAAP, chair of the AAP Committee on Pediatric AIDS (COPA) and lead author of the policy statement from COPA and the AAP Section on International Child Health.

Geographic disparities

An estimated 540,000 children under age 15 were infected with HIV in 2006, mostly through mother-to-child transmission during pregnancy, delivery or breastfeeding. Effective HIV prevention services, including prenatal testing, perinatal ARV prophylaxis and safe alternatives to breastfeeding, are offered to fewer than 10% of pregnant women worldwide. As a result, approximately 2.3 million children were living with HIV at the end of

2005, including 2 million children in sub-Saharan Africa.

Medical advances during the past decade ensure that children living in the United States and other resource-rich countries are quickly diagnosed with HIV and treated with highly potent antiretroviral therapy (ART), giving them a 90% or greater chance of survival into adulthood. In contrast, about 53% of HIV-infected children in Africa die before age 2



“We hope that early adoption of these principles by American drug companies will mean that antiretrovirals in formulations more appropriate for children will be available for use in children throughout the world.”

— Peter L. Havens, M.D., FAAP,
chair of the AAP Committee on Pediatric AIDS

because testing and treatment are not readily available.

“This means two things. We need to diagnose these kids to get them treatment, and we need to treat them at an earlier age,” said Lynne Mofenson, M.D., FAAP, liaison from the National Institute of Child Health and Human Development to COPA, and a contributor to the new policy statement.



Dr. Mofenson

The barriers to optimal care of very young children with HIV, according to the statement, are a lack of RNA or DNA nucleic acid tests, expensive and complex procedures required to definitively diagnosis children under age 18 months with HIV; few pediatric-trained medical staff in remote areas; and

an absence of affordable, solid, easy-to-transport ARVs in appropriate child dosage.

“One of the largest barriers to treatment is that only half of the available drugs have pediatric formulations for use,” said Dr. Mofenson.

“You need solid formulations that you can crush and/or split in half,” said Dr. Mofenson. Because no other drugs are available, countries and physicians often are forced to split unscored adult tablets into halves or quarters, which can over- or under-dose a child.

Many U.S.-manufactured ARVs are in liquid form, which while easier to administer to infants and young children than solid ARVs, are difficult to transport and keep refrigerated in sub-Saharan Africa and other remote areas of the world.

Optimally, Dr. Mofenson said, drugs for children should

be smaller, fixed-dose combinations offering multiple ARVs in one pill, as are currently available for adults.

Part of the lag in developing drugs in different forms and dosages comes from ethical considerations involving children and drug testing, said Dr. Havens. “How do we stimulate the testing of drugs in children early on so that they can be available for use in children at the time they are first available for use in adults?”

Improving testing, treatment

The new policy statement makes recommendations for improving HIV testing and treatment in children, including:

- ARV drug formulations and dosage;
- developing pills in smaller milligram amounts and pill sizes;
- configuring tablets so they can be easily

divided, and creating other alternatives to liquid medication, including chewable tablets or sprinkle formulations;

- expediting the availability of new drugs for child use by requiring that pediatric formulations (liquids and/or tablet dosage forms and sizes) be available at the same time a country approves a drug for use in adults, unless there is a biological reason not to develop the drug for use in children;
- developing formulations and performing studies to allow once-daily dosing in children at the same time as planned for adults;
- requiring studies of drug pharmacokinetics in infants, children and adolescents at the time phase 2 and 3 studies are being conducted in adults, so that when drugs are approved for adult use, they also can be dosed for children; and
- providing drug administration devices and tools along with medications (syringes, bottle tops, tablet crushers, etc.).

HIV testing:

- enhancing early identification of infants with HIV infection by making appropriate virologic testing technologies available throughout the world; and
- supporting political, religious and other community leaders in endorsing the value of HIV testing linked to prevention and treatment.

Care of children with HIV:

- expanding the education and number of health care practitioners caring for HIV children; and
- integrating pediatric HIV care into comprehensive child health programs and facilitating collaboration among health experts to build capacity and expand expertise throughout the world.

Global effort

Dr. Mofenson said U.S. drug companies are receptive to working with the world health and pediatric communities to improve anti-retroviral treatment and availability for children.

“The pharmaceutical companies have said: ‘tell us what we need to do,’” said Dr. Mofenson. “They’re looking for some direction, and this policy statement provides it.”

The international health community’s unprecedented support and input for the new policy statement adds considerable weight to its recommendations.

The statement was based on a paper presented at a WHO conference by Diana M. Gibb, M.D., co-author of the new AAP policy statement, and a series of lectures in Kenya by Joseph Mbutia, M.D., Ruth Nduati, M.D., and Dorothy Mbori-Ngacha, M.D., all on barriers to testing and treating young children with HIV, said Dr. Havens.

The four physicians served as consultants during the statement’s editing process, ensuring “that we were really meeting the needs of the large number of pediatricians caring for children with HIV throughout the world,” said Dr. Havens. “It was a very important collaborative effort that resulted in a strong document.”

“I’ve never seen a statement with so many organizations signing on in support, said Dr. Mofenson. “This is not just a U.S., but a global effort” in the fight against HIV in children.

Endorsing organizations

- African Network for the Care of Children Affected by AIDS
- Baylor International Pediatric AIDS Initiative
- British HIV Pharmacy Association
- British Paediatric Allergy, Immunity and Infection Group
- Canadian Paediatric Society
- Children’s HIV Association of UK and Ireland
- Elizabeth Glaser Pediatric AIDS Foundation
- Paediatric European Network for Treatment of AIDS
- Pediatric Infectious Diseases Society
- Indian Academy of Pediatrics
- International Pediatric Association
- Latin American Pediatric Association
- Pediatric Association of Jamaica
- Pediatric Society of Thailand
- Royal College of Paediatrics and Child Health
- South African Paediatric Association
- Southern African HIV Clinicians Society
- Union of National African Paediatric Societies and Associations
- World Health Organization