

FOCUS: How the BHP Came to Be

Maybe it all started with Deeda Blair, an early (and constant) supporter of the Harvard AIDS Institute. She introduced Max Essex, Chair of HAI, to Maurice Tempelsman in the 1980s.

Because of his business and personal interests in Africa, Mr. Tempelsman's knowledge and contacts were essential in helping establish HAI's research and prevention collaborations in Senegal. Studies with a cohort of commercial sex workers yielded the identification of HIV-2 and evidence that it was less virulent than HIV-1. Senegal has been cited by the World Health Organization as a major success story, having the lowest rate of HIV/AIDS in sub-Saharan Africa. The program continues to this day, under Dr. Phyllis Kanki, making it the longest prospective study of HIV in Africa.

Fast forward to June 1996. Maurice Tempelsman, now Chair of the HAI's International Advisory Council, was hosting a dinner at Washington's celebrated Cosmos Club. The dinner was in honor of President Ketumile Masire of Botswana. Knowing of the growing AIDS crisis in Botswana, Mr. Tempelsman invited Max Essex to the dinner and introduced him to President Masire. The two spoke briefly. The President asked Dr. Essex if he could meet with him the next morning. Essex, who had a class to teach at Harvard the next day, said no, but that he could meet later that evening.

When the meal was over and the formal goodbyes said, President Masire and Dr. Essex went back to the President's hotel suite. The President knocked on the door of his Personal Physician, who was also a

Consultant Physician, heading one of the Medical Units at Princess Marina Hospital in Gaborone. As Essex remembers, Dr. Joseph Makhema had already retired for the night when he was roused by the President's knock. Still wearing his bathrobe, Dr. Makhema joined the two men for a discussion about the growing AIDS crisis. At the end of the conversation, it was decided that Essex would travel to Botswana as soon as his schedule allowed.

A few weeks later, in the summer of 1996, Max Essex landed in Botswana for the first time. He was met by Ria Madison, who worked for Maurice Tempelsman as Personnel Officer at Lazare Kaplan Botswana, a diamond polishing operation that employed several hundred people. Many of the employees were young women

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The Players. Top row: Deeda Blair, Dr. Max Essex, Maurice Tempelsman, President Masire. Bottom row: Dr. Joseph Makhema, Ria Madison, Dr. Ibou Thior, President Mogae.

An Interview with Dr. Max Essex



Photograph by R. Feldman

Drs. Max Essex and Joe Makhema

Dr. Max Essex is Chair of the Harvard School of Public Health AIDS Initiative (HAI), the Lasker Professor of Health Sciences, and Chair of the Botswana-Harvard Partnership for HIV Research and Education (BHP). As the BHP celebrates its 10th anniversary, Martha Henry, Editor of Spotlight, asked Dr. Essex to reflect on past accomplishments and future goals of the BHP.

Spotlight: What major accomplishments were achieved during the first ten years of the Botswana-Harvard Partnership?

Essex: We treated the first AIDS patients with antiretroviral drugs (ARVs) in Botswana. Bill Wester and Hermann Bussmann, who work at the BHP, were the first physicians to administer ARVs through the government health system. The Minister of Health at the time, Joy Phumaphi, wanted to demonstrate that lives could be saved through three-drug combinations. This led to a government program that is by far the largest in Africa, setting the example that a country can treat a lot of their AIDS patients if they really want to.

In our research work we showed that the virus in Botswana and southern Africa is different. This taught us that when making a vaccine or designing drugs for the epi-

dem in southern Africa, we should do it with the virus most representative of that region, rather than accept what was done for the West.

We also made major progress in learning how to prevent mother-to-child transmission of HIV and we ran the first vaccine trials in southern Africa.

Spotlight: What else?

Essex: Building the Botswana-Harvard HIV Reference Laboratory, the largest AIDS-dedicated laboratory in Africa, was a major accomplishment.

Through the KITSO program, we trained more than 5000 clinical AIDS workers, including doctors, nurses, midwives, counselors, pharmacists and lab workers. Approximately 80-90% of all healthcare workers who serve AIDS patients in Botswana have received KITSO training.

“Botswana is an example of what hopefully will occur in much of the rest of Africa.”

- Dr. Max Essex

Spotlight: What are the future goals of the Botswana-Harvard Partnership?

Essex: We need to develop better prevention approaches for adults at risk of HIV infection. We need to do more with vaccines, microbicides and other biological approaches to prevention.

We need to determine whether the established drug regimens will work as well in the medium and long term in Botswana, especially if drug-resistant HIV variants begin circulating in the population.

