FOCUS: No More Waiting to Know

Inside the Game City Shopping Centre along the new Lobatse Road in Gaborone, Botswana, passersby see a poster of a striking young man. The man looks apprehensive about the possibility of being exposed to HIV. In a country where about one in three adults is HIV-infected, his odds of becoming infected are high but so are the chances of fighting the disease – if he gets tested early for HIV.

His decision to find out about his status would benefit not only himself but also Botswana’s efforts to fight the disease, and an ongoing study that could generate interventions to prevent progression to AIDS. Tshedimoso, which means “to reveal new information” in the Setswana language, aptly describes some of the goals of the Botswana-based study.

The main goal of the study is to examine the acute and early phases of HIV-1C infection and how the body’s immune system responds to HIV from the very beginning of infection. Because early HIV disease behaves very differently from chronic HIV infection, researchers are measuring profiles of the amount of HIV in blood and the differences among HIV subtypes or strains. These data should indicate a correlation between the quantity of the virus and the point at which HIV viral levels plateau (or viral set point). Also, the magnitude, breadth, and diversity of virus-specific CD4+ and CD8+ T-cell immune responses are being analyzed. The study results may provide knowledge on how to reduce HIV replication during the acute infection phase, and pave the way for early treatments and vaccine design.

The Tshedimoso team launched the “No More Waiting to Know” campaign to encourage people to find out about their HIV status. Knowing their status would empower them to care for themselves, alter any risk-taking behavior, and help protect their families and their communities.

The team raised this HIV/AIDS awareness at clinics, schools, ministries, malls, and in local publications and newspapers. They also held seminars at clinics and other sites to educate potential participants about the safety and goals of the study.

Thus far, they have helped more than 1,380 people learn their status, and enrolled 37 participants. These participants may be the key to help stem the epidemic in Botswana and save millions of lives in southern Africa.
In 1983, I was appointed as head of the Department of Immunology at the TDRC. I started developing and establishing immunological assays for sero-epidemiological surveillance for the African trypanosomiasis, malaria and schistosomiasis with the support of WHO-TDR in Geneva and various experts from Switzerland and UK. What was interesting and challenging at that time was that I had to prepare my own antigens, conjugates and purification of antigens and immunoglobulins. I also served as a member of the WHO Steering Committee of Immunology and Immunopathology of African Trypanosomiasis in Geneva from 1989 to 1991.

When AIDS first emerged in Zambia more than 20 years ago, Dr. Rosemary Musonda knew that the disease, without intervention, was capable of becoming the epidemic that it is today. Dr. Musonda continues to dedicate her extensive experience, both in the scientific arena and in international HIV/AIDS strategic planning, to fight HIV/AIDS. She was recently recruited to work as the head of research laboratory at the Botswana Harvard School of Public Health AIDS Initiative Partnership for HIV Research and Education (BHP).

**Spotlight:** When you began your scientific career, you were originally interested in working on malaria. What made you decide to focus on HIV/AIDS?

**RM:** My scientific career started in January 1980 at Tropical Diseases Research Centre (TDRC) in Ndola, Zambia where I was seconded by the Ministry of Health of the Republic of Zambia as a staff development fellow. At that time, TDRC was organized under the World Health Organization (WHO-TDR) special program for research and training in tropical diseases. The mission of the TDRC was research and training on tropical diseases such as malaria, African trypanosomiasis (sleeping sickness), schistosomiasis, and leprosy which were part of the six tropical diseases of WHO-TDR’s concern. Of course AIDS was not known to exist at that time.

I worked on a collaboration to develop assays for HIV testing with several experts from the Uganda Virus Centre, the German Primate Centre, and the laboratory at the TDRC. We conducted some comparisons of different viral antigens and a recombinant peptide called ENV-80 ELiza using Zambian sera. The assays revealed what were then very frightening figures of about 5% HIV prevalence rate in pregnant women in Ndola and equally high rates in blood donors.

Over the course of the following years, I concentrated on studying the immunology and virology of HIV. The dynamics of the disease were like no other I studied and it posed an important new challenge.

I wanted to find easier and more cost effective treatment regimens for HIV/AIDS, monitoring of drug resistance, understanding the pathogenesis of the diseases and preventive vaccines including microbicides. This would help reduce incidences of HIV/AIDS in southern Africa especially in vulnerable groups, and women in particular.

**Spotlight:** In what ways will you be able to further the mission of the BHP?

**RM:** My experience has prepared me to contribute to research in HIV/AIDS in Botswana as part of the capacity building of the southern African region as a whole, which has been hardest hit by the HIV/AIDS pandemic. I am confident that with the experience I had from the TDRC, I will be able to motivate local scientists to enhance their capability to respond to relevant and important research needs of Botswana and southern Africa.

My responsibilities will include ensuring the smooth running of the laboratory, in collaboration with various principal investigators and study directors. We’ll also manage sample processing, analysis, storage and shipping and work closely with the data management centre and the clinical investigators.

There is no doubt in my mind that the scope of work at BHP is quite significant and the facilities and infrastructure are excellent. With the present support from the Government of Botswana and the Harvard School of Public Health and other collaborating partners, there is a great opportunity to make progress investigating the dynamics of HIV genotypes and the development of drug resistance. Understanding the HIV/AIDS epidemic and the importance of immune responses with other factors, and how they affect transmission and disease progression are also important. These studies will generally contribute to treatment and prevention of HIV infections in southern Africa and the world at large.
Every day at 8PM, Angela Ntswana* makes sure her mother, Kgomotso*, takes her prescription of antiretroviral medications to manage her HIV. Although her mother is hardly ever forgetful, Angela’s role as mopati, which means “partner” in the Setswana language, is to remind Kgomotso that this treatment and care will keep her healthy and thriving. Angela is one of 325 partners, or bapati (plural of mopati in Setswana), who agreed to become adherence assistants in the Tshepo Study.

