The Rise and Fall of Projet SIDA

An international research project based in Zaire provided many early insights into AIDS; its premature demise in 1991 has left a potential treasure trove of data

KINSHASA, DEMOCRATIC REPUBLIC OF THE CONGO—It's easy to see that many things are missing from Kinshasa General Hospital. Overcrowding is so severe that some patients are forced to share a bed. People are rolled around on World War I–vintage wheelchairs that have only three wheels. Holes in the walls mark the places where electrical boxes have been torn out. Tiles have fallen from the walls and are missing from parts of the floors. In the plaza that separates the wards, multicolored lizards crawl over charred wooden stumps, the remnants of trees that once provided much-needed shade. Except for the cellular phones owned by some doctors, there is no communications system. But there is one, less obvious, thing missing that a decade ago made this hospital, then known as Mama Yemo, a focal point for scientists from Europe, the United States, and Africa: AIDS research.

Mama Yemo Hospital was a critical component of Projet SIDA (French for AIDS Project), a Zairian-American-Belgian research program that began in 1984 and quickly shed much light on the emerging epidemic. "The epidemic of AIDS, not only in Africa but in other parts of the world, became known because of the work here," says cardiologist Bila Kapita, who helped establish the Zairian side of the collaboration. "And many Zairian doctors learned how to do research." Says Claudes Kamenga, who worked with the program for 5 years and is an epidemiologist in the behavioral research unit at Family Health International in Arlington, Virginia, "Zaire was shining because of Projet SIDA."

To the dismay of many scientists, however, Projet SIDA suddenly ended in 1991, a victim of the civil unrest that tore Zaire apart in the 1990s. The machine-gun fire that rang through the city that September led to the project's demise and signaled the beginning of the end for Zairian dictator Mobutu Sese Seko, who finally was ousted from power last May. Today, says Kapita, with a mixture of sadness, frustration, resignation, and finality, "Projet SIDA is dead." As Eugène Nzilambi Nzila, a key clinician in the project from its outset, says: "We don't think about research now."

Outsiders who launched and ran Projet SIDA provide a glowing eulogy. "It's one of the things I'm really proud of in my life—that I contributed to this project and made it happen," says Belgian epidemiologist Peter Piot, who now heads UNAIDS, the United Nations AIDS program. James Curran, former acting director of the Division of HIV/AIDS Prevention of the U.S. Centers for Disease Control and Prevention (CDC) in Atlanta, the project's main funder, calls his involvement "a tremendously enlightening experience." Says Curran, now head of Emory University's School of Public Health in Atlanta: "During many of its early years, it was the preeminent AIDS research project in Africa in terms of number of people involved and quality of research coming out." Thomas Quinn of the U.S. National Institute of Allergy and Infectious Diseases (NIAID), another key contributor to the project, says, "The number of papers we generated out of there was just incredible."

MALCOLM LINTON

Overcrowding. Patients in Kinshasa General Hospital sometimes have to share beds, and many basic facilities are missing.

But, in spite of its many accomplishments, Projet SIDA—which at its peak had a $4 million annual budget—also provided some object lessons in the difficulties of conducting research in poor, conflict-ridden countries, where the scientific objectives of the studies don't always mesh with urgent public health needs. It also left behind an unexploited legacy: a vast accumulation of blood samples from patients—some of whom are still being followed today—that could offer valuable insights into preventing and treating the disease. And it left in its wake trained medical investigators and technicians who, like Kapita and Nzila, would love to do research once again. "We in Congo are at the heart of the problem," says Kankienza Muana'mbo, head of the National Institute of Biomedical Research (INRB), which once housed a main Projet SIDA lab. "We have human beings and we have biological materials, but we don't have fresh resources to look at the problem. And we think that doing research here in Congo can bring some solutions for the whole world."

