HARVARD PRESIDENT VISITS THE BOTSWANA–HARVARD PARTNERSHIP

Harvard President Drew Faust toured clinics and laboratories of the Botswana–Harvard AIDS Institute Partnership (BHP) on the first visit of a sitting Harvard president to Africa. Established in 1996, the BHP is a collaborative research and training initiative between the government of Botswana and the Harvard School of Public Health AIDS Initiative (HAI).

On the morning of November 25th, Faust was met at the airport in Gaborone, the capital of Botswana, by Max Essex, Chair of both the BHP and HAI, along with other researchers and clinicians.

The first stop on Faust’s daylong visit was Mochudi, a village of 40,000 that has an adult HIV prevalence of about 25%. The village is the site of a new HAI research study called the Mochudi Project, a comprehensive, community-based approach to HIV prevention that emphasizes the detection and treatment of acute (recent) HIV infections.

Faust toured the Mochudi hospital and visited BHP clinics on the hospital grounds where clinical trials are underway. She talked with young mothers in the Mma Bana Study, an NIH-funded trial designed to determine the optimal drug regimen to prevent mother-to-child transmission among breastfeeding women in Botswana.

In the afternoon, Faust returned to Gaborone to meet with young Harvard-trained researchers now working at the BHP, including Dr. Neo Tapela, a native of Botswana who is studying HIV and chronic diseases. Faust toured the Botswana–Harvard HIV Reference Laboratory that serves as headquarters for the BHP. The Laboratory houses research on a number of projects, including prevention of mother-to-child transmission of HIV and the genomic analysis of HIV-1C, the viral sub-type predominant in southern Africa.

Dr. Rebeca Plank is the Principal Investigator of a new clinical trial, Infant Male Circumcision in Gaborone, Botswana, and Surrounding Areas: Feasibility, Safety and Acceptability. Plank is an Infectious Disease and HIV specialist who trained at the Brigham and Women’s Hospital in Boston. She recently spoke with Martha Henry, Editor of Spotlight.

What is the history of circumcision in Botswana?

PLANK: Circumcision had traditionally been practiced into the 19th century to mark the transition from boyhood to manhood. This practice was discouraged through the influence of Western medical missionaries. As of a few years ago, up to 15% of men in Botswana were circumcised, only rarely as infants.
**Q&A**

**Rebeca Plank** *(cont’d from front)*

**Why do we need this study?**

**PLANK:** Botswana has one of the world's highest rates of HIV infection. Education programs and campaigns to promote condom use have done little to decrease the prevalence of HIV there. Finding effective prevention measures is essential.

In three randomized controlled trials, circumcision reduced a man's risk of HIV infection through heterosexual sex by 60%. Circumcising a baby is easier, safer, cheaper and faster than circumcising an adolescent or adult, but we don’t know which method of infant circumcision is most appropriate for Botswana and other developing countries. That’s why we’re doing this study.

**What are the aims of your study?**

**PLANK:** In the first phase, our aim was to determine if infant male circumcision is acceptable in Botswana. If parents are offered the option, what percentage will actually have their babies circumcised? In the second phase we are examining the feasibility and safety of two different infant circumcision techniques: Mogen clamp versus Plastibell. No study has ever compared the two methods.

**You’ve finished the first phase. What were your findings?**

**PLANK:** Our study found that among mothers of newborn male infants interviewed in the maternity wards in four towns in Botswana, 92% responded that they would circumcise, primarily to prevent future HIV infection, if the procedure were available free of charge in a clinical setting.

**Why spend money circumcising infants who are less than a month old when you could be circumcising men who are already sexually active?**

**PLANK:** That’s a very reasonable question. The government of Botswana aims to circumcise 80% of HIV-uninfected males aged 0–49 years over the next several years as part of the country’s HIV prevention efforts. Currently there are wait-lists for adolescents and adults seeking the procedure. Infant circumcision has not yet been scaled-up. The Ministry of Health is awaiting the results of our study before deciding which method to adopt for the national program.

Circumcising a baby is about one-tenth the cost of circumcising an adult. Not only is it cheaper, it’s also much safer to circumcise a baby than an adolescent or adult. Another factor to be taken into consideration is that if an adolescent or adult resumes sexual activity before the wound is fully healed, they have an increased risk of getting infected or of passing the infection on to someone else.