The Tshepo Study, known as “the study of hope”, is the first large-scale research study in southern Africa to assess the emergence of drug resistance to, and the tolerability of, different protease inhibitor – sparing highly active antiretroviral therapy (HAART) regimens. The study also compares two different strategies to enhance patient adherence to these treatments in Botswana. One strategy is the standard of care (SOC), and the other is the community, or family-based, daily directly observed therapy (Com-DOT). Each strategy is designed to offer consistent HIV/AIDS care to the HIV-infected patient.

In the SOC strategy, the patient receives medication and counseling in the same way that the Government of Botswana is providing these services through the National ARV Treatment Program. At the Infectious Disease Care Clinic (IDCC), the patient picks-up his or her monthly medications and receives counseling and education from the IDCC staff. The staff consists of pharmacists, pharmacy technicians, nurses, medical officers, and social workers.

In the Com-DOT strategy, the medication and counseling services are the same as the SOC strategy, but the patient also has a mopati. The mopati is a family member or close friend, chosen by the patient, and is trained to help the patient take his or her medications on a daily basis. The mopati also takes notes of each medication administration and monitors the general health of the patient, ensuring that the patient is well enough to continue to take this powerful therapy.

Both patient and mopati prepare for this assistance with training in HIV care, either in their community, at one of their homes, or at a location of their choosing. After this training, both receive additional private trainings for the first month, then group trainings every four months for the duration of their involvement with the study. The mopati is also encouraged to accompany the patient at his or her monthly visits at the IDCC.

Although both patient adherence strategies are being followed, the Tshepo researchers are taking a deeper look into the role and responsibilities of the bapati. The goals of this sub-study are to describe comprehensively the bapati’s interaction with their study participants and their daily practices, as well as to identify factors that may positively and/or negatively affect the mopati-patient relationship. The team plans to enroll about 285 bapati participants. The results of this sub-study may offer important insights into enhancing ARV adherence for Botswana and other resource-scarce countries.

*Names are pseudonyms to protect the identities of the study participants.

New BHP Advisory Board

In strengthening the continuing efforts to fight HIV/AIDS in Botswana, the Botswana-Harvard School of Public Health AIDS Initiative for HIV Research and Education Partnership (BHP) gathered a wide range of in-country expertise. The group of local leaders has formed the BHP Advisory Board, which will help identify and meet immediate and long-term HIV/AIDS needs, such as building sustainable capacity and infrastructure in Botswana. The members include Sir Ketumile Masire, former president of the Republic of Botswana, Justice Unity Dow, the first woman on the High Court, Dr. Patson Mazonde, the former director of National Health services, and Dr. Leonard Manthe, lead treatment support manager of the African Comprehensive HIV/AIDS Partnerships. The Board has already provided valuable advice about improvements for the program, and suggestions about how to use the results in Botswana as a model for southern Africa.

American Students in Botswana

Students from the US lend their assistance in helping the research that will ultimately stem the epidemic in sub-Saharan Africa. In a new collaboration with the Princeton-in-Africa Program, the BHP provides an extraordinary opportunity for students from Princeton University to learn first-hand about the AIDS epidemic. The fellows work in year-long positions in Botswana to assist program officers, write grant proposals and reports, monitor projects in the field, represent organizations at coordination meetings, and review funding proposals. They also help support institutional capacities of local partners, teach basic skills, and guide donors in the field.
Storage and Transport of ARV Medications

Since the Tshepo Study began, a number of issues concerning the storage and transport of ARV medicines by the patients themselves have become apparent to Tshepo physicians and pharmacists. Patients in both the Tshepo Study and the National ARV Program come to the IDCC monthly to get refills of their medications.

Study team members found that many patients carry their medicines in a wide variety of ways, because some patients are anxious about their HIV status being discovered by family members or co-workers. For others, the size of the pills and occasional requirements for cool storage may lead to a reduction in adherence. As a result of this anecdotal information, the study team is examining ARV medication storage and transport, an issue that has never been systematically studied or reported in the literature among ARV patients in sub-Saharan Africa.

The goal of this sub-study is to determine the prevalence of ARV transportation and storage issues in the adult, HAART-treated population seen at the Tshepo clinic. The findings can potentially lead to targeted educational and training initiatives that may help patients better adhere to their treatment regimens, and could help pharmacy staff design more patient-friendly packaging for patients’ medications. Information from the sub-study might also inform the development of simple, low-cost adherence reminders that are well accepted in Botswana.

Drug Resistance in HIV-Infected Women

Christopher F. Rowley, a research fellow in the Department of Immunology and Infectious Diseases at the Harvard School of Public Health and the BHP, is conducting a study on nevirapine (NVP) resistance in Botswana women who are given the drug to help prevent mother-to-child transmission of the HIV virus during labor.

Dr. Rowley’s research focuses on implementing improved laboratory tests that would be able to detect NVP drug resistance in HIV-1C infected women. The current tests are not sensitive enough to detect minor populations of the virus which may be clinically important as they can lead to treatment failure.

If successful, these new laboratory tests could lead to a better understanding of the development of resistance mutations, which can have a negative impact on an HIV-infected woman’s health when she begins treatment with antiretroviral therapy. Additionally, the knowledge gained through the study may lead to better policy decisions on prevention of mother-to-child transmission initiatives, and to improved general care of patients who are increasingly receiving antiretroviral care in resource-poor settings.

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