Botswana’s situation is unique. Nowhere else in the world has a significant fraction of the population been involved in both ARV treatment for AIDS and chemoprophylaxis to prevent transmission of HIV/AIDS from mothers to infants. This affects the kinetics of transmission.

The questions about how drug-resistant variants develop and get transmitted among people to interfere with one program or another have not been addressed. If women and infants are getting infected for the first time with a drug-resistant variant, then the standard chemoprophylaxis won’t work. We already know that if women and infants are getting chemoprophylaxis with one or two drugs to block mother-to-infant transmission, then the antiretroviral treatment that they will need later may not work. Drug resistance feeds off itself in different ways when you have a combination of chemoprophylaxis and treatment going on in the same population at the same time.

Spotlight: How long do you think the collaboration between HAI and Botswana will continue?

Essex: I think it will continue for a long, long time. I hope it will continue for another 20 years at least because many of the problems we are now addressing need great attention. Harvard has experts in different aspects of these problems. We are committed to helping the situation in Botswana.

Botswana is an example of what hopefully will occur in much of the rest of Africa. It’s the first place where a large program was launched to cover most of the affected population of a country, and in some ways an easier case because of its good government and economic resources, but it’s clearly an example of what has to happen in the rest of Africa to control HIV/AIDS. ○

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How the BHP Came to Be *(continued from front page)*

whose small hands enabled them to do the precise work of cutting and polishing diamonds. Later, young women as a group were found to have one of the highest incidences of HIV/AIDS in Botswana.

After hours of discussions, planning and negotiations, the idea of a collaboration between HAI and the Republic of Botswana became a reality. In October of 1996, an official agreement was signed.

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On that first trip, Essex made presentations about his research and met with government officials to discuss potential areas of collaboration. Blood samples from HIV-positive individuals were collected for Essex to bring back to Boston.

When the samples were analyzed back in the lab, researchers discovered that the virus in Botswana was different from the virus found in the U.S. and Western Europe. “As soon as we knew that the rates of HIV infection were high and that the virus was different, which we didn’t know until then,” said Essex, “we decided that it was important to set up a program and have a lab.”

Dr. Ibou Thior, a researcher who had played an important role in HAI’s work in Senegal, was appointed as the first Project Director. Ria Madison formally became the Project Administrator, the first official employee of the Botswana-Harvard AIDS Institute Partnership for HIV Research and Education (BHP). Doctors, nurses, lab researchers and pharmacists soon joined the project.

Fast forward ten years to the present. Today the BHP employs 204 people, of whom 163 are Botswana. HAI was renamed in 2004 and is now the Harvard School of Public Health AIDS Initiative. Dr. Joseph

Makhema, who was present at that first meeting between President Masire and Dr. Essex, is the current Project Director of the BHP. One of his long-term goals is to see more African senior scientists employed by the BHP.

Botswana elected a new president in 1998, His Excellency Festus Mogae, who continues his government’s tradition of strong leadership and support in the fight against AIDS. President Masire is now chair of the National BHP Advisory Committee.

As President Mogae said at the time of the BHP’s 10th anniversary, “Through close collaboration with the BHP clinicians, the first public ARV therapy clinic was piloted in 2001. This pilot provided many valuable lessons and later grew into *Masa*, the first public and nationwide ARV therapy program in the region. It is encouraging to know that as a result of this program, many people who were on their deathbeds are back on their feet and are productively engaged and providing for themselves and their families.” ○

NEWS & EVENTS

Educating Southern African Parliamentarians about HIV/AIDS

The Conference on AIDS Action and Botswana: Lessons in Capacity Building and Importance of Research took place in Gaborone, Botswana in late January.

Under the auspices of The Southern African Development Community Parliamentary Forum (SADC) and the Botswana-Harvard Partnership, in collaboration with the National Assembly of Botswana, the conference was attended by delegates from the 14 SADC countries.

The conference focused on basic scientific information on HIV/AIDS with a view towards facilitating policy formulation, de-

velopment and implementation of programs for HIV/AIDS. Sessions covered the benefits and challenges of research performed in southern Africa, the ability of research to build scientific and medical capacity, and suggestions of how to better coordinate responses for combating HIV/AIDS in SADC countries.



Politicians networked with scientists and clinicians. Members of Parliament, influential leaders, and high-ranking government officials were provided with the knowledge and tools necessary to support and implement successful national HIV/AIDS research programs. The conference detailed the latest HIV/AIDS research results and emphasized the need for countries to participate in local HIV/AIDS research for their own benefit.

