Focus: The Mashi Study

Over the past decade, the United States has seen a dramatic decrease in the number of HIV-infected children. In 2003, there were only 59 pediatric AIDS diagnoses, less than a third of the estimated number in 1999. Much of this decrease is attributed to several factors including enhanced voluntary HIV testing and counseling, altered social perceptions of HIV/AIDS and readily accessible antiretroviral treatment such as zidovudine, commonly known as AZT, by HIV-infected pregnant women and their newborn infants.

Yet in resource-poor countries, like those in sub-Saharan Africa, the number of infants infected with HIV remains at an all-time high. Governments continue to struggle to overcome financial and technical challenges in order to make critical drugs available to pregnant women. In Botswana, an estimated 35.4% of pregnant women are HIV-infected, and 7,000-9,000 infants are infected with HIV annually.

In March of 2001, HAI researchers began enrolling 1,200 HIV-infected pregnant women in the Mashi Study to evaluate the best treatment to block mother-to-child transmission of HIV (MTCT) in Botswana. The study worked with the Botswana government’s national program, which provides AZT free of charge to HIV-infected pregnant women and their infants.

The first goal of the study was to determine whether administering a single dose of the drug, nevirapine (NVP) to both mother and child around the time of delivery would further reduce the transmission of HIV from mother to child.

The word “mashi” means “milk” in Setswana and reflects the second goal of the study, which is to compare two different infant feeding techniques to prevent postnatal transmission of HIV. Over the course of six months, scientists compared exclusive breast-feeding and six months of AZT to formula feeding and one month of AZT.

In August of 2002, data presented at the XIV International AIDS Conference strongly suggested that the treatment regimen of NVP and AZT is superior to AZT alone in preventing MTCT. Subsequently, the Botswana study was redesigned so that all babies received a single dose of NVP. Scientists examined the effect of giving this new treatment to the mothers. The study was completed in 2004.

Drs. Roger Shapiro and Ibou Thior presented the findings at a late breaker session at the 2005 Conference on Retroviruses and Opportunistic Infections in Boston. They concluded that adding NVP to the mother’s drug regimen was not superior to AZT alone as long as the newborn infant received NVP, but that the results need to be interpreted in the context of feeding strategy and in utero infection rate. HAI researchers will continue to study the effect of NVP on mothers’ health through the Mashi Plus Study, which will assess the response of women to antiretroviral therapy after receiving single-dose NVP.

In the breast-feeding arm of the study, researchers found that breast-feeding had higher HIV infection rates but lower mortality rates by seven months. High rates of HIV-free survival through 18 months were achieved with both infant feeding strategies. HAI researchers will also examine the effect of breast-feeding on mother and infant health through the Mashi Plus and Infant Health Outcomes Studies.

HAI researchers hope that the results of the Mashi Study will help inform the national AIDS policy in Botswana and other sub-Saharan African countries. Dr. Carolyn Wester, the Mashi Study coordinator, believes that studies like Mashi are making a difference on many levels. Dr. Wester said, “First, they are being designed for and implemented within the context and the population they are most likely to benefit. Furthermore, research that is conducted alongside government programs also serves to complement and strengthen these services, particularly when they are first being introduced to the community.”

How You Can Help...

HAI’s efforts depend upon your support. Contributions are tax deductible. To make your contribution to HAI online, please visit the Harvard School of Public Health giving page at http://www.hsph.harvard.edu/give/.

Sign up for free email updates!

Sign-up to receive free email updates from HAI. Simply send an email to info@eci.harvard.edu to receive electronic news and details about upcoming events.
Carolyn Wester moved to Botswana in 2000 to join the Botswana-Harvard School of Public Health AIDS Initiative Partnership for HIV Research and Education. In her position as study coordinator for the Mashi Study, she oversees daily operations including training and protocol adherence of study personnel at the Mashi Study sites in Gaborone, Molepolole, Lobatse and Mochudi.

Spotlight: How is the Prevention of Mother to Infant Transmission situation different in Africa than in America? What are the challenges?

CW: The challenges in preventing mother-to-child transmission of HIV, or MTCT, are certainly unique to the context in which one is living whether in Africa or America. In areas of high HIV prevalence like Botswana, it is particularly important to recognize that preventing the spread of HIV begins with enabling individuals to know and protect their HIV status and, subsequently, to make informed reproductive decisions.

