FOCUS: HIV Transmission and Genital Herpes

Developing new strategies to stop HIV transmission is one way to curb the AIDS epidemic. In addition to vaccine research and HIV/AIDS training, researchers at the Botswana-Harvard School of Public Health AIDS Initiative Partnership for HIV Research and Education (BHP) are involved in various studies to accomplish this goal. The Basadi (which means “women” in the Setswana language) Study, in particular, is examining the role of genital herpes in HIV transmission in HIV-infected women starting highly active antiretroviral therapy (HAART).

Genital herpes, which is caused by the herpes simplex virus type 2 (HSV-2), is a common sexually transmitted infection around the world. There is no cure for this disease, which may consist of painful genital sores that recur several times a year (called recurrent genital herpes), but treatment can prevent and lessen outbreaks.

Scientists initially found that people co-infected with both HIV and HSV-2 tend to experience recurrent genital herpes more often than individuals who are HSV-2 infected only. They also discovered that co-infected individuals have higher amounts of HIV in their genital tract than HIV-infected individuals without HSV-2. These findings suggest that co-infected people may be more likely to transmit HIV to their partners than people who are only HIV-infected.

Although HAART manages HIV infection and reduces the amount of HIV in blood, there is no evidence demonstrating that antiretroviral treatment (ART) is able to reduce the amount of HIV in the genital tract in HIV–HSV-2 co-infected women.

The Basadi Study, which will enroll 500 HIV-infected women starting HAART, will evaluate the influence of HSV-2 infection on the ability of HAART to reduce the presence and quantity of HIV in the genital tract. The study will also develop recommendations on genital herpes suppression among co-infected individuals on HAART.

All women in this study will receive medical care and treatment following Botswana Government guidelines, including antiretroviral medications and routine laboratory testing through Botswana’s National Program for ART. Participants and their partners will also be provided treatment for sexually transmitted infections following government guidelines.

The study is conducted by the BHP and supported by the National Institutes of Health in the United States.

HIV Infection Among Pregnant Women in Nigeria

Nigeria has one of the largest populations in Africa and although HIV prevalence is low compared to other African countries, there are more than 3.6 million people living with HIV. Pregnant women are one of the vulnerable populations to become HIV-infected. Researchers at the Harvard School of Public Health and at the Jos University Teaching Hospital collaborated on a study to determine the risk factors for HIV among pregnant women receiving antenatal services in Jos, Plateau State, Nigeria.

Researchers found that, of the 2,657 study participants, 8.2% were HIV-positive. Women in the 20-29 age group were four times more likely to be at risk for HIV infection when compared to women less than 20 years of age. The study also found women of the Catholic and Pentecostal faiths were more likely to be HIV-infected than Moslem women. Women who had multiple marriages and women who were married to a banker or an accountant were at a much higher risk of HIV-infection.

Researchers hope that the results will support the development of effective interventions, which would include behavioral change, expansion of perinatal HIV prevention services and sexually transmitted infection control in this part of Nigeria. These findings were published in the July 2005 issue of the International Journal of Gynecology and Obstetrics.

Anemia and HIV in Tanzania

In a recent study collaboration between the Harvard School of Public Health and the Muhimbili University College of Health Sciences, researchers examined the relationships between anemia and HIV in Tanzania.
This approach was a kind of litmus test for assessing just how involved males were in PMTCT interventions. It turned out that only approximately 6% of male partners tested for HIV at our facility. The HIV discordance rate among these couples was notably high at about 23%. It was then that I decided to team up with a laboratory scientist to draft a research concept paper which we presented to Prof. Max Essex, who in turn linked us to this Multi-Center Phase III trial initiative among HIV discordant couples.

**Spotlight:** You completed your annual enrollment targets for the Netefatso Study within four months from the beginning of the study – a feat no other study site was able to accomplish. What was your strategy and greatest challenge?