Delegates appreciated the opportunity provided by the Botswana-Harvard HIV Reference Laboratory to share experiences, expertise, and best practices within southern Africa. The Bill and Melinda Gates Foundation provided major funding for the conference. ○

Semester Abroad: First Harvard Undergraduates in Botswana *(continued from page 3)*

research, policy, healthcare, or advocacy.” Amy will remain in Gaborone this summer to work with the Clinton Foundation on a rural lab expansion initiative.

The three students also visited clinics associated with the Botswana-Harvard Partnership in Mochudi, Molepolole, and Lobatse. The Program Coordinator, Bukamu Hulela, a native of Botswana and graduate in the Harvard Class of 2005, arranged field trips to Jwaneng Diamond Mine and the Okavanga Delta.

All three students mention a trip to Khutse Game Reserve in the Kalahari desert as a high point of their semester. On a drive in the bush they came across conservation workers darting a male lion to collar him to keep him from being shot by local farmers. “They let us get out of the truck when he was sedated, so we have pictures with this huge lion,” said Jamie.

Lisa, Jamie and Amy were, in many ways, experimental subjects themselves in Harvard’s first undergraduate program in Botswana. The next group of students arriving in Gaborone will benefit from their experiences and suggestions for improvements.

“I have always heard that people from Botswana are incredibly nice and friendly,” said Amy, “but it was still a surprise when I came here. My U.B. friends were excited to

teach me about their traditional foods and culture. I will really miss walking down the street and greeting ‘Dumela!’ to almost everyone I pass by.” ○

Lisa, Jamie and Amy were, in many ways, experimental subjects themselves in Harvard’s first undergraduate program in Botswana.



Lisa Flannery inspects a sedated lion on an excursion in the Kalahari Desert.

SPOTLIGHT



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AIDS INITIATIVE



WHAT'S NEW: Semester Abroad: First Harvard Undergraduates in Botswana

This spring, three adventurous young women were the first Harvard undergraduates to study abroad in Botswana. The three biology majors lived on the campus of the University of Botswana and took classes there. The greater part of their education took place at the Botswana-Harvard Reference Laboratory.

To learn standard HIV diagnostic techniques, the students spent the first weeks of the semester rotating through the basic laboratories—the CD4 cell count lab, the viral load lab, the serology lab and the PCR lab. For the rest of the term, the students worked on independent research projects.

Jamie Greenwald is a junior from St. Louis. Though—or perhaps because—her father is a physician, she grew up thinking she would be anything but a doctor. She changed her mind in her sophomore year at Harvard and switched to pre-med.

Jamie's research project evaluated a serologic diagnostic test to distinguish between early and chronic infection of HIV. A related test was developed using HIV-1 subtype B populations in the U.S. She is trying to develop a test for subtype C, the HIV subtype in Botswana. Jamie also played soccer with the University of Botswana girls' team.

"I thought it might be a little out of my comfort zone, but I wanted to experience something completely different from how and where I had been living."

- Lisa Flannery

When asked why she was studying in Botswana, Lisa Flannery, a junior from Sterling, Massachusetts, replied, "I thought it might be a little out of my comfort zone, but I wanted to experience something completely different from how and where I had been living. I also think that it is a phenomenal environment in which to study the HIV/AIDS epidemic. It is a country that has dealt remarkably well with the current issues



BHP Viral Load Lab. From left: Monica Phiri, Amy Wu, Jamie Greenwald, Lisa Flannery, Fredah Mulenga. Kneeling: Pong Phillimon Sebogodi.

and getting the chance to see how it works from the inside was one I could not pass up."

Her work in the lab concerned HIV infection of the central nervous system. She was interested in HIV/AIDS-related dementia rates amongst viral subtypes. For subtype B, the predominant subtype found in the U.S., rates are known to be high, but less is known about subtype C, found in Botswana and most of southern Africa. She wants to know if a possible difference in rates is influenced by the difficulty in diagnosing dementia in the presence of more pressing opportunistic infections with subtype C, or if it is based in the virus's inability to actually infect/affect the cells of the central nervous system.

"After spending time in Botswana," said Lisa, "I feel like I will be more willing to return to Africa later in my life. It has opened up new possibilities for me when I think about living and working abroad and has served as a gateway to taking chances that I wouldn't have even considered before." This summer, Lisa will continue her research at the BHP on the molecular aspects of cell tropism with the hopes of developing a senior thesis project.

