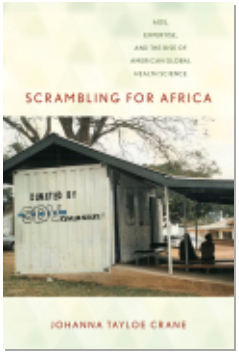
Scrambling for Africa

Johanna Tayloe Crane



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Chapter 1

Resistant to Treatment

As I entered the Oakwood Hotel in San Francisco's Tenderloin District, I was greeted by the incongruous scents of body odor and Indian curry. The Oakwood was one of many single-room occupancy, or "SRO," hotels populating San Francisco's Skid Row neighborhood. Originally built around the turn of the century to house unmarried and migrant industrial workers, by the late twentieth century the hotels were occupied primarily by the elderly, poor, addicted, and mentally ill (Groth 1994). Some residents established long-term homes in these hotels, redecorating their tiny rooms to their taste and paying monthly rent out of their disability checks. Others paid for only a week or two before they ran out of money, and bounced back and forth between the hotels and the street. It was the close quarters and proximity to homelessness that gave the Oakwood and other SROs their distinctive human odor. The curry scent came from the kitchens of the Indian immigrant families who owned most of the hotels and often lived in apartments on the ground floor.

I had come to the Oakwood to visit William, a young, gay, HIV-positive African American man who had lived in the hotel for the past eight years

and was enrolled in the HIV research study that employed me. A native of Georgia, William still spoke with a soft Southern drawl. His small room in the Oakwood was crowded but orderly. His narrow single bed was covered in a homey afghan blanket, and the walls were decorated with birthday and Christmas cards from his family. Somewhat incongruously, a large plastic wall lamp in the shape of E.T. hung high up next to his doorway. In one corner of his tiny room, he kept a hot plate for making himself home-cooked meals. He kept a family photo album handy, and would sometimes pull it out and show me pictures of his mother and siblings in Atlanta.

My job as a research assistant was to pay monthly visits to William and other study participants taking anti-HIV drug combinations (antiretrovirals) for the treatment of their disease. During the several years that I worked for the research study in the late 1990s, I visited residents of San Francisco's SROs and homeless shelters every month to assess their "adherence" to HIV medications—in other words, whether or not they were taking their antiretrovirals as prescribed. Many were. William was not. As I got to know him, I came to learn that his seemingly orderly life was punctuated by periodic crack binges and, later, episodes of mental confusion. During one visit, he complained about a fractured cheekbone, an injury he told me was given to him by a "friend." Nonetheless, he was working to improve his situation, and spoke excitedly about his pending Section 8 application, which, if successful, would provide him with a housing subsidy to move out of the hotel and into his own apartment.

When I asked him to show me his HIV medications, William would pull out a plastic shopping bag filled with a dozen half-filled bottles of pills. Looking at the prescription dates, I would try to puzzle out which were old and which were current. Often, the combinations of pills he told me he was taking seemed to make no sense. William himself was confused and inconsistent about what the doctor's instructions had been, and as the jumble of pill bottles continued to accumulate in number and variety over the months, it became clear to me that he was overwhelmed. I worried that he was mixing pills from his old regimens in with his more recent prescriptions, and suspected that his doctor was poorly equipped to manage a patient living on the edge of homelessness, as William was. My employer, Dr. Jason Beale, an HIV physician himself, gave the doctor the benefit of the doubt and guessed that William's hodgepodge of drugs was an intentionally prescribed "sal-

vage" regimen, a last-ditch effort at saving a patient whose virus had become resistant to multiple antiretrovirals.

William eventually moved out of the Oakwood, not because he got an apartment, but because the hotel caught fire and his room—as well as his possessions—were destroyed. After the fire, he moved from hotel to hotel. His appearance became unkempt and he became less and less mentally lucid. Finally, he returned home to his family in Georgia, where he eventually died of AIDS.