**PN:** Building a strong team that shared my vision and commitment. In this case we had the motive, will power and passion for what we were doing. I believe these were the essential ingredients that got us from a pre-study initiation ranking at the bottom to a post-study initiation ranking at the top among all eleven international sites involved in this study.

Every research effort needs to have a clear vision of the challenge ahead in recruitment. This for us was effected through conducting an initial formative research and baseline data search on the feasibility of our research intervention. The feasibility data armed us with the necessary information for designing recruitment and retention strategies that were community centered rather than investigator driven recruitment choices.

One significant challenge was getting stakeholders to appreciate the value of couple testing as an HIV prevention strategy. Through aggressive advocacy we were able to get couple HIV testing into mainstream HIV prevention efforts on a national level.

**Spotlight:** Stigma plays a large role in preventing people from coming forward to find out their status and get the help they need. How can sero-discordant couples overcome this barrier?

**PN:** Unfortunately HIV related stigma was institutionalized right at the start of the epidemic, and what we see at the community and individual level interventions is a trickle down effect. HIV is one of those few diseases where “the right not to know” overshadows the benefit of knowing one’s disease status. Nonetheless, a significant aspect of stigma particularly in regard to couples is pseudo-stigma attributed to provider perception. There is no stigma attached to ARV clinic facilities yet providers thought branding such clinics as HIV specific would limit responsiveness. We need to get providers to a level where they are comfortable addressing couples on HIV issues, including discordance. Only then shall they be able to embrace HIV partner notification/prevention issues the way they have done for the syndromic STI management approach.

In Botswana, just over 40% of HIV-positive individuals in stable relationships have an HIV-negative spouse and yet there was little effort being made to prevent these impending HIV transmissions. The impact of addressing couples on the HIV epidemic can never be over-emphasized particularly in sub-Saharan Africa, where UNAIDS estimates over 75% of new infections are acquired from a stable partner. If only most country HIV programs had data on HIV discordance, we would all embrace couple testing as an HIV prevention intervention.

Our experience with over 200 HIV discordant couples seen at our facility was extremely enriching regarding the stigma misconception. Discordant couples were always able to accept their status and in my anecdotal re-collection, there was one case of discordance related domestic violence which we had to deal with. I believe failure to address couple testing is like failure to accept that unmarried people have sexual intercourse. A significant proportion of couples anyhow get to learn of their discordance status with or without any couple intervention. We learned that providing couple services was a much more welcome alternative for discordant couples, as information clears their misconceptions and brings about relationship stability.
Today, more than 52,000 HIV-infected Botswana citizens are on antiretroviral (ARV) treatment, making Botswana the leading African country in providing free HIV/AIDS treatment and care. The national ARV therapy program, called Masa (which means “new dawn” in the Setswana language), was created in 2002 and aims to treat more than 150,000 HIV-infected citizens by the end of 2009. The Botswana Government also plans to roll-out 32 ARV sites to provide treatment and care throughout the country.

As these scale-up efforts are underway, the Government has identified three critical areas of need that would potentially compromise the quality of, and access to ARV treatment through Masa. The critical areas are: 1) the need for a sustainable training capacity in clinical care and treatment at ARV sites, 2) the expansion of HIV laboratories throughout the country to perform CD4 and viral load tests in the public sector, and 3) improvement in the tracking and reporting of ART patients through the establishment of a Monitoring and Evaluation Unit within Masa.

Through a cooperative agreement with the Botswana Government, HSPH, and the President’s Emergency Plan for AIDS Relief (PEPFAR), the project, referred as BHP-PEPFAR, was established to develop and implement a comprehensive ARV site support program to address these needs (see Figure 1).

The Clinical Master Trainer/ARV Site Support program is designed to create a sustainable training capacity in the clinical care of HIV/AIDS patients. The program designates and trains site-level doctors, nurses, and pharmacists as site Master Trainers, who can provide on-going, hands-on training tailored to the specific needs of their ARV site.