Though born in Beijing, sophomore Amy Wu grew up in Corvallis, Oregon. In

the summer of 2006 she returned to Beijing to work as an intern in the HIV/AIDS Division of the China Center for Disease Control. After her research experience in China and involvement with the Harvard AIDS Coalition, she wanted to visit a place where HIV has a major impact on the population and see firsthand what was happening. "This research abroad program to Botswana was the opportunity I had been waiting for," said Amy.

She began an HIV immunology project to see whether certain genes related to immune responsiveness are associated with viral suppression in AIDS patients on drug therapy. She is studying samples from patients in a large treatment trial that involves four different drug combinations. She analyzes samples from patients who have failed their first line of drug therapy, as well as patients who were the best responders, having successfully suppressed their viral load for at least two years after HAART (Highly Active Antiretroviral Therapy) initiation.

"My experience in Botswana has only strengthened my plans to work in international health and medicine in the future," said Amy. "Coming here has made me realize just how many ways are possible to contribute to this field, whether through basic

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Using Nevirapine More Effectively

A study published in the January 11th issue of *The New England Journal of Medicine* found that for mothers given a single dose of nevirapine during labor to reduce the chance of HIV transmission to their children, waiting six months after birth before taking a nevirapine-based antiretroviral treatment dramatically reduced their chances of developing resistance to nevirapine.

The use of single-dose nevirapine has successfully reduced mother-to-infant transmission of HIV, but with a significant drawback. Research has shown that 20 to 69 percent of women who take a single dose of nevirapine during labor subsequently develop resistance to the drug—a situation that may undermine the patients' ability to respond later to nevirapine-containing antiretroviral therapy. And nevirapine, or a closely related drug that shares the same resistance, is used for almost all AIDS treatment in Africa. A single dose of nevirapine

during labor is frequently all that is accessible to pregnant women in resource-limited settings where more expensive treatments multi-drug treatments are not available.

The team of researchers led by Shahin Lockman, Assistant Professor in the Department of Immunology and Infectious Diseases at Harvard School of Public Health and at Brigham and Women's Hospital, and Max Essex, Chair of the Harvard AIDS Initiative, followed 218 HIV-infected women who received a single dose of nevirapine during labor, as well as a short treatment of anti-retroviral drugs during pregnancy. Sixty women started a nevirapine-based treatment within six months of giving birth, while the remaining 158 women started on the drugs six months afterward.

The outcomes were dramatically different. Of those women taking the drugs soon after giving birth, 41 percent experienced treatment failure. Of those women



Photograph by Graham Ramsay

Drs. Max Essex and Shahin Lockman

who waited, just 12 percent had the treatment fail.

Dr. Lockman speculated the better results were because the amount of nevirapine-resistant HIV in the body decreases as time passes from the single-dose exposure to nevirapine during labor. The findings will affect treatment approaches during pregnancy for millions of HIV-infected mothers. ○

KITSO Update

In 2001 the Government of Botswana, in an initiative unprecedented in Africa, announced that it would provide antiretroviral (ARV) therapy free of charge to all qualifying patients. At that time, few physicians in Botswana had experience prescribing ARV drugs.

That same year the Botswana Ministry of Health, in collaboration with the Botswana-Harvard AIDS Institute Partnership, established the KITSO AIDS Training Program. KITSO was developed to train doctors, nurses and other health

professionals to implement Botswana's ambitious goals in a sustainable, standardized national ARV treatment program.

In 2002 the first four ARV treatment sites were opened. Today 32 main treatment sites are operating throughout the country. From its inception, KITSO-BHP has carefully incorporated monitoring and evaluation methods to assess the quality and integrity of the program's structure, content and implementation. This commitment to constant evaluation has helped to create a program that is capable of adapting

quickly to new research information and changing national public health guidelines.

The central course in KITSO's training program is AIDS Clinical Care Fundamentals, which includes lectures, case study discussions, practice exercises for pediatric ARV dosing, question and answer sessions, and a final exam. Other courses include Medication Adherence Counseling, and Advanced HIV/AIDS Care and Treatment.

KITSO's training of over 5,000 health professionals has supported Botswana's national program, which now provides ARV therapy to over 80,000 patients and serves as a model for HIV/AIDS care and treatment throughout Africa.

KITSO-BHP's training efforts are made possible through the support of the African Comprehensive HIV/AIDS Partnerships (ACHAP), a collaboration between the Government of Botswana, the Bill and Melinda Gates Foundation, and The Merck Company Foundation/Merck & Co., Inc. ○

How You Can Help...

The research, training and education efforts of the Harvard School of Public Health AIDS Initiative depend upon your support. Your contribution will make a difference. Contributions are tax deductible.

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