Spreading HIV/AIDS research

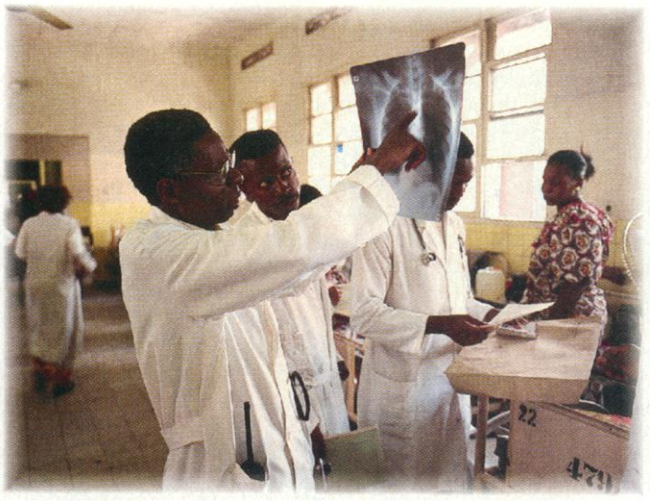
Turn back the clock to the summer of 1983. HIV had just been isolated, but scientists had yet to prove conclusively that it caused the disease. AIDS itself, which had first been recognized 2 years earlier in Los Angeles, was labeled a disease of "the four H's": homosexuals, heroin addicts, hemophiliacs, and Haitians. Mosquitoes were still a suspected vector of AIDS. And the impact of the disease on the African continent had yet to be described. One afternoon that summer, Quinn and NIAID then-director Richard Krause met at a cafe in Vienna with Piot, who at the time was with Belgium's Institute of Tropical Medicine (ITM). The topic of discussion: hints from a variety of sources that AIDS had struck Zaire.

Piot had seen Zairian patients at the ITM who had AIDS. "I was dying to go to Kinshasa and see what was going on, but I didn't have the money," says Piot. And Quinn and Krause had recently returned from Haiti, where they learned that many Haitians had worked in Zaire after it became independent from Belgium in 1960, and then were forced out in the '70s. "With that history I said, hey, we've got to get into Zaire," recalls Krause, now a scientific adviser at the Fogarty International Center, a branch of the U.S. National Institutes of Health (NIH). They decided there and then to form a collaboration. "I was committed to devoting substantial funds to that," says Krause.

The trio met again that fall in Belgium to map out the collaboration. They were joined

by the CDC's Joseph McCormick, who had much experience working in Zaire and had independently received official clearance to investigate AIDS there. On 18 October, Piot, McCormick, and Quinn set out for Kinshasa. "Our first problem," says Piot, "was to see whether we were welcome or not." They met with the minister of health, who, says McCormick, spelled out all the other diseases plaguing Zaire. "He said, 'You're welcome to go look, but this is not going to take on any priority.' " They took that as a green light to meet with Kapita, who then was head of internal medicine at Mama Yemo. "It's really thanks to him that the whole project could start," says Piot.

Not only did Kapita welcome the foreigners, he also deeply impressed them with his independent observations about AIDS, taking them around the wards of Mama Yemo and pointing out patients who he thought had the disease. Analyses of these patients' immune cells proved Kapita right. Says Quinn: "He's probably one of the first Africans to recognize the disease." The work, which was published in the 14 July 1984 *Lancet*, also helped clarify the importance of heterosexual spread of the disease. As the authors wrote, "The findings of this study strongly argue that the situation in central Africa represents a new epidemiological setting for this worldwide disease—that of significant transmission in a large heterosexual population."



MALCOLM LINTON

AIDS pioneer. Bila Kapita, one of the founders of Projet SIDA, examining x-rays of an AIDS patient for signs of lung damage.

In the winter of 1984, the project gained what ended up being a major source of support when CDC epidemiologist Jonathan Mann, a newcomer to AIDS research, visited Piot in Belgium. At the time, Piot was writing a grant proposal to NIAID to launch a joint project. Much to Piot's surprise, Mann said CDC was planning to launch its own project. "Being a pragmatic guy, I said let's work together and see how we can collaborate," says Piot. CDC became the project's major funder: Of its final $4 million budget, roughly $2.5 million came from CDC, $1 million from NIAID, and $0.5 million from ITM.

Projet SIDA officially began in June 1984 with Mann at its head. In the beginning, it consisted of Mann and two Zairian physicians, Bosenga Ngali and Nzila. Mann emphasizes that they contributed significantly to the direction the nascent project took. "Nzila and Ngali didn't hesitate to say what they thought," says Mann. "We were in a canoe. And we were all paddling." They soon were joined by NIAID's Henry "Skip" Francis, who ran the project's lab, and ITM's Bob Colebunders, who headed the clinical work.