Project staff (“Core Master Trainers”) will train and provide on-site continual support to the site Master Trainers using a curriculum adapted from the WHO guidelines for Integrated Management of Adolescent and Adult Illnesses. Through the development of this curriculum, the project substantially contributes to an integrated approach to HIV/AIDS care and treatment (combining ARV treatment with tuberculosis care, PMTCT, sexually transmitted infections, and other HIV/AIDS-related programs) and paves the way for the eventual roll-out of ART to lower-level clinics staffed primarily by nurses. This is a critical next step in improving access to all patients requiring ART.

As of October 2005, the program conducted comprehensive needs assessments at 11 ARV sites, provided on-site training to 55 health professionals at five sites on specific topics, and began providing intensive on-site support.

BHP-PEPFAR is playing an important role in creating laboratories throughout the country with CD4 and viral load testing capabilities. This will relieve the burden on the country’s two HIV reference laboratories and quicken the time needed to obtain test results. While the Botswana Government and African Comprehensive HIV/AIDS Partnerships are providing the equipment and funds for constructing or expanding these laboratories, BHP-PEPFAR is responsible for the training in the use of these tests, using the same Master Trainer/site support approach as for the Clinical Master Trainer program.

To date, 12 laboratory technicians designated as site Laboratory Master Trainers from six new labs have received viral load or CD4 training and CD4 training is currently underway for lab technicians from two additional sites. Piloting of viral load testing is taking place at one of these labs and the launching of CD4 testing is underway at four others. In all, with the training support from BHP-PEPFAR, nine decentralized labs will be fully functional in performing these two critical tests in the near future.

A key to implementing a successful ART program is the ability to obtain timely data on treatment outcomes – including side effects, patient adherence, and drug resistance – in order to monitor the program’s effectiveness and make necessary changes. BHP-PEPFAR is helping the Botswana Ministry of Health to establish a uniform, computerized patient tracking and reporting system, which includes both the public and private sectors. This will also link the central Masa office with ARV sites, HIV laboratories and local pharmacies.

These significant and vital efforts will enhance the ability of the Botswana Government to provide high-quality treatment and care to all HIV-infected persons throughout the country.

Researchers found that anemia was associated with an increased risk of both AIDS-related and all other causes of deaths in a study of 1,078 HIV-infected pregnant women. These participants were enrolled and followed up in a clinical trial of vitamin supplementation from 1995-2003. There was also a significant association between anemia and the rapid decline in CD4 cell counts.

Researchers concluded that anemia is a strong predictor of HIV disease progression and that HIV/AIDS care initiatives should include anemia screening, along with prevention and treatment efforts, especially in programs that target women.
12th HIV Vaccine Think Tank Symposium

With a growing problem of accessing treatment in the developing world, limited drug access and drug resistant HIV strains, a viable HIV vaccine is in demand more than ever. An emergent research approach investigates a virological and immunological analysis of the earliest stages of HIV infection. This research may provide clues for developing an efficient and effective vaccine design. This was the focus of this year’s twelfth think tank, HIV Vaccines for Developing Countries: Analysis of Acute and Early Infections, held in Nairobi, Kenya, Thursday, October 13 to Saturday, October 15, 2005. Leaders in HIV vaccine research from various African countries and the US shared important information about acute infection and vaccines. A summary report of the think tank findings will be available soon on HAI’s website.

Multivitamins and AIDS

Researchers are examining how supplementation with multivitamins and/or selenium may improve immune function and delay the onset of AIDS or mortality in HIV-infected adults in Botswana. In addition, the pilot of the Dikotlana-Basadi (which means “multivitamin-women” in the Setswana language) Study follows 50 women to determine whether taking nutrient pills will change the amount of the HIV virus in the fluid of their genital tract. The process, also known as genital HIV-1 shedding, may ultimately reduce HIV-1 infectivity.

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