For HIV-infected pregnant women, MTCT can occur any time during pregnancy, delivery or breast-feeding. Although antiretroviral medications, or ARVs, and formula feeding have been shown to reduce MTCT, in order to implement these strategies women must have access to a number of services which may be taken for granted in other contexts, such as health care facilities, ARVs, personnel trained in the provision of ARVs, infant formula and clean water.

In Botswana, over 90% of pregnant women receive antenatal care and deliver in health care facilities, government-sponsored programs are available to citizens (including free ARVs and infant formula), and clean water is readily accessible throughout the country. All these services contribute to making Botswana unique, certainly within the African context. However, significant challenges exist in Botswana and elsewhere in getting these programs to the individuals who are most likely to benefit from them.

One of the initial challenges in Botswana was very low acceptance rates of HIV testing. Fortunately, HIV testing rates subsequently dramatically increased for a variety of reasons, including wide-spread access to ARVs and the advent of “routine” HIV testing in all health care facilities.

Another challenge has included the community’s reluctance to embrace formula feeding as a medically and socially acceptable way to feed an infant. For many years community members have understood that “Breast is Best,” particularly with respect to preventing other infectious diseases that contribute to infant illnesses in the region. As a result, many community members were understandably reluctant to embrace formula feeding – even in the context of HIV – as an acceptable alternative to breast-feeding. Also, as formula feeding is advocated in the context of HIV, women electing to formula feed risk disclosing their HIV status and may suffer the stigma associated with that disclosure. This continues to be a very real challenge in Botswana and elsewhere.

Spotlight: What impact will the findings of the Mashi Study have on the ways that women and infants are treated around the world?

CW: I believe that the findings of the Mashi Study will reinforce the importance of performing research studies among the populations that they are most likely to benefit. The Mashi Study suggests that it is important to consider both the HIV subtype as well as the population affected when interpreting study results. I also believe that the findings of the Mashi Study reinforce that high quality data can be expected from clinical trials conducted in the developing world.

The specific findings of the Mashi Study are being considered carefully by policymakers inside and outside of Botswana. Specific areas being considered in the context of MTCT include the optimal time to start ARVs, which ARVs to recommend to both mother and baby, and the best method of infant feeding. I do not want to speculate at this time as to what policies will be adopted locally as a result of the Mashi Study, but I do know that the government of Botswana is committed to implementing the most effective and safest strategies for preventing the spread of HIV.

HIV and Breastfeeding: Mashi Plus and the Infant Health Outcomes Study

For an African mother living with HIV, the decision to breast-feed her child is complex. If she breast-feeds, there is a 5-20% chance that the infant will be infected with HIV through breast milk. However, if she formula feeds, her child is six times more likely to die of an infectious disease in the first two months of life. The lack of access to clean water and formula, and the societal pressures to breast-feed only make the decision more difficult.

HAI scientists designed two studies to help shed light on the complex issues of breast-feeding: The Infant Health Outcomes Study and Mashi Plus. Both studies were conducted simultaneously with the (continued on next page)
Essential Networking in HIV/AIDS Research

As the healthy HIV-infected participant from the Tshepo Study leaves the clinic, Dr. Okechukwu Okezie reviews his notes from their consultation. The participant has been on antiretroviral therapy for only a few months and already is responding well. Dr. Okezie completes the case report form (CRF) and faxes it to the Data Management Centre (DMC) at the Botswana–Harvard School of Public Health AIDS Initiative for HIV Research and Education Partnership (BHP). Now Dr. Okezie is ready to see the next study participant and help people stay on their antiretroviral therapy.

Mashi Study, using the same data gathered from mother and infant participants.

The Mashi Plus Study examines the effect of breast-feeding on the health of HIV-infected women in the developing world. The two goals of the Mashi Plus Study are to examine whether breast-feeding by HIV-infected women in the developing world.

The two goals of the Mashi Plus Study are to examine whether breast-feeding by HIV-infected women is associated with a higher rate of disease and death, and to assess the present among each of these groups, and the rate of infant mortality for formula-fed and breast-fed babies.

Scientists hope that these studies will provide a more complete picture of the benefits and risks of breast-feeding for African women living with HIV, and help inform infant feeding strategies for the future.

HIV Negative Profiles Study

The two goals of the Mashi Plus Study are to examine whether breast-feeding by HIV-infected women is associated with a higher rate of disease and death, and to assess the present among each of these groups, and the rate of infant mortality for formula-fed and breast-fed babies.