Although infant circumcision would have a delayed impact on the HIV epidemic, it would be one way to introduce the procedure in a safe, systematic, and sustainable way to Botswana and in other resource-limited settings. If you take all of those factors into consideration, infant circumcision makes a lot of sense.

**Circumcision has been shown to reduce HIV infection in men by 60%. Does it have a significant effect in reducing infection for the female partners of infected males? Does male circumcision have any impact on women?**

**PLANK:** The evidence is not clear about whether the female partners of HIV-infected males have a reduced rate of infection if their male partners are circumcised. However, one should look at the larger picture. If fewer men get infected with HIV because of circumcision, fewer men will pass on infections to women. And when fewer women are infected, fewer babies will be born infected. Eventually circumcising enough men will reduce the population prevalence of HIV, which will reduce the number of women who get infected.

**How will your study results be used?**

**PLANK:** The World Health Organization (WHO) and UNAIDS have stated that countries with severe, generalized HIV epidemics but low rates of male circumcision should offer this surgery as an important, evidence-based HIV prevention intervention, including among newborns. Governments now need to make decisions about implementing circumcision services. They must develop policies that are based on international best practice and respectful of human rights.

Our study will provide the WHO with data on the safety and sustainability of two established methods of circumcision. It is important to consider not only the cost and safety of each procedure, but also how easy it is to train people and maintain the supply chain.

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If it hadn’t been for public health, Rebeca Plank might not have been conceived. Her parents met through a common interest in public health during a medical conference in the late 1960s.

Her father, Stephen Plank, a physician from the U.S., did his medical residency in the Panama Canal Zone. While there, he was dismayed to discover that he had to send people out from the hospital to the same conditions that had brought them there in the first place. He began to understand that while clinical medicine was important, the best way to make a lasting difference in people’s lives was to address root problems. He went back to school and earned a doctorate from the Harvard School of Public Health (HSPH).

Plank’s mother, María Lucila Milanesi, grew up in rural Brazil, one of nine children. At a time when few children went to school, Milanesi, a determined young woman, attended medical school and became a pediatrician. Then, as Plank puts it, “She got tired of watching kids die of preventable causes so she, too, decided to address the root of the problem and obtained a doctorate in public health from the University of Sao Paulo.”

Plank’s parents met at a research conference when they were both living and working in Santiago. They married and Rebeca was born. The young family left Chile in 1970 and Plank spent most of her childhood in Salvador, Bahia, Brazil, before moving to California at the age of ten. She attended Pomona College.

“About halfway through college I decided I would become a medical anthropologist because I was fascinated by the intersection of health care and culture—how the two can help and hinder each other,” said Plank. Her goal was to work in international public health. For her senior project, she analyzed HIV prevention posters from all over the world.

When her anthropology professors encouraged her to go to medical school, she followed their advice, getting an MD from the University of California, San Francisco in 2001. During medical school, she worked in Brazil, first on a clinical rotation in infectious diseases and then as a research assistant. She also spent a year working on a research project in rural Vietnam.

After graduation, Plank headed to the Brigham and Women’s Hospital in Boston to complete her training, first as a resident, then as chief medical resident, and finally as a clinical and research fellow.

It was at the International AIDS Society Conference in Rio in 2005 that Plank found a focus for her work. At that meeting, Dr. Bertrand Auvert announced the results of the first randomized trial of circumcision in adult males in South Africa. “When I heard him say that circumcision reduced the incidence rate of HIV infections in adult men in their study by more than 60%, I thought, finally we have something that works that can actually change the course of the epidemic.”

With the help of HAI researcher Dr. Shahin Lockman, Plank began planning a research project to examine infant circumcision in Africa. Plank’s hard work and tenacity led to her becoming Principal Investigator of the clinical trial, Infant Male Circumcision in Gaborone, Botswana, and Surrounding Areas: Feasibility, Safety and Acceptability.

Plank is quick to credit the mentors in her life, especially Lockman, who gave her invaluable guidance as a clinician/scientist with experience setting up clinical trials in Botswana. Plank also praises Prof. Max Essex, Chair of HAI, and Dr. Roger Shapiro for their generous help with her research.

These days, Plank splits her time between conducting HIV prevention research in Botswana and seeing patients in Boston. She is an attending physician in the Division of Infectious Diseases at the Brigham and Women’s Hospital where she has won a number of awards for excellence in teaching medical students and residents. She is on the faculty of Harvard Medical School and is also a Research Associate at HSPH. She was awarded an NIH Career Development Award to support her work in Botswana.