In 2003, a few years after William's death, I found myself in the back seat of a taxi in Kampala, Uganda, being interviewed by an American radio reporter. I was in Kampala for the summer at the request of Dr. Beale, who had asked me to interview patients enrolled in his new study of adherence to HIV treatment in Kampala, where antiretroviral drugs (ARVs) were just beginning to become available. For the first decade following the discovery of effective HIV therapy, the only antiretrovirals that had been available in Uganda were what one Ugandan doctor described to me as "briefcase drugs" brought back from trips to Europe in the personal luggage of the wealthy. However, by 2003 Uganda was importing ARVs from Cipla Pharmaceuticals, a generic drug manufacturer in India, and selling them to patients nearly at cost. The price was about $30 a month, and although this was still quite expensive for most Ugandans, it was much more affordable than the $1,000 a month that equivalent drugs cost in the United States (Whyte et al. 2004). Dr. Beale's study was documenting the impact of these drugs on patients' health, as well as their adherence to the regimen. The American journalist was an acquaintance of Beale's scientific mentor and a health correspondent for a nationally broadcast news program.

The reporter rode in the front seat, and awkwardly turned around and pointed her shotgun microphone towards the back where I was sitting with my colleague and friend Idah Mukyala. She had just accompanied Idah and me on a visit to a study participant named Esther, an unemployed mother of three. During our visit, Idah had surveyed Esther about her adherence to the medications, asking her questions nearly identical to those I had asked William four years earlier: "How many doses of your medication did you take yesterday? How many doses did you take the day before that?" Unlike William, Esther had only one bottle of pills, labeled "Triomune." She took only one pill twice a day. (Unencumbered by Western intellectual property

rights, the Indian company had engineered a single pill containing three different antiretrovirals, a formulation not possible in the United States, where each drug was owned by a separate, competing pharmaceutical company). And also unlike William, she said she almost never missed a dose of her medication. The one exception had been just after she lost her job as a maid, when she had missed four days of the drugs because she couldn't afford to purchase a new bottle. Fortunately, she had been able to get support from a charitable organization that agreed to sponsor her medications from then on. However, she was still struggling to find enough money to buy food and to pay for her children's schooling. In words more distressing than reassuring, she told us, "It is only that I don't have a job and enough to eat—otherwise I'm not stressed anymore."[1] The visit ended with the reporter discreetly handing Esther several folded bills, uncertain of how else to respond to the situation.

During our conversation in the taxi afterwards, the reporter asked Idah and me about the research. The study that employed us was one of a growing number of projects studying antiretroviral treatment in Africa, most of which were finding very high levels of adherence to the drugs—much higher, in fact than average rates in the United States. I found myself repeating this finding into the microphone, telling the reporter that I had worked for a similar HIV treatment study back in the United States, and that people "here"—in Uganda—"take their pills more correctly than in America." Idah described how patients who owned mobile phones would set the phone's alarm twice a day as a reminder. A few months later, our words would be nationally broadcast on U.S. news radio as part of the reporter's story on HIV treatment in Africa.

That same fall, the *New York Times* published a front-page story summarizing the results of studies conducted in four countries across the African continent. The headline declared, "Africans Outdo U.S. Patients in Following AIDS Therapy" (McNeil 2003). The article described research conducted in Botswana, Uganda, Senegal, and South Africa in which patients were found to be taking over 90 percent of their antiretroviral medications. Several doctors quoted in the article emphasized that this was

1. See Kalofonos 2010 and Weiser et al. 2010 on food insecurity and ARV treatment in Africa.

significantly higher than typical adherence rates in the United States, which tended to be around 70 percent. These were surprising findings, as prominent health experts and policymakers had long assumed that adherence to the medications would be poor in Africa. Just two years earlier Andrew Natsios, the chief administrator of the U.S. Agency for International Development, had asserted that many patients in Africa "don't know what Western time is" and would therefore be unable to take HIV medications as scheduled (Donnelly 2001). Similar comments were made by an unnamed senior U.S. Treasury official (Kahn 2001). Because poor adherence was believed to cause the virus to become drug-resistant, a number of scientists had cautioned against expanding access to ARVs on the continent on the grounds that it could create a secondary epidemic of drug-resistant HIV. Now, by contrast, it seemed that Africans were being "made up" as "good adherers" (Gilbert 2005, 6; Hacking 1999).

The studies turned the prevailing Western assumption about HIV treatment in Africa on its head. Yet, I read the *New York Times* article and listened to my own assertion in the radio reporter's story with discomfort. It was good news that antiretroviral treatment in Uganda and other African countries was going well, but it was troubling that this finding was always presented in contrast with the comparatively poor performance of patients in the United States. Why were we so intent on framing Africans as model patients? And why, in order to do so, had I been so quick to throw American HIV patients—patients like William—under the bus?