Scientists hope that these studies will provide a more complete picture of the benefits and risks of breast-feeding for African women living with HIV, and help inform infant feeding strategies for the future.

While dedicated people, like Dr. Okezie, are on the front lines fighting the crisis, investigators, researchers and data managers help attack AIDS through science, analysis and technology. One integral group of crusaders is the team that manages the data collected from the field. This group forms the BHP’s DMC, which was designed to serve multiple simultaneous clinical and research studies since 1996.

The DMC plays several key roles in each study. As each study is formed, the DMC helps develop realistic project timelines for data collection and processing, and informs study budgets for the resources used. For ongoing studies, the DMC enters, cleans, edits and codes data while efficiently managing thousands of CRFs every month.

All information gathered from the field must meet stringent quality controls for accuracy and precision. The DMC constantly performs integrity checks on datatypes, patterns, inter-CRF skip logic, and cross-CRF logic throughout the data management process. Once the data is keyed, additional complex integrity checks are processed by the data managers using on-line query and reporting tools to further reduce any potential errors. The paper CRFs are then filed and secured within the main DMC room which is only accessible through security clearance.

In addition to the day-to-day processing of new data, the DMC assists in producing interim reports on study progress as well as generating progress reports for each study participant. This reporting facilitates efficient follow-up for study physicians and nurses who care for and consult with study participants each day.

The DMC not only serves as an important network nexus with researchers including study physicians, principal investigators, lab technicians, clinicians and statisticians in Botswana, but also has helped several organizations in Africa which plan to establish their own DMC.

Erik Widenfelt, the director of the DMC at BHP, has lent his expertise at a recent workshop held in Dakar, Senegal. The workshop focused on scaling up capacity and establishing information infrastructure to support clinical trials and data management. Mr. Widenfelt said, "It is important that study sites in Africa develop the capability to efficiently manage and organize the vital data they collect from the field. This is a good way of both maintaining critical communication and sustaining research in fighting AIDS."
Upcoming HAI-related Events on summer hiatus. Look for new events in the next issue.

Support the Botswana Harvard School of Public Health AIDS Initiative Partnership

Wear the AIDS in Africa Ribbon - Handmade by HIV+ Women in Botswana

By purchasing this beautiful, handmade beaded AIDS ribbon, you will help us battle AIDS in Africa. The proceeds from the sale of these ribbons contribute to research in Botswana, including programs that prevent HIV+ mothers from passing the virus to their infants. Hundreds of babies’ lives have been saved already. But we have so much farther to go...Please help us help them.

To order the AIDS in Africa Ribbon, please go to www.aids.harvard.edu/orderform, download the order form and mail to HAI at 651 Huntington Ave, Boston, MA 02115, or fax it to us at 617-432-4545.

News & Events

Women and AIDS in Africa: Hope for the Future

In May, HAI held its first online auction: “Women and AIDS in Africa: Hope for the Future.” The auction celebrated the courage of women living with AIDS in Africa and fostered hope for a healthy future for themselves and their children. Items in the auction ranged from a spectacular wildlife safari adventure in Botswana and a fishing expedition on the Botston Harbor to a dazzling set of South Sea pearl and diamond earrings and a handcrafted gemstone globe. All items were donated by members of the HAI International Advisory Council and other HAI supporters. The auction raised over $16,000, which will provide researchers and scientists at HAI the tools they need to continue their global efforts to fight the AIDS epidemic through research, education, and training. HAI thanks all its supporters for participating in this exciting event.

AIDS Research in Africa: Opportunities and Challenges

Africa continues to carry the greatest burden of the AIDS epidemic. More than 80% of the world’s total number of HIV-infected women and infants live in sub-Saharan Africa. Dr. Max Essex, chair of HAI, spoke about efforts of HAI scientists to address the crisis at a recent June lecture, sponsored by the Office of International Programs at Harvard Medical School Division of AIDS. The lecture was entitled, "AIDS Research in Africa: Opportunities and Challenges." Dr. Essex spoke about the high rate of genomic variation of the HIV virus which is a significant impediment to AIDS research. Although this complicates vaccine design and ARV therapy efforts, scientists devise innovative strategies to meet these challenges. From developing a vaccine candidate that is based on a recombinant anthrax protein to formulating a new treatment strategy to avoid drug resistance for HIV-infected mothers and their infants, scientists will continue to tailor interventions and chemoprophylaxis to target the specific subtypes that are predominant within African countries.