Cutting-Edge Study Launches

“We strongly believe that with this project we have the chance to make history in the fight against AIDS,” said Michelle Gavin, U.S. Ambassador to Botswana, at the November 8th press conference in Gaborone announcing the launch of the Botswana Combination Prevention Project.

The project is called *Ya Tsie* in Setswana, the language of Botswana. The name comes from a proverb that roughly translates as “Teamwork bears more fruit than individual effort.” *Ya Tsie* is a collaboration with the Botswana-Harvard Partnership, Botswana’s Ministry of Health, and the U.S. Centers for Disease Control and Prevention.

In Botswana, where 24% of the adult population has HIV, about 12,000 new infections occur annually. Botswana has reached a tipping point where the annual increase in adults receiving antiretroviral treatment is greater than the annual number of adults becoming infected with HIV.

Elton John Receives HAI Award

Sir Elton John received HAI’s Leadership Award on October 15th. The award is presented to individuals who have exhibited extraordinary vision, leadership, and courage in the worldwide struggle against AIDS. Past recipients include tennis star Arthur Ashe, Diana, Princess of Wales, President Festus Mogae of Botswana, and President Olusegun Obasanjo of Nigeria.

Since the creation of the Elton John AIDS Foundation (EJAF) in 1992, John has spoken out against stigma and advocated for the rights of people living with HIV/AIDS, especially those on the margins of society. EJAF has raised more than $300 million to combat stigma, prevent infections, provide treatment and services, and motivate governments to end AIDS.

John received the award at EJAF’s fall gala in New York City. *Today Show* host Matt Lauer hosted the event. Julio Frenk, Dean of the Harvard School of Public Health, Max Essex, Chair of HAI, and Deeda Blair and Maurice Tempelsman, Co-Chairs of HAI’s International Advisory Council, presented the award to John.

“When I think of the extraordinary people who have received this honor before me, including my dear, dear friend Princess Diana, I am humbled to be counted among such august company. But I am also tremendously inspired by their courage, vision, generosity, dedication, and grace under fire,” said John upon receiving the award. “What I hope to add to their legacy is my own special brand of pig-headed stubbornness.”

As part of the evening’s program, John presented the EJAF Founder’s Award to former Secretary of State Hillary Rodham Clinton. In her remarks, Clinton praised Harvard’s leadership role in AIDS research. “I was delighted to hear that Harvard will begin the trials that we have been promoting and planning for very shortly,” she said, referring to the *Ya Tsie* project that was initiated through the President’s Emergency Plan for AIDS Relief (PEPFAR) when Clinton was Secretary of State.

(continues on page 4)
When the Botswana–Harvard AIDS Institute Partnership (BHP) was launched in 1996, the official goal was collaborative research and training between the Republic of Botswana and the Harvard School of Public Health AIDS Initiative. But for Dichaba Siane—a 40-year-old hospital worker in the capital, Gaborone, who chairs the local Community Advisory Board (CAB)—the scientific teamwork has transformed not only his community and country, but also himself.

According to Siane, the BHP has dramatically improved health and health care management in Botswana. Clinical trials using antiretrovirals to prevent mother-to-child transmission, for example, have shown that the rate of children born HIV-positive can be cut from 40 percent to less than 1 percent. “The research was done mainly in Gaborone,” he said, “but the benefits have cascaded through the entire country.”

Treatment for tuberculosis—a ubiquitous and deadly opportunistic infection that has shadows the AIDS epidemic—has also advanced. “The care has improved so much that if you are on treatment, you will complete your treatment and you will be cured,” said Siane.

But the most impressive development may be that thousands of Siane’s countrymen have volunteered for studies. Batswana, as people from Botswana are called, were reluctant to participate in early clinical trials because they feared having blood drawn. “Blood plays a very important role in the culture. It’s sacred. My blood should be with me—it should not be taken and kept somewhere else,” Siane explained. “However, we’re working through that. Now there are quite a number of people who are comfortable with blood draws, because they realize the importance of blood in terms of research and possible help for the future generation.”

For Siane—who as CAB chairperson has informally served as educator, translator, diplomat, organizer, and advocate—the rewards have also been personal. “Working with the CAB has changed me. I’ve learned a lot about science. And I’ve learned that I have a responsibility to be in constant communication with my community.”

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**Clinical Trials: When Research Gets Personal**

When the Botswana–Harvard AIDS Institute Partnership (BHP) was launched in 1996, the official goal was collaborative research and training between the Republic of Botswana and the Harvard School of Public Health AIDS Initiative. But for Dichaba Siane—a 40-year-old hospital worker in the capital, Gaborone, who chairs the local Community Advisory Board (CAB)—the scientific teamwork has transformed not only his community and country, but also himself.

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And randomized trials using antiretrovirals to prevent viral transmission when one person in a couple is infected and the other is not have also altered the social and emotional landscape. “The study proved without any doubt that it is possible to protect oneself and one’s partner,” Siane added.

Supplements to Slow Disease Progression

Will taking a daily multivitamin and selenium help if you have HIV, but your CD4 count isn’t low enough to qualify for antiretroviral treatment?

In a double-blind, randomized, placebo-controlled trial of 878 HIV-positive men and women in Botswana, Dr. Richard Marlink, Executive Director of HAI, and colleagues showed that a single supplement containing specific multivitamins (vitamins B, C, E) and selenium was safe and significantly reduced the risk of immune decline and death over a two-year period. The supplements cost just pennies per week.

“The likelihood that you would get AIDS or die was reduced by 50% over the two-year follow up, said Marlink. “If you’re a person with HIV and you don’t yet qualify for treatment, this is a very cheap and non-toxic way to slow the damage that HIV could cause to your immune system, though it shouldn’t be looked upon as a replacement to get on antiretroviral treatment if you need it.”

The paper was recently published in the *Journal of the American Medical Association (JAMA)*. The findings replicate an earlier finding by Harvard School of Public Health researcher Dr. Wafae Fawzi and colleagues in Tanzania among pregnant women.

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**spotlight**

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651 Huntington Avenue, 6th Floor
Boston, MA 02115

Phone: 617-432-6106
Email: mshenry@hsph.harvard.edu
Web: www.aids.harvard.edu
Chair: Dr. Max Essex
Executive Director: Dr. Richard Marlink

**PUBLICATIONS STAFF**

Editor: Martha Henry
Print & Web Designer: Lucia Ricci
Thanks to: Lendsey Melton
Three Harvard undergraduates spent last summer at the Botswana–Harvard Partnership (BHP). Under the direction of Max Essex, Chair of HAI, the students worked in the laboratory and designed research projects. They also kept a blog. Here are a few excerpts.

ARRIVAL IN GABORONE • Charlotte Kreger

Our first week in Botswana has been an adventure (sometimes), surprisingly relaxing (sometimes), and fun (all of the time). Yanick, Melody, and I are living in a beautiful apartment, working in a welcoming environment, and exploring the beautiful city of Gaborone.

It’s “winter” here, which means that the nights get to be around 40 degrees and the afternoons can reach past 70 degrees. I’ve been going for a run almost every day and trying to get lost in a good way in order to orient myself in the city. Unfortunately, the days are short here so I have limited time after work gets out to run long distances. Regardless, it’s fun to run through the city, smile and say, “Dumela” to passersby.

WEEK ONE • Melody Guan

Yanick and Charlotte and I began our internships by rotating amongst the diagnostic labs at BHP to learn about the role of each lab in the management of HIV/AIDS and to learn some useful lab techniques. I started off in the DNA/PCR lab, in which blood samples of infants born to HIV-positive mothers were tested for HIV infection.

On the weekend, feeling adventurous and wishing to explore our new surroundings, the three of us climbed Kgale Hill. The hike featured a troop of baboons at the hill’s base, scenic views along the trail, and the thunderous prayers of a large crowd of Pentecostal Christians during our descent.

WEEK TWO • Melody Guan

This week at work we continued our lab rotations. In the viral load lab, there is a really cool machine called the Abbott M200SP that automates almost the entire process of determining the quantity of viral RNA in plasma samples, from pipetting to ensuring that everything is in the right place by scanning barcodes. It even checks that reagents are present in sufficient volumes! BHP is a very high-tech laboratory!

At local restaurants we’ve been able to sample traditional Botswana cuisine with delicious food items like samp (creamy white corn kernels), pap (ground maize porridge), and seswaa, the national dish (boiled, shredded meat). We’ve also developed a craving for magwinya or “fat cakes,” a deep-fried treat sold at the many street-food stalls in Gaborone.

THREE-DAY HOLIDAY • Yanick Mulumba

Dr. Musonda, the Lab Director, invited us to her home and treated us to some Zambian food. Two other colleagues from work and her two daughters were also present. I felt this was a good experience, especially for Melody and Charlotte, to learn more about Botswana and Zambian cultures. Amongst the many discussions was how marriage preparations are generally carried out.

HALFWAY POINT • Charlotte Kreger

For the past few weeks I’ve been working on samples from recently infected patients to sequence them, which means determining the virus’s DNA, base by base. I’m working for Mr. Moyo, one of the lab directors here. He’s looking into the genetic diversity of a section of the viral DNA to eventually genotype and create a phylogeny of the variants of the disease. He’s also looking to find early founder viruses—those which are the initial infectors in a person, which is why using samples from recently infected people is important.

Right now I’ve been working on samples to sequence them. But unlike sci-fi movies like Gattaca, sequencing doesn’t entail putting a piece of hair or drop of blood into a machine and waiting for it to spit out the pattern of nucleotides. It is a three- to four-day process of various protocols.

For the first weeks, Yanick, two interns, and a BHP employee, Terrence, were working with me. It’s always fun to work with other people. They’re good for reminding you when you’re at risk for contamination or when you’ve accidentally skipped a step in the procedure. Now I’m working on the sequencing alone, which is nice, but I miss all of my assistants!

The lab work is good for acquiring useful lab techniques and understanding, first of all, what it takes to complete a research project, and secondly, what doing all of this means and why it’s important. It’s also good for connecting with the other interns/workers here at BHP and working for a common cause. I never thought I’d be so elated when getting a 100% success rate on my first round of PCR! I can’t wait to continue the work and eventually get enough data to analyze and answer some interesting questions. ☺
The more people who are on treatment, the less chance there is for the virus to spread within a community.

The goal of Ya Tsie is to determine whether combining and strengthening HIV prevention methods can prevent the spread of HIV within a community more effectively than using standard methods alone. If the hypothesis is correct, the interventions should have a mutually reinforcing effect that is greater than the sum of the parts.

Ya Tsie will run for four years in 30 villages and involves over a 100,000 people. Participants will receive household visits and services that may include HIV testing and counseling, antiretroviral treatment, male circumcision, and treatment for prevention of mother-to-child transmission of HIV. Some prevention services will be expanded to reach HIV-infected individuals with high viral loads. The goal is to significantly reduce the number of new HIV infections within a community.

Max Essex, Chair of HAI and the Principal Investigator of the study, has spent much of the last year on the enormous task of planning Ya Tsie. “The project includes two innovations—targeting HIV carriers who are the most likely to transmit based on viral load and evaluating transmission networks based on viral mutation patterns,” said Essex.

In Africa and around the world, we urgently need better ways to stop the spread of HIV/AIDS. Ambassador Gavin stressed the importance of Ya Tsie in addressing that need. “If this combination prevention strategy is shown to be effective and affordable, Botswana will be a global leader in providing scientific evidence needed to turn the tide on this epidemic.”

HAI: The Movie

A just-released short video marks the 25th anniversary of the Harvard AIDS Initiative, recapping accomplishments and outlining work that remains to be done. Fast-paced and featuring interviews with Max Essex, Harvey Fineberg, Deeda Blair, and others, you’ll find the 10-minute video online at https://vimeo.com/76450441.