In short order, Projet SIDA began addressing the most fundamental of epidemiological questions: How many people were infected? Who got the disease? Was AIDS the same in Zaire as seen elsewhere? Could mosquitoes transmit HIV? The project also helped the country come to terms with its epidemic. "We were living through the time when the government [went from] denying the problem to accepting the problem and dealing with it," says Francis, who now is the chief of clinical medicine at NIH's National Institute on Drug Abuse. "Jon Mann was politically eloquent and could get the message out without frightening people." And Zaire's response to AIDS caught the attention of its neighbors, says Colebunders, who is now back at ITM: "It's because of Projet SIDA that the other countries started to talk about AIDS."

In 1985, Mann recalls attending the first international AIDS conference, held in Atlanta, with Kapita, who had never been to the United States before. "There was such a good feeling of working together," says Mann. "It was really a new world and we were in it together. In the beginning, we were all discovering everything everyday."

Grand aspirations and limitations

Mann left in 1986 to head the World Health Organization's new Global Programme on AIDS. He was replaced by Robin Ryder, an epidemiologist who had previously worked in The Gambia. During Ryder's 4-year stint, Projet SIDA branched into many new areas, employing nearly 300 people—only seven of whom were expatriates. In all, says Ryder, who's now at Yale University, Projet SIDA had more than 20 Landcruisers, a better computer system than the one used by the CDC, and state-of-the-art machines that could separate one type of immune system cell from another. "It was a research factory," says Quinn. Ryder says 15 or so Zairian physicians were the "backbone" of the project. "It was sort of like a plant when you give it water and it really perks up," says Ryder. "They just thrived."

A steady stream of scientific insights began to flow from the program, which now included a clinic devoted to the study and treatment of prostitutes. With help from ITM's Marie Laga, Projet SIDA proved that preventing and treating sexually transmitted diseases (STDs) decreases the incidence of new HIV infections. Careful investigations of HIV-infected pregnant women documented the rates of transmission to their infants and attempted to explain why the majority of babies remained virus free. Projet SIDA also rigorously measured both the prevalence of HIV and the rate of new HIV infections in thousands of people, critical work for establishing "cohorts" that can participate in vaccine trials. To date, more than 120 publications have come from Projet SIDA, and more than 1000 abstracts have been presented at scientific meetings.

Yet Projet SIDA was not, in Piot's words, "a honeymoon." One source of unease was the Zairian government. In 1986, at the second international AIDS conference in Paris, Kapita gave an address about AIDS in Africa at the opening plenary session. A quiet and modest man, Kapita was deeply honored by the opportunity. But after he spoke, a Zairian doctor came up to him with a warning. "You think you're here to be a star," Kapita recalls being told. "You must know that all you're telling here is being transmitted to Kinshasa. We're waiting to decide what to do with you."

When Kapita returned to his office at Mama Yemo Hospital, an officer from the Ministry of Health was there waiting, with instructions to take him to prison. Fortunately, a friend in the ministry intervened, and Kapita says he never faced political problems again. But the episode underscores that the difficulties facing AIDS researchers in Zaire went far beyond struggling to find a working phone line or a clean pair of latex gloves.

For many Projet SIDA members, the problems intensified over time. "There were lots of fights," acknowledges Piot. Oddly, the main battles had little to do with Zaire; instead,

they broke out between NIH and CDC.

Tensions between these two research heavyweights, both of which are part of the U.S. Department of Health and Human Services, surfaced from the moment Mann first set up shop in Kinshasa. "Since he spoke fluent French, he had everything worked out with the minister of health that CDC was in charge," recalls one NIH insider who asked not be named. "That really pissed off NIAID because it was our idea." Piot says he stayed clear of the power brokering: "I never understood the politics. For me. it was not a real problem. ... And after all, CDC has more field experience than NIH." But the rift between the American agencies was real—and it grew, complicating the difficult decisions that had to be made about research priorities.