Plank plans on staying in the field of HIV prevention. Building upon her circumcision research is the next step for her. “Botswana is stretched thin with regard to physicians, especially now that adult male circumcision services are in place. There are just not enough doctors to meet the demand,” she explains. “Wouldn’t it make sense to have the already highly trained and skilled nurse/midwives in labor and delivery also circumcise the babies before they go home? That’s the next thing we’d like to look at because it might be more sustainable in resource-constrained settings.”

Rebeca Plank with her parents in Bahia, Brazil
BEST PRACTICES IN HIV/AIDS PROGRAMS

Dr. Richard Marlink, Executive Director of the Harvard AIDS Initiative, is the Executive Editor of the recently published From the Ground Up: Building Comprehensive HIV/AIDS Care Programs in Resource-Limited Settings. This three-volume collection of best practices and lessons includes contributions from over 320 distinguished HIV/AIDS professionals from around the globe, with a special focus on sub-Saharan Africa. The book is being offered free-of-charge so that it will reach the widest possible audience, especially those involved with program implementation work "on the ground" in resource-limited settings.

"In this era of expanded funding to help implement AIDS care and prevention efforts in poor regions of our world, From The Ground Up represents the combined efforts of hundreds of experts, sharing their experiences in how to build comprehensive AIDS programs," says Marlink. "Those 'on the ground' experts show that building programs is possible, and that in doing so, healthcare access and delivery is expanded."

Each of the three volumes is named after an essential step in HIV/AIDS program implementation. Volume One, "Laying a Strong Foundation," highlights the key elements that should be in place prior to program initiation. Volume Two, "Establishing a Framework for Success," touches on the scientific and practical considerations for the provision of HIV-related care, treatment, and prevention services. Volume Three, "Developing Pathways and Partnerships," looks at how, once programs have been established, implementers can ensure that services reach those who need them most.

HERPES & HIV: NOT WHAT YOU THINK

It is always a shock to find out that what you had assumed was true simply is not. That is why clinical trials are so important in science. The unexpected results of a recent trial examining herpes and HIV demonstrates the importance of carrying out controlled trials to test preconceived beliefs.

Up to 90% of women with HIV infection in southern Africa also have genital herpes (HSV-2). Most people who are infected with HSV-2 do not know that they have the virus, which causes symptomatic genital sores and breaks in the skin but is frequently active without symptoms. Multiple studies had shown that infection with herpes was associated with an increased risk for HIV infection. However, whether treatment to suppress HSV-2 would decrease HIV transmission had not been tested.

The Partners in Prevention HSV/HIV Transmission Study, led by the University of Washington and funded by the Bill & Melinda Gates Foundation, looked at whether the use of acyclovir, a drug widely used for the safe and effective suppression of HSV-2, by persons who are infected with both HSV-2 and HIV could reduce the likelihood that they would transmit HIV to their HIV-uninfected partners.

The study was conducted among 3,408 African HIV-discordant couples, in which one partner had HIV and the other did not. In all the couples, the partner who had HIV also had HSV-2 infection. The study took place in seven countries in Africa (Botswana, Kenya, Rwanda, South Africa, Tanzania, Uganda and Zambia). In sub-Saharan Africa, the majority of new HIV infections occur among heterosexual HIV-discordant couples, many of whom are in stable partnerships and unaware that one partner has HIV and the other does not.

The study results, published in The New England Journal of Medicine in early February, were both surprising and disappointing. Researchers concluded that daily acyclovir therapy did not reduce the risk of HIV transmission when taken by people infected with both HIV and HSV-2. In other words, controlling the herpes of someone infected with HIV did not decrease the chance that he/she would infect a partner with HIV.

The Botswana portion of the study was conducted by the Botswana–Harvard AIDS Institute Partnership, under the direction of Dr. Max Essex. Though Essex was disappointed, he said the results are still useful. “It is important, first of all, because it shows that although the risk for infection by herpes and HIV go together, controlling the herpes infection with treatment does not reduce risk for infection with HIV. People should not treat herpes specifically to control HIV spread, but should treat to control the pain and symptoms of herpes.”

Essex said the study was also important for showing how viral genetic sequencing can be used to determine if a study participant became infected from his/her partner or from someone outside of the study. “The study showed how effectively researchers can use viral sequencing genetic linkage to verify the source of the infection. We found that two-thirds of the newly infected people who didn’t get acyclovir did get infected from their partner.”

