

## J. Brooks Jackson '82: Taking aim at AIDS

By Anne Bennett Swingle

Johns Hopkins AIDS researcher Brooks Jackson, M.D., could be forgiven if he had mixed emotions about a huge clinical trial he ran in Uganda. It cut the transmission of HIV from mother to infant by almost 50%. But the project also made the 1982 Dartmouth Medical School graduate the subject of fierce public attack.

There are far easier ways to make a living than by running a clinical trial in the developing world. Just building the infrastructure, making the contacts, and training the staff can take years of toil and require millions in grant funding. Then, when all the groundwork is laid, some catastrophe—a revolution, a coup—can wipe out everything. Still, scientists generally agree that the key to finding better treatments for the diseases that batter struggling nations lies in testing promising drugs on their stricken populations.

When Jackson opened his big AIDS trial in Uganda four years ago, none of the usual obstacles stood in the way. He had ample funding from the National Institute of Allergy and Infectious Diseases (NIAID), key contacts in Uganda's government, a well-trained staff, and a state-of-the-art lab. What's more, Uganda, after years of deadly guerrilla warfare and brutal dictators, was relatively calm. Officials in other African countries had turned their backs on the tens of thousands dying from AIDS, but Uganda's government was spending time and money educating people about how HIV is transmitted. Jackson's study moved smoothly into its first stages. But within months, his protocol had thrust him into the midst of a worldwide melee.

Remarkably, Jackson is not a typical international-health type. He's a specialist in neither public health nor infectious diseases, but a pathologist—interim chair, no less, of Hopkins's huge department of pathology. For him, directing a clinical trial overseas is all the more formidable because the work must be blended with the grinding demands of academic medicine to teach, publish, and see patients. Still, since the early 1980s, when he was a resident in transfusion medicine and AIDS was first identified, Jackson's been committed to helping rid the world of this scourge. There was no more obvious place for him to make an impact than in the downtrodden nations of Africa, where the disease was striking up to one in three people.

By the early '90s, Jackson was keen to find a simple, affordable way to cut the spread of AIDS from mother to child in the developing world. Transmission of HIV from a woman to her newborn takes place about 700,000 times a year, usually during the birthing process or through breast-feeding. Yet in the U.S., because infected pregnant women are given AZT starting early in pregnancy, only about 200 babies annually develop AIDS. At \$1,700 a case, however, the AZT regimen used in this country is too costly for most developing nations.

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Jackson had two drug regimens he wanted to try in Uganda, both considerably less expensive than the U.S. method. The first was a much shorter course of AZT, which he would give to infected women and to their infants; the second was a course of the antiretroviral nevirapine, a drug used in combination "cocktail" treatments that have proven highly successful in staving off the disease in this country.

By 1997, Jackson's trial—known as HIVNET 012 because it was part of a National Institutes of Health (NIH)-sponsored network of HIV-prevention trials—was ready to go. It would enroll more than 600 mother-infant pairs. Some would receive AZT, some nevirapine, and some—and this would eventually prove the fire keg—a placebo.

Then, early in 1998, Harvard researchers in Thailand demonstrated that a short, four-week course of AZT could reduce transmission of HIV between mother and infant by 51%. Jackson knew, though, that that regimen would be unaffordable in Uganda and decided to forge ahead with his own protocol. It would allow him to compare nevirapine's results with AZT's and also to show how subjects treated with both drugs fared in contrast to those who received nothing—the standard of care at that point in Uganda.

But within weeks, he was being attacked by a watchdog group called Public Citizen. For Jackson to continue to use a placebo on some subjects in the 012 study after knowing the results of the Thai study, Public Citizen wrote in the prestigious British medical journal *Lancet*, was "deeply unethical."

Brooks Jackson is a mild-mannered, amiable man known as a superb collaborator. "Unethical" is not a word that had ever before been used to describe him. Still, Jackson felt strongly that he didn't want to drop the placebo part of his protocol. Testing the two drugs against nothing, instead of only against each other, was the only way to make a valid scientific assessment of the worth of both medications.

It had taken Jackson nearly a decade to get this big trial off the ground. When he first arrived in Uganda in the late 1980s, he was an associate professor at Case Western Reserve. Mulago Hospital in Uganda's capital city of Kampala had erratic electrical power, few supplies, and no running water. Almost no HIV testing was being done, and clinicians weren't even allowed to tell patients they were HIV-positive for fear they would commit suicide. Before Jackson could even think of starting a clinical trial, he knew he'd have to establish a modern laboratory to support his research.