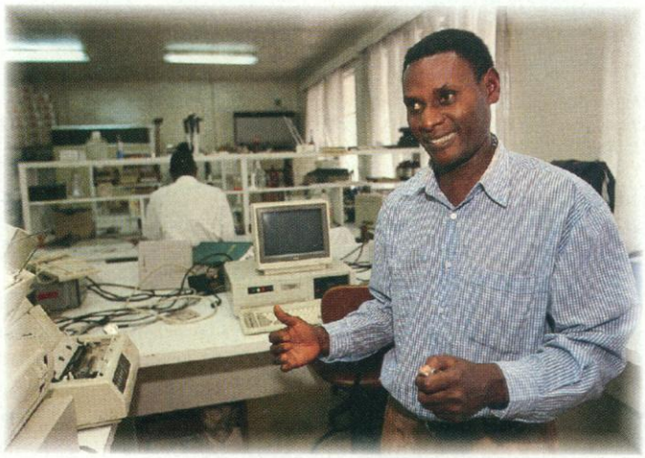
By the time Ryder took over, the wrangling had become more than a nuisance. "It was the bane of my existence," says Ryder. "I never had problems with the Africans." According to Ryder and others, a difference in outlook between the two U.S. agencies fueled the conflict. "People from the CDC were ready to think big, big, big. But 'big big big' means there are lots of lab samples to be tested, and NIH ran the lab. So there was some real push and shove because they'd say, 'You can do the study, but we're not going to do the lab work.' " The NIAID researchers had their own projects that they wanted to pursue, Colebunders and others explain. "They wanted to do more sophisticated virological and immunological work, and that was not the interest of CDC and Zaire itself," Colebunders says.

Although the involved Zairians—who now call themselves Congolese—view the project as hugely successful, they have their own complaints. One critical weakness, says Kakanda Kanjinga—a clinician who, like many of her colleagues, went straight from medical school to a Projet SIDA study—is that the program made little explicit effort to teach locals about research. "When I was at Projet SIDA, I didn't even know I was doing research," says Kanjinga, who subsequently earned a master's of public health at the University of California, Berkeley. "I really didn't understand the purpose of what we were doing."

CDC's William Heyward, who took over from Ryder in 1990, says the project was on its way to filling that gap, noting that it helped send a dozen Zairians to the United States for advanced degrees. He and his colleagues had hoped these "team leaders" would then do "trickle down" training. "I feel quite proud about how much we did do," says Heyward.

Kapita has a different complaint: Projet SIDA paid too much attention to epidemiology and not enough to treatment and prevention. "I'm sorry to tell you that Projet SIDA had very little impact for infected people here," he says. "It would have been useful for them to ask us about what was the useful thing for us they could do here." Kapita is particularly disappointed that the Americans and Belgians didn't budget money to screen the blood banks for HIV. "We knew that AIDS was transmitted by blood transfusion, but nothing was done about it," he charges. Money to clean the country's blood eventually came from the German government's international aid program, Gesellschaft für Technische Zusammenarbeit.

Projet SIDA's limited emphasis on treatment even caught the attention of Mobutu (who died of prostate cancer in September). In the summer of 1988, Jack Whitescarver, former deputy director of NIAID, said he was summoned to the Madison Hotel in Washington, D.C., to meet Mobutu. When he entered the Zairian president's hotel suite, Whitescarver says, "a long line of enormous guys with guns closed in on us" and shunted them over to Mobutu, who wanted to know about treatments. Whitescarver explained that Projet SIDA was addressing the problem. "I've never been so terrified," he says. "I wasn't sure I was going to get out with my life."



MALCOLM LINTON

Long-term data. Eugène Nzila has a decade's information and sera from prostitutes exposed to HIV but who remain uninfected.

Piot says those involved with Projet SIDA were acutely aware of the tensions between research needs and public health needs. "That's a big discussion we always had: What is the responsibility of what is primarily a research project working with research funds in terms of doing something for the country?" The cost of screening the blood supply, notes Emory's Curran, turned out to be roughly equal to the entire Projet SIDA budget. Project officials also point out that the clinic for prostitutes, opened in 1988 in the Kinshasa neighborhood of Matonge, helped many by providing drugs for their STDs and condoms and education to prevent them. "Before there was the Matonge clinic, I would get infections all the time and miss work," confirms "Alpha," a prostitute who works dance clubs in one of Kinshasa's many downscale neighborhoods. Support from Médecins Sans Frontières (MSF) has kept the clinic alive to this day, and it now serves the public at large.