From The Ground Up also features profiles of individuals on the front lines of the pandemic—from a community health nurse in western Kenya to the first African religious leader to publicly disclose his HIV-positive status.

For more information and to order the free three-volume set or searchable CD-ROM (shipping charges apply), visit our website: www.aids.harvard.edu.
Not many undergraduates have the opportunity to conduct their own laboratory research projects. Harvard students who spend a semester abroad at the Botswana–Harvard AIDS Institute Partnership (BHP) are a rare exception. Last year, Carlos Becerril, a pre-med social anthropology major, researched drug resistance among antiretroviral-naïve patients with recent HIV infection in Botswana.

Born in Morelia, Mexico, Carlos was 13 when he received a life-saving kidney transplant from his mother. The experience made him want to become a doctor. Because of the transplant, he takes immunosuppressant drugs every day and has to be careful about infections. “If I get the flu, I get the flu for four weeks. It takes a long time for my body to recover.”

After his freshman year at Harvard, Carlos spent the summer in Peru, working at an orphanage for HIV-positive children. The experience motivated him to go to Kenya after his sophomore year, where he volunteered in several HIV clinics around Lake Victoria. He took vital signs, updated records, and helped dispense drugs from the pharmacy. He also spent time counseling people with HIV.

“Doing this helped me realize how similar I am to HIV patients,” he said. “We take similar medications to help prevent us from getting sick because our immune systems aren’t that strong. We have the same issues. I felt so connected to them. That’s why I decided to study abroad in Botswana and do HIV research.”

Carlos did get very sick while in Kenya, possibly from food poisoning, and ended up in the hospital. “I’ve been through that,” he said. “If it happens again, I know how to respond. You grow from the experience.”

Unlike other students, Carlos had never worked in a lab before arriving in Botswana, but that did not stop him from pursuing his goal. Part of the semester abroad program involves working closely with mentors. Carlos’s junior mentor was Rebecca Mitchell, who earned a biology degree at Harvard in 2003 and was doing research at the BHP while pursuing her DVM/PhD in epidemiology from Cornell.

“Carlos came to the lab with no experience and a limited biology background,” says Mitchell, who spent hours teaching Carlos the fundamentals of laboratory science. “I was surprised at the dedication he demonstrated once he began seeing the results of our work. By the end of the semester, he had a solid understanding of the technical processes he was performing in the laboratory, as well as the underlying biology.”

For his research project, Carlos analyzed samples from four patients with early HIV infections who had not yet begun antiretroviral therapy. The samples were from a previous BHP study and had been taken between 2005 and 2008. Using the latest laboratory techniques, Carlos tested the samples for drug-resistance mutations, which would have indicated the possibility that a patient had become infected with a drug-resistant strain of HIV. He found no transmitted drug resistance in the four samples, which helped confirm research from other scientists indicating that transmitted drug resistance is not prevalent in Botswana at this point in time.

Now back at Harvard, Carlos continues to do HIV laboratory research. After graduation this May, he hopes to get a Master’s in Global Health, and then attend medical school. He continues to pursue his goals and also to take his pills.

Carlos Becerril

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The Laboratory also serves as a facility to train HIV/AIDS researchers.

Faust met with Botswana’s Minister of Health to discuss Harvard’s continuing commitment to the Botswana–Harvard Partnership. She also met with the University of Botswana’s Vice Chancellor to explore future collaborations between the two schools.

At a dinner in the evening to celebrate the cooperation between Botswana and Harvard, Faust spoke about the importance of leadership, acknowledging the two former Botswana presidents in attendance, President Masire, who was instrumental in establishing the partnership, and President Mogae, who launched Botswana’s national antiretroviral drug program.

In her remarks, Faust spoke of the university-wide scope of the Botswana–Harvard Partnership. “It has been so clear to me since the earliest days of my presidency,” she said, “indeed when I was at Harvard before my presidency and heard about this remarkable collaboration, that it was a partnership that honored and privileged and served us at Harvard—our students, our faculty, at every level of the institution, from the undergraduates who have been part of the project, to the researchers, to the medical students, to the faculty themselves.”

“We have come together in fields that have ranged from fundamental science to medicine to anthropology, marking a kind of partnership of the intellect and a partnership of inquiry that have broken down boundaries in how we understand the way to go about our work.”

-President Drew Faust on her visit to the Botswana–Harvard AIDS Institute Partnership

See page 1 for full story.