In this chapter, I address these questions by examining the politics and science of antiretroviral therapy during the early years of the "treatment era." This was a time of great uncertainty as efforts to understand the biological mechanisms of the new drugs evolved contemporaneously with efforts to describe the risks and benefits of international ARV access. During this period, the ethical imperative to treat everyone in need appeared to be distinctly at odds with the duty to shield the public from disease threats, revealing a tension between two different forms, or "regimes," of global health (Lakoff 2010). Advocates of wider access to antiretroviral therapies invoked a global health aligned with humanitarian medicine, arguing that the scope and severity of the AIDS epidemic constituted a medical emergency and that action must be taken to alleviate suffering. In contrast, those cautioning against treatment in Africa relied upon a global health regime rooted in

health security, in which drug-resistant HIV constituted an emerging infectious disease from which the world must be protected (King 2002; Lakoff and Collier 2008).

In this context, evidence suggesting that patients in Africa could (or could not) adhere or would (or would not) cultivate a drug-resistant "doomsday strain" was inherently political (McNeil 2003). Sociologist of science Dorothy Nelkin has argued that although scientific controversies typically take the form of debates over technical issues, they are often, at heart, arguments over moral and political questions (Nelkin 1995). This chapter explores two of these seemingly technical debates in an effort to foreground the political and moral questions at their cores. First, I recount the scientific and policy disputes surrounding HIV treatment access and drug resistance as they played out in relation to (first American and then African) patients perceived as unlikely to take antiretrovirals properly. Although on the surface this appeared to be a debate about medication adherence and missed pills, I argue that it was ultimately about inequality, citizenship, and Africa's relationship to globalization and modernity. Second, I explore the rise and fall of drug-resistant HIV as a potential "superbug." The perception of drug-resistant HIV as easy to transmit but very difficult to treat fed Western anxieties about antiretrovirals in Africa. However, this perception was based in part on an erroneous assumption that HIV treatment would mirror tuberculosis treatment, where poor adherence had led to the development and spread of a lethal, multidrug-resistant bacterium. As scientific understandings of the mechanisms of antiretroviral resistance developed, researchers instead found that viral resistance could develop even among highly adherent patients, and that drug-resistant virus was often treatable (though certainly not benign). Moreover, the arrival of a candidate "nightmare strain" of HIV in New York City forced a public reckoning with assumptions about the global geography of antiretroviral resistance and the framing of Africa, rather than America, as the location from which drug-resistant HIV would emerge and spread.

The chapter concludes by considering the perspectives of Ugandan doctors on the debates over antiretroviral adherence, drug resistance, and Africa. Their opinions about antiretroviral adherence and resistance among their own patients are diverse, but collectively their reflections suggest that the long-awaited arrival of internationally-funded HIV treatment in their country signaled not only new hope for patients, but a form of global recog-

nition and inclusion for a continent still struggling for respect and legitimacy in the postcolonial era.

A Divided Epidemic

For the first fifteen years of the epidemic, HIV was a death sentence in slow motion. Initial HIV infection was typically accompanied by a bout of flu-like symptoms, followed by a symptomless period that could last for several years—even a decade—before the virus's gradual attack on the immune system led to AIDS, a syndrome marked by extreme weight loss, disabling and sometimes disfiguring infections, and other "opportunistic" illnesses, eventually ending in death. Beginning in the 1980s, doctors and researchers began testing a variety of experimental medications against the new disease, but even the most promising drugs worked only temporarily. Patients given AZT (zidovudine), the first drug to show any efficacy against the virus, initially improved, only to decline rapidly upon developing resistance to the medicine. The same thing happened with subsequent anti-HIV drugs. Researchers learned that as a retrovirus,[2] HIV was prone to rapid genetic mutation. This tendency posed a major barrier to the development of effective AIDS treatment, as HIV's mutability allowed it to quickly evolve into variants that were genetically resistant to AZT and other similar antiretroviral drugs.

This changed in the mid-1990s, when researchers developed additional classes of HIV medications that attacked the virus in new ways. When prescribed in tandem with the older drugs, these combinations—dubbed highly active antitretroviral therapy, or HAART—were able to stave off drug resistance and preserve patients' health for the long term in ways that had been previously impossible. The remarkable recovery of AIDS patients very near death following treatment with HAART was widely described as "the Lazarus effect." In the United States, the regimen's high cost—between ten and fifteen thousand dollars a year—was covered by insurance companies and the AIDS Drug Assistance Program, a federal funding mechanism

2. Retroviruses are viruses that carry their genetic information in the form of RNA rather than DNA.

initiated to ensure that even the uninsured could access treatment. As a result, by the end of 1996 the death rate from AIDS in the United States declined for the first time since the onset of the epidemic fifteen years earlier (CDC 1996).

Elation over the success of the new treatment dovetailed with a rising awareness of the global scope of the AIDS pandemic. Because AIDS was first documented in California and New York City, it was initially viewed primarily as an American disease, especially by those outside the United States[3] (Farmer 1992). Within a short time, however, it became clear that AIDS was global. Reports from sub-Saharan Africa, in particular, grew increasingly alarming as time passed. In East Africa, a zone of political instability and black-market trade between Uganda and Tanzania created a perfect storm for an explosive epidemic in the 1980s and early 1990s (Iliffe 2006). In the late 1990s, it became clear that southern Africa was even more severely impacted, and reports from the region began to border on the apocalyptic. In Botswana, for example, one-third of the adult population was infected by the year 2000, up from about 3 percent only a decade earlier (ibid., 39). A U.S. National Intelligence Estimate report released in January of 2000 predicted that a quarter of the population of southern Africa was likely to die of AIDS, and warned of the possibility of "demographic catastrophe" in some African nations.

Escalating reports of the epidemic's devastating effects in Africa clashed with sentiment in the United States that the discovery of HAART meant AIDS was on the brink of being conquered. In 1996 a *Newsweek* cover story ran the hopeful headline, "The End of AIDS?", and in the months that followed, HIV became increasingly described as a "manageable, chronic disease" (Leland 1996; Jacobs 1997). But not long after, reports from Africa warned that as many as one in four people might be infected in the hardest-hit countries (Altman 1998). In his ethnography of the epidemic in West Africa, anthropologist and HIV doctor Vinh-Kim Nguyen describes his personal experience of this moment in AIDS history from his vantage point in a Canadian hospital:

3. In some African countries, there was a running joke that the acronym AIDS stood for "American Invention to Discourage Sex" (Schoepf 2003).

> I remember the first clinical trial in 1994 that used one of the new drugs—saquinavir—in combination with two of the older drugs we used to prescribe singly. The results were stunning. In our hospital, patients stopped dying. Some patients were literally resurrected from their deathbeds by the new drugs. I wondered how these miraculous new treatments would get to Africa. But in the AIDS conferences I attended, this was not discussed. The drugs were too expensive. In Africa, it would have to be prevention and perhaps palliative care (Nguyen 2010, 3).

Indeed, the African experience of the discovery of HAART was one of being "on the outside looking in" (Mugyenyi 2008, 96). Dr. Peter Mugyenyi, a Ugandan HIV expert and leading advocate of treatment access in Africa, described the sentiment at the 1996 International AIDS Conference in Vancouver as "either that of indifference or open discouragement—just in case the Africans got carried away with ideas of introducing the highly sophisticated designer drugs to their miserable set up" (ibid). The AIDS epidemic was dividing in two: a treated epidemic in wealthy countries, and an untreated one in poor countries. For activists and supporters of treatment, the contrast was difficult to bear, and as the 1990s wore on advocates around the world grew increasingly vocal about the imperative of making HIV treatment accessible in Africa and other regions in the global South.

Initially, it was the high cost of AIDS medications that appeared to be the primary barrier to global treatment access. With governments in the United States and other wealthy countries struggling to cover the new drugs at home, it was difficult to imagine funding treatment abroad. But before too long, lower- to middle-income countries like Brazil, South Africa, and India began manufacturing generic ARVs for domestic use and export (Grady 2001). Sometimes described as "copycat" drugs, these pills were developed using reverse-engineering and were produced in nations where law did not require observance of American and European patent protections.[4] Generic antiretroviral combinations could cost as little as a dollar a day per

4. In the United States patent protection is granted for a period of twenty years, during which the manufacturer enjoys market exclusivity. Only once a patent expires is it legal for other companies to make and sell generic versions of a drug. Though generic ARV production initially faced aggressive opposition from the multinational "branded" pharmaceutical industry, it was eventually upheld by the World Trade Organization as allowable under the group's Trade-Related aspects of Intellectual Property, or TRIPS, Agreement (Westerhaus and Castro 2006).

person, and although this price was still out of reach for many individual African patients, it made the possibility of external, donor-funded treatment in Africa much more economically feasible.