Over the next few years, he imported practically every single piece of equipment—generators, water distillers, computers—necessary for a health-care clinic. He did it all without a reliable airline, customs procedures, or refrigerated shipping. In the meantime, he had to train Ugandan technicians to perform sophisticated assays and to make certain that each technician became familiar with U.S. concepts like in-

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formed consent, follow-up, data management, and quality control. Now, just as all that was about to pay off, it looked as if the meticulously planned study might have to be canceled.

As pressure mounted, Jackson dropped the two placebo arms of his clinical trial, a step that still riles him today. "No researcher," Jackson says, "can assess a drug's effectiveness with scientific certainty without testing it against a placebo. That's the only way we can know for sure if a short course of AZT or nevirapine is better than nothing."

Working abroad in a study like his can present a Catch-22 for American investigators, Jackson says. "If the trial had been done exclusively by Ugandan investigators who had decided simply to test nevirapine against a placebo, no one would have batted an eye. But because we're Americans and NIH-funded, all of a sudden we're unethical. These kinds of barriers can make it almost impossible to find good solutions for medical dilemmas facing developing nations.

"The real nub of the issue," he adds, "is this: Should a clinical trial be obliged to provide the same drug regimens in developing nations as we do in the United States, even though those regimens won't be affordable or easy to administer in those countries once the trial is over?"

As the 012 study lurched on, Jackson was resigned to simply producing enough preliminary data to determine which of the two drugs he would ultimately test against other potential drug regimens. In the summer of 1999, after the trial had enrolled more than 600 mothers, the NIH got ready to unblind the data; until then, neither the subjects nor the physicians knew who was receiving what.

The data proved stunning: nevirapine was 47% more effective than AZT, reducing the rate of infection in infants from 25% to 13%. Best of all, nevirapine was inexpensive—just \$4 for both doses. If implemented widely, the drug could prevent HIV transmission in more than 300,000 newborns a year. Jackson's findings were announced jubilantly in Kampala by the Ugandan Minister of Health and in the U.S. by Vice President Gore. Many called the study a perfectly constructed clinical trial by a superb academician.

Nevertheless, academic medicine appeared late on Jackson's radar screen. After graduating from Kenyon College with a degree in his-



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*DMS alumnus Brooks Jackson, a pathologist at Johns Hopkins, has spent a lot of time in Africa investigating ways to cut the HIV transmission rate.*

tory, he earned an M.B.A. at Dartmouth, then joined the family coal-mining business in Cincinnati. That lasted less than a year. In 1977, after he'd been on the job for six months, there was a violent United Mine Workers strike that dragged on and on. "I thought, this is not the life I want to have," he remembers.

Jackson returned to Dartmouth, this time to round out his premed requirements. To support himself, he took a job as administrative manager of the pathology lab at Mary Hitchcock Hospital. It was a life-defining decision. Even before entering medical school at Dartmouth, he knew his subspecialty would become transfusion medicine.

By the time Jackson graduated from DMS and entered a pathology residency at the University of Minnesota in 1982, AIDS was a worldwide problem and Jackson had jumped with both feet into HIV research. Four years later, he was providing laboratory support for the national AIDS Clinical Trials Group. "You're in all these conference calls for these clinical trials," he says, "and you start to realize, 'Boy, I could do a clinical trial.'"

**T**he early 1990s found Jackson jetting back and forth regularly between Cleveland and Kampala as he pursued that possibility. A year before his big trial in Uganda opened, he and his wife and three young sons moved to Baltimore, where he'd been recruited to become Johns Hopkins's deputy director of pathology for clinical affairs. Jackson arrived at Hopkins with all the underpinnings for a kind of HIV research—mother-to-infant transmission—that had never been practiced at Hopkins. He brought an American pediatrician he had worked with in Uganda, his HIV lab, a couple of staff members, and a sky-high pile of research dollars.

Jackson has one more big asset: he has the energy of someone half his age. He's been known to arrive on the other side of the world at midnight after a 15-hour flight, check into a hotel, and be out on the streets jogging 10 minutes later. He's a marathon runner and has completed nearly a dozen races, though these days, with a raft of departmental responsibilities in addition to his overseas projects, he has little spare time in which to train. He also continues to serve as an attending physician on Hopkins's blood-bank service. "It's a way to keep

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