Salaries for local researchers created another thorny issue—one that often bedevils international research projects. Skyrocketing inflation in 1990 and 1991 drove down the standard $1000 per month salary—which, according to U.S. State Department rules, had to be paid in local currency—to less than $200. "I couldn't live on that," says Kavuka Luwy Musey, a former Projet SIDA physician who is now at the University of Washington, Seattle. Kanjinga's husband, Yadiul Mukadi, a clinician who was studying tuberculosis treatment with Projet SIDA, says the inflation problems had a dramatic impact on the program. "We had a very bad period where our attention was shifted from talking science to talking salary," says Mukadi, who now works on TB at the California State Department of Health in Berkeley.

Heyward and his top CDC colleague in Kinshasa, Michael St. Louis, fought hard to solve the currency problem. "That was one of the most terrible things during the time I was there, to watch our colleagues suffer," says St. Louis. "We knew they were having shrinking buying power and income, but we had these absurd rules. The amazing thing to me was that it didn't have more impact on their work." Heyward adds, "The State Department was just totally unsympathetic to the problem, and we were just totally frustrated."

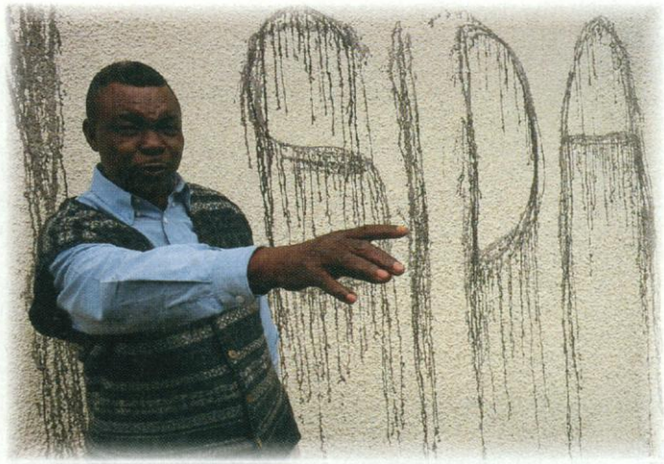
A bad fall

The inflation problem was also tearing apart the rest of the country. In September 1991, Zairian soldiers, angry that they hadn't been paid, decided to turn Kinshasa upside down, leading to widespread looting and mayhem. St. Louis well remembers the night that soldiers started firing their machine guns outside the American compound where he lived with his wife and two infants. "We didn't know what the intent was," he says. "There was one very scary

time when people massed outside our gate and were banging on the door."

At the Projet SIDA laboratory housed at the INRB, Delfi Messinger, an American zoologist, made a decision that many credit with saving masses of data and samples that had been accumulated. Frightened by the machine-gun fire and people running in the streets, Messinger decided to kill a sheep, put its blood in a 50-cc syringe, and squirt "SIDA" in dripping, meter-high letters on the wall outside the institute. (She repeated this with paint during later periods of unrest.) She also put snakes in cages in front of the entrances to all of the institute's buildings and, to "booby-trap" her car, put a snake in it, too. "It was scary," says Messinger, who works on the conservation of a rare chimplike ape called a bonobo. "It was worse than a nightmare."

A few days later, with the city under the guard of Belgian paratroopers and the French Foreign Legion, Heyward, St. Louis, and the other Projet SIDA expatriates were evacuated across the Congo River to Kinshasa's sister city of Brazzaville, and they returned to the United States. Eight months later, the CDC and NIH leaders, convinced that the country was still in a quagmire, pulled the plug on Projet SIDA.



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Protection. Kankienza Muana'mbo, head of the National Institute of Biomedical Research, stands in front of a warning painted on the old Projet SIDA lab building to deter looters.

To this day, several Congolese researchers cannot understand why the project had to end so abruptly. "I wish they could have tried more to keep that project alive," says Kamenga. "There should have been more trust in those who were remaining there, the locals. They just assumed because the Americans and Belgians were leaving, they couldn't continue."

In 1992, Skip Francis, who had left the project 4 years earlier, found himself back in Kinshasa shutting it down. In part because he was a black American, Francis was asked to return and retrieve equipment, half the stored sera, and data. "It was extremely controversial," says Francis. "You now had a completely Zairian operation, and now [the Americans] are going to send someone back to take half their stuff."

Francis encountered trouble even before he reached Kinshasa. He took the Brazzaville ferry into Kinshasa, and, at the border, a soldier hit him with a garden hose. He says he "almost got shot," too. "I had the misfortune to be wearing the pants that military people wear with all the pockets," says Francis. "A soldier said to me, 'The pants or you die.' " The soldier settled for $10 instead.

The Projet SIDA team was none too happy to see him. "Basically, they hadn't had a lot of communication [from the Americans]," says Francis. "They were extremely upset. I remember very vividly that first meeting: You had 10 Zairians yelling at me in two languages. It was an agonizing process." During the next few days, the Zairians told Francis which pieces of equipment they wanted to keep and which ones they didn't think they could use. They also shared data and sera that ended up being used in further studies done in the United States.

Musey, who was the lab leader then, wishes they had adopted "a more responsible attitude" with Francis. "Skip was a very nice person and said, 'This is what I'm asked to take. What do you think?' " remembers Musey. "The key was how can we get something if we give them the samples? That's where we failed one more time. We needed to give the samples and get something in return, like funding for 5 years so we can continue to do research even at low levels of, say, $50,000 a year."

Francis, for his part, wishes the United States had a more visionary approach to conducting research in countries like Zaire, where there's great sensitivity about foreign scientists doing "safari research"—swooping in, bagging the data, and leaving. "The way we're committed to do research, we're always going to be at risk for safari research because we work in blocks of 5 years," says Francis, noting that the U.K.'s Medical Research Council has funded foreign projects for 25 years.

Mukadi thinks the CDC in particular made a "big mistake" by not continuing to fund the project. "They could at least have kept some life there," he says, noting that the Belgians and MSF have continued to send some support. "People were coming to work every day even if they didn't have salary. They kept coming. ... There are some people I know who are very angry."

Heyward says, "It's a shame that it happened this way," but stresses that the agency could not figure out a way to keep sending in money, which had to go through the U.S. Embassy. "If you have to point the finger at anyone for the way Projet SIDA ended, it was President Mobutu," says Heyward. "It wasn't CDC or the U.S. government's fault. We would love to have Projet SIDA today."

Restarting research

A painful part of Projet SIDA's denouement is that almost everyone involved at the end was delighted with the direction the program was taking. Zaire was one of four developing countries that, with the World Health Organization's imprimatur, was readying itself for trials of AIDS vaccines—trials that would have relied heavily on Projet SIDA. The Zairian researchers were maturing as well, with many of the bright lights ready to return from their training in the United States. As Francis says, "Over time, we would have done more things for the Zairians, and over time, it would have been more and more of a Zairian project."

McCormick, who left the CDC in 1995 and now heads the new epidemiology program at France's Pasteur Institute, still holds out hope for the project. "I wonder if Projet SIDA could be revived," he says. "If Nzila's still there, there are many things to be done that are important. That's a reasonable question to ask."

Nzila is still there. Last month, he showed a visitor to the Matonge clinic a computer print-out that lists 26 prostitutes, followed by the project since 1988, who have never become infected with HIV. Nzila well recognizes that only a few other similar cohorts of "exposed, uninfected" people have been identified, and researchers have studied them intensively looking for clues that might help determine how the immune system can thwart infection—information that might be the key to an AIDS vaccine. He says they still have stored sera from these women that could be analyzed. "We can't do research," shrugs Nzila. "You have to have a lot of money to expand."

Still, Nzila and several Congolese researchers now in the United States hope they'll soon be able to find funds for a collaborative project. And Nzila wants AIDS vaccine researchers to consider once again staging efficacy trials in his country. "If they think they're ready, we'll get ready," says Nzila. "It's important for us to be involved so we will not be outside of the loop."

–Jon Cohen