In the Name of Public Health

Even as drug pricing became less prohibitive, the political will necessary to allocate aid dollars in support of antiretroviral therapy in Africa remained largely absent in the United States and other wealthy donor nations. Once global treatment became economically possible, the debate about expanding ARV access to the "developing" world, and in particular to sub-Saharan Africa, shifted to questions of feasibility at the technical and behavioral levels. In this shift, concerns about economics became reframed as concerns over global public health. First, researchers and policymakers asked, would it be technically feasible to safely and consistently administer high-cost, high-tech, multi-pill regimens in areas with limited physical and health infrastructure? And second, would patients with little education and few resources be willing and able to adhere to (i.e., "comply" with) the regimens? Concerns about consistent drug supply and adequate adherence were both rooted in the fear of drug resistance: if patients missed doses, their HIV could easily mutate into a drug-resistant strain, rendering the drugs ineffective and, as one medical journal article argued, "making the developing world a veritable 'petri dish' for new, treatment-resistant HIV strains" (Popp and Fisher 2002).

Within HIV medicine, the belief that missed medication doses would lead to viral resistance was hegemonic from early on. In the United States, anxiety surrounding antiretroviral adherence and drug resistance was fed by recent failures in tuberculosis control. In the late 1980s and early 1990s, tuberculosis rates in the United States began to climb at an alarming rate, spurred on by Reagan-era cuts to anti-TB programs and rising cases of HIV (which made infected individuals more susceptible to TB by weakening their immune systems).[5] In 1991 the TB population in New York topped

5. Global rates of tuberculosis and drug-resistant TB were also on the rise at this time, leading the WHO to advocate a policy of "directly observed therapy," or witnessed dosing, for TB treatment (Harper 2010).

4,000 for the first time since 1967, and many more of these cases were drug-resistant than ever before (Specter 1992). One outbreak of multidrug-resistant TB (MDR-TB) killed thirteen inmates in New York prisons (McFadden 1991).

Experts argued that resistant TB was on the rise because many patients were failing to complete the months-long regimen of antibiotics required to cure active tuberculosis, often because of mental illness, drug abuse, or homelessness. As a result, New York City began to impose enforced hospitalization on "recalcitrant" tuberculosis patients who repeatedly failed to complete their treatment. These modern-day Typhoid Marys were often patients like William: African Americans from the most marginal fringes of society (Navarro 1992).[6] Similar issues arose in other U.S. cities as they confronted their own growing rates of tuberculosis. Health officials justified the medical detention of noncompliant patients as necessary for public safety. One Denver professor of medicine put it this way: "Say I'm totally drug-resistant and I still like going to movies and I like going to restaurants and I like getting in buses and I like teaching in schools," he told a *New York Times* reporter. "If I had a gun and I waved it around in all those places you would lock me up. This is no different than a loaded gun" (Belkin 1991). This coding of incomplete adherence as a threat to not only one's own health but to the general public, as well as the public image of the nonadherent patient as poor and dark-skinned, would play a significant role in subsequent debates over the threat posed by drug-resistant HIV.

Like TB treatment, successful HIV treatment required patients to take a combination of several drugs over an extended period of time. From early on, the guidelines for HIV treatment echoed those for tuberculosis treatment and stressed the importance of assuring "near-perfect" patient adherence—95 percent or higher—as a key tool for warding off the development of drug-resistant virus (Chesney 2003; DHHS 2003). Understandably, adhering to such regimens was challenging for many patients—especially given that

6. Of the thirty-three tuberculosis patients detained by the NYC Public Health Dept. between January of 1988 and April of 1991, 79 percent were black, 79 percent were drug users, 49 percent were homeless, and 61 percent were men. Many were also mentally ill, and had been hospitalized for TB several times previously. Seventy-three percent had drug-resistant tuberculosis (Navarro 1992). The law under which tuberculosis patients were forcibly hospitalized dates from the era of Mary Mallon—"Typhoid Mary"—who was believed to have infected fifty people with typhoid fever prior to 1915 (Barbanel 1991).

the treatment for HIV was indefinite, with no endpoint in sight. Furthermore, the "pharmaceuticalization" of HIV care that came with the development of HAART effectively sidelined broader issues such as nutrition, housing, poverty, and mental health from patient care, as the drugs came to be seen as a "magic bullet" for treating the disease (Biehl 2007). This made it easy to frame patients like William as "noncompliant" or "poorly adherent" rather than socially and economically marginalized.

Having witnessed the recent upsurge of MDR-TB, many AIDS doctors feared the development of drug-resistant strains of HIV among their poorly adherent patients, and some went so far as to withhold ARVs from homeless or drug-using patients they believed would be unable to adhere (Collins 1996; Waldholz 1996; Sontag and Richardson 1997).[7] (Indeed, Dr. Beale's initial research among homeless people living with HIV was spurred by his desire to "prove" that even the homeless could succeed on the new drugs. And, in fact, for every patient in the study who struggled like William did, there were several more who did very well on ARVs). A spirited debate ensued as to whether this practice was a breach of the Hippocratic oath, or a professional obligation necessary to protect the public's health (Baxter 1997; Bayer and Stryker 1997; Lerner, Gulick, and Dubler 1998; Sollitto et al. 2001; Senak 1997).

Once pressure began to mount for antiretroviral treatment in Africa, similar fears resurfaced with a new international slant, shifting the locus of concern from patients like William to patients like Esther. Experts feared that antiretroviral treatment in Africa would backfire. At stake was both the health of individuals, who would gain little benefit from the drugs if they became resistant to them, and the greater public, who could be faced with the threat of untreatable, drug-resistant strains of HIV. The World Bank urged caution, asserting that "Problems with patient compliance are likely to be worse in low-income countries due to low education and the many other problems that poor people in developing countries face" (World Bank 1999, 180–181). A 2001 commentary in the medical journal *The Lancet* raised the specter of resistant virus, arguing, "Widespread, unregulated access to antiretroviral drugs in sub-Saharan Africa could lead to the rapid

7. Studies later showed that clinicians' estimates of who would and would not be adherent were no more accurate than random guessing (Tchetgen, Kaplan, and Friedland 2001; Paterson et al. 2000).

emergence of resistant viral strains, spelling doom for the individual . . . and leading to transmission of resistant virus" (Harries et al. 2001). This article, authored by a team of British and Malawian researchers, is typical in its focus on technology, infrastructure, and expertise—all of which were seen to be lacking in Africa. This and other scientific opinion pieces warned of the possibility of antiretroviral or therapeutic "anarchy" if HIV treatment in Africa were not carefully monitored and controlled (Horton 2000; Stevens, Kaye, and Corrah 2004). While experts who cautioned against global treatment access did not make direct comparisons between the U.S. urban poor and patients in Africa, it seems noteworthy—as Dr. Beale told me, with intentional irony—that the targets of fear remained "poor black people."

Concerns about adherence and drug resistance in Africa were echoed in the press, where writers argued that low-income African patients could not be expected to comply with the multi-pill regimens that even middle-class American patients found challenging (Sullivan 2001). "Unsupervised" distribution of antiretrovirals in Africa would be "dangerous," one physician and medical writer argued, because it could encourage the rapid emergence of drug-resistant HIV that might then "boomerang back to the West" (Mukherjee 2000).[8] This argument was picked up by the multinational "branded" pharmaceutical industry, which in the late 1990s was coming under increasing attack for its pricing practices and its aggressive efforts to block the manufacture of cheaper generic antiretrovirals in poor countries (McNeil 1998).[9] For example, the website of the Pharmaceutical Research and Manufacturers of America (PhRMA), the leading U.S. pharmaceutical industry group, made liberal use of both scientific and journalistic assertions about barriers to adherence in Africa and the associated danger of

8. The author of this article, Siddhartha Mukherjee, would later become a well-known medical writer, and was awarded the 2011 Pulitzer Prize in nonfiction for his book *The Emperor of All Maladies: A Biography of Cancer*.

9. In 1997 a consortium of forty branded pharmaceutical manufacturers filed a suit against the South African government—then headed by Nelson Mandela—in an effort to stop the country's production of generic antiretrovirals. Their lawsuit was supported by the Clinton administration, which, at the urging of the U.S. Pharmaceutical Research and Manufacturers of America, threatened to enact trade sanctions against South Africa (McNeil 1998). In 1999, the Clinton administration withdrew its support of the lawsuit after AIDS activists repeatedly picketed Vice President Al Gore's presidential campaign stops, chanting "Gore's Greed Kills" (Cooper, Zimmerman, and McGinley 2001). The lawsuit was eventually dropped.

drug resistance. "Unfortunately," the industry site claimed, "few developing nations until now have made public health programs a priority. In the case of HIV/AIDS, 'the therapies require taking a dozen or more pills every day at precise intervals without fail, plus high-tech monitoring for viral resistance, plus still more drugs to control side effects,' says *National Journal*. 'Try that in an African town with dirty water and mud roads' " (PhRMA 2006). In passages such as this, the barriers to AIDS treatment in Africa were strategically reframed. It was not international trade policy or corporate drug pricing that stood in the way of treating African AIDS patients, but rather Africa itself—its weak governments, lack of trained physicians, poor laboratory facilities, impoverished and malnourished patients, and "dirty water and mud roads."

Some of these worries had merit. For example, recent research conducted in Uganda has documented that some patients may miss medication doses for lack of easy access to clean drinking water in a private setting (Kawuma 2011), and new ARV distribution programs have had to devise means to ensure drug delivery in areas with few paved roads (Weidle et al. 2006; Bajunirwe 2011). Health care services in many parts of Africa are underfunded, understaffed, and undersupplied—although it is important to recognize that Western structural adjustment policies have played a considerable role in shaping this reality (Pfeiffer and Chapman 2010). Also, as I discuss in chapter 3, the laboratory technologies that are fundamental to HIV care in the United States (CD4 and viral load testing) are not available in many African health care settings. Moreover, it is well known that patients in the United States and other wealthy countries have struggled with the demanding ARV regimens and their side effects, even under the best of circumstances. However, in the U.S. context, even those who argued that denying treatment to patients like William could be justified specified that such decisions should only be made on an individual, case-by-case basis, and not on broad sociodemographic criteria (Bayer and Stryker 1997). In contrast, the argument against treating AIDS in Africa was remarkable in that it succeeded in framing the withholding of treatment from millions of people—indeed, an entire continent—as beneficial for public health. Judging by its publication in leading medical journals, this view was considered scientifically legitimate (though certainly not universal; see, for example Nkengasong, Adje-Toure, and Weidle 2004). How did this come to be?

African Time and "'Africa' Talk"

Science studies scholars have demonstrated that the sanctioning of knowledge as scientifically legitimate is deeply contingent upon the historical and social context in which truth claims emerge (Shapin and Shaffer 1987). In this vein, we can understand the successful framing of antiretroviral treatment in Africa as a threat to health security rather than a humanitarian public health imperative as dependent upon the continued social resonance of deeply held stereotypes positioning Africa and Africans outside "Western" modernity. For centuries, the dominant Euro-American imaginary of Africa has been one of a "dark continent" characterized by disorder and, in particular, disease (Vaughan 1991). Within this discourse, Africa was and continues to be seen as "the world par excellence of all that is incomplete, mutilated, and unfinished"—a foil of "absolute otherness" against which the West has constituted its own norms and subjectivity (Mbembe 2001, 1–2). The implication of African alterity (Mudimbe 1988) can be seen in expert warnings framing the continent as a place unsuitable for modern antiretroviral drugs.

This historically entrenched imaginary of African difference—"dirty water and mud roads" dysfunction, lack of "Western time,"—was handily accessible to those who argued against expanding antiretroviral treatment on the continent, and it bolstered their ability to frame the high-tech drugs as inappropriate, even dangerous, for deployment in African settings depicted as primitive. Also at work in the statements of Andrew Natsios and others was a version of what Charles Briggs and Clara Mantini-Briggs have called "medical profiling." Africans were deemed to be "unsanitary subjects," who were "incapable of adopting [a] modern medical relationship to the body, hygiene, illness, and healing" (Briggs and Mantini-Briggs 2003, 10). Placing expensive, powerful medications into such unreliable hands would be both wasteful and dangerous.

The power of this kind of discourse of difference is an instructive example of how representations of "Africa," or what James Ferguson dubs "'Africa' talk," can engender consequences independent of any relationship to empirical reality (Ferguson 2006, 2). "Africa"—always offset in quotation marks—Ferguson argues, is "a category through which a 'world' is structured" (ibid., 5). Though "Africa" conceived this way is more imagined than

real, he argues, it nonetheless has very tangible and material effects: "Fantasies of a categorical 'Africa' (normally, 'Sub-Saharan' or 'black' Africa) and 'real' political-economic processes on the continent are interrelated"—for example, when negative perceptions actively discourage meaningful private investment in African economies (ibid., 7). Arguably, this was also the case with AIDS treatment at the turn of the millennium, where perceptions of "Africa" as a place of "antiretroviral anarchy" and a potential "petri dish" of drug resistance actively worked to maintain the status quo of Africa as a treatment-free zone. Moreover, what began as "'Africa' talk" facilitated the emergence of what we might call "public health talk," in which the nontreatment of a fatal illness was justified as protecting the global public's health. In this way, "Africa" is, as Ferguson says, "a category within which and according to which people must live" (ibid., 5). And perhaps, in the case of AIDS treatment, also a category according to which people must die.

It was within this discursive environment—in which the ability of Africans to tell time was publicly called into question by high-level U.S. policymakers—that the well-publicized findings that African patients were, in fact, highly adherent to antiretrovirals, emerged. The results of the adherence studies profiled in the *New York Times* and on U.S. national radio in 2003 seemed to provide righteous scientific fodder for those, myself included, who found U.S. reticence to support ARV treatment in Africa profoundly unjust. If American patients who took, on average, only three-quarters of their medications had unfettered access to ARVs, it made African patients who took nearly 95 percent of their drugs seem undeniably "deserving" of equal access to HIV treatment. In addition, science seemed to offer a redemptive narrative: the African patient—formerly seen as a danger to global public health—was now redeemed as exemplary in his or her pill-taking behavior. The former "unsanitary subject" was now a model "sanitary citizen . . . credited with understanding modern medical concepts and behaving in ways that make them less susceptible to disease" (Briggs and Mantini-Briggs 2003, xvi).

In this new scenario, it was American patients who didn't match up—a comparison made all the more damning by the fact that they were getting their drugs for free, making their missed doses seem not simple indications of absentmindedness or disorganization, but ungratefulness. "If the whole family is pooling its resources to pay for you," said one American doctor quoted in the *New York Times*, "you damn well better take your drugs.

That's a whole different scenario from the U.S., where patients get free medicine, and if they change therapy, will let a month's worth go to waste" (McNeil 2003). It was the notion of "deserving" treatment that would eventually make me uncomfortable with the *New York Times* coverage and my own brief statements about adherence on American news radio. If, as I had told the radio reporter, it was true that Ugandans took their HIV drugs "more correctly" than Americans, what did this say about American patients struggling to survive, such as William? If adherent African patients deserved treatment, did that mean that poorly adherent African American patients like William did not? Were Africans now model patients, the "worthy poor" whose diligence in taking their pills justified funding the treatment programs that kept them alive? Were impoverished American patients comparatively "unworthy" of these expensive, lifesaving drugs? Was treatment a question of merit, or of human rights? In retrospect, I see this valorization of African over American patients as a tactical move—a "politics of strategic reductionism" (Comaroff 2007). It was a gamble that treatment advocates took in the hopes that it would advance the cause of antiretroviral access in Africa without endangering treatment opportunities for socially and economically marginalized patients in the United States.

Fortunately for William, what ultimately determined his ability to get treatment was not a symbolic "sanitary citizenship" but his actual, legal membership in a country that subsidized the drugs for its citizens. As a citizen of a functioning, wealthy state, William got treatment for his HIV through a federal system designed to provide care for indigent patients—whether or not he was adherent. Although any given individual physician might have hesitated to prescribe ARVs to him, the state supported his antiretroviral treatment even as it failed to provide him with adequate care in other ways. Esther, as a member of a poor, donor-dependent state enfeebled first by colonialism, then despotism, and most recently by structural adjustment and privatization, found that her legal citizenship did her little good in treating her HIV. She, instead, was forced to turn to the "thin" citizenship that Nguyen (2005, 2010) calls therapeutic citizenship, relying on her international contacts within research projects, charitable groups, and even a chance encounter with an American radio reporter to cobble together the resources she needed to keep herself alive. At the same time, as a research subject in an adherence study framed as proof that Africans could take ARVs successfully, her exemplary pill-taking contributed to the construction

of a form of sanitary citizenship for all Africans with HIV. While this rehabilitation of the African patient was a boon in the fight for global treatment access, it came at the cost of providing discriminatory health policies and practices with scientific legitimacy. By allowing drug resistance to continue to be framed as the outcome of individual failure, this positive re-imagining of the African patient reinforced the same bitter logic as its negative predecessor: that some people merited treatment, and others did not.

Historicizing resistance

The public discