Susan Allen: Confronting HIV in Africa

Despite opposition from a secretive government and the horrors of a genocidal war, Susan Allen established one of the most important cohorts for the study of HIV transmission.

In the early years of the HIV epidemic, researchers and health workers assumed that the partners of HIV-positive individuals would also be infected. But in 1988, Susan Allen, then a researcher at UCSF, made a startling discovery. While tracking HIV in pregnant Rwandan women, Allen found that 14% of her 1,500 research subjects did not share the same HIV status as their partners (1). To Allen, this discordance made these women and their partners an ideal cohort both to understand the factors that determine virus transmission and to identify strategies to prevent it.

Allen soon started a program in which both partners received counseling about prevention strategies and were routinely tested. Her approach had a huge payoff: HIV incidence among counseled couples is 50–70% lower than among non-counseled couples (2).

Allen's progress came to a brutal stop during the Rwandan genocide. Hundreds of her subjects and half of her program's staff were killed. But rather than return to the United States, she used research funds formerly bound for Rwanda to start a similar program in Zambia.

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Today, Allen's program—known as the Rwanda Zambia HIV Research Group—includes the largest and longest-standing cohort of HIV-discordant couples in the world. It has helped to identify strategies that reduce HIV transmission and to uncover the effects of the host's genotype and immune response on the evolution of the virus (3, 4).

JOURNEY TO AFRICA

You were poised to start a surgical career after finishing medical school. How did you end up as a HIV researcher in Africa instead?

When AIDS started to hit the radar in 1984, I was doing my residency in pathology in San Francisco, which turned out to be one of the epicenters of the epidemic. One of the guest speakers at the hospital where I was doing autopsies on young, AIDS-ravaged gay men was a Belgian internist who had treated African AIDS patients. The internist described otherwise healthy people dying of diseases that shouldn't have been lethal—something that we were also seeing among the AIDS victims in San Francisco. The patients were different, but the mortality was the same.

This doctor had access to blood samples from AIDS patients in Kigali, the capital of Rwanda. But these were the times before the virus had been isolated, before there were blood tests to detect it. So the doctor and his colleagues in Rwanda had a hard time figuring out if this new disease was different from other endemic tropical diseases.

I approached the speaker and suggested that they needed a pathology lab to diagnose the infections. He offered to write me a letter of introduction to the Rwandan Ministry of Health if I could find the funding to set up a diagnostic laboratory in Kigali. 18 months later, I landed in Kigali with seed money from UCSF and the state of California.

Had your medical training in the States prepared you to cope with the realities of doing science in Rwanda?

Because one doesn't learn very much about tropical medicine during medical school in the US, I did a three-month intensive course in this subject at the Liverpool School of Tropical Medicine in the UK.

But it was really my childhood that made it easy for me to settle in. I grew up in Brazil and Lebanon. My parents had put me in French schools wherever we went because these schools had the same books and curriculum everywhere, unlike the American schools. So I spoke fluent French, which was a must to survive in Rwanda in those days.

Susan Allen

Going solo like that, did you ever feel like you were stepping into the unknown?

The people at the hospital in Kigali made me feel very welcome, so I never felt alone or abandoned. And my mentors back at UCSF—people like Jay Levy and John Ziegler—were very supportive of my work, although they thought I was a little crazy for choosing to do this overseas project. But I never felt like I was embarking on some new and foreign adventure. Having grown up overseas, going to Africa was like going home.

There were some limitations however. Communication with the outside world was one. Political interference was a bigger problem.

DISRUPTIVE POLITICS

Why did the government interfere with your work?

HIV was a politically sensitive issue in the early days. The first antibody tests for HIV detection were faulty and generated what later turned out to be a lot of false positive results. But the press coverage of these bloated numbers set off a panic, which can be very destabilizing to African governments that are already just hanging on by a thread.

The Rwandan officials did not want any discussion of HIV because they thought it would kill foreign investment and scare off the tourists who came to see

HIV-discordant couples are counseled at an HIV testing center.

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mountain gorillas—an industry that constituted a significant part of the economy. The government, which later became the regime responsible for the genocide, had a very active secret service that began to follow me around, tap my phone, and open my mail. I wasn't allowed to publish my results from 1986 until 1991.

How did you cope with such an effective gag order?
Growing up in places like Lebanon, I'd developed a sense of discretion very early on about some things, like government corruption. I thought that it was too bad that I wasn't allowed to discuss my work but figured that it was alright as long as I could keep working. I made concessions such as calling my program "Project San Francisco" because it wouldn't do me any good to put up a sign that said "Project HIV."

Scientists working elsewhere in Africa were also under the same kind of pressure from other governments and were prevented from publishing. We finally got to the point where our funding was threatened because the NIH and other agencies demanded to see results.

Because the group of scientists working on HIV in Africa was very small at that time, we met in closed door sessions with no press around. That was the only way we could communicate with each other and with our funding agencies.

Given your troubles with the authorities, how hard was it to recruit people into the studies?
The recurrent theme in the 22 years that I've been doing this work is that the target population is never the problem. The obstacles are usually the bureaucracies, and to some extent, the healthcare workers, who are more concerned with stigma and social issues and end up projecting their pessimism onto their patients. We approached the community directly with our intentions, and they were overwhelmingly eager to be tested.

When we set up Project San Francisco to counsel the women who were coming in to be tested, I sat in on the first 700 or so counseling sessions to get a feeling of what these women were able to grasp from what we were telling them about how to protect themselves from HIV or how to prevent its transmission. I was very surprised by how quickly they understood the bottom line. They told me, "Thanks for the information, but you really need to talk to our husbands, because they are the ones who make decisions in our marriage about sexual matters."

Is that how your idea of studying discordant couples came about?
That's right. We encouraged the men to come in, and a third of them showed up despite having no incentives; we didn't even reimburse their transport costs. That's when we discovered the phenomenon of discordant couples. We were making good progress in terms of recruiting and educating people until the genocide forced us to flee. We relocated the program to Zambia, and soon after, I shifted base from UCSF to the University of Alabama system.

REBUILDING CAREER AND COHORT

Why did you move?
I had to leave UCSF because there was no tenure there, and San Francisco was an incredibly expensive place for a single mother with two young kids and a career that depended on the stability of war zones. So I moved to Alabama in 1996 until financial troubles forced the closure of my department. And without students interested in international health, I could not recruit interns for our sites in Africa. So my husband, whom I met there, and I decided to move to a place where there were more people interested in global health. We came to Emory University in 2004.

What's the current status of the discordant couples study project?
We went back to Rwanda after things calmed down and now have about 2,000 couples spread over three sites there and in Zambia. We have money from a variety of sources, including the International AIDS Vaccine Initiative. We've done clinical trials both of behavioral interventions like condom use and family planning as well as of antiviral drugs like acyclovir. The sites are also ready for vaccine trials.

"We are uncovering risk factors for HIV infection and ways to prevent the spread."

Our biggest focuses at the moment are the prevention of transmission and the study of the natural history of the disease. The cohort is a great source of samples to study the characteristics of the transmitted virus and the virus that establishes infection in a new host, because this information is likely to help in the design of effective vaccines.

Are you closer to understanding why discordancy exists, that is, why some people are resistant?
We're working with virologists and geneticists to answer that question. Basically, everyone is vulnerable, and everyone who gets infected is contagious to some degree. Our collaborators have identified HLA types that are associated with being contagious or being vulnerable. So we are uncovering risk factors for HIV infection and ways to prevent the spread of HIV, but there is a lot more left to learn.

1. Allen, S., et al. 1992. *BMJ.* 304:1605–1609.
2. Allen, S., et al. 2003. *AIDS.* 17:733–740.
3. Dorak, M.T., et al. 2004. *Lancet.* 363:2137–2139.
4. Derdeyn, C.A., et al. 2004. *Science.* 303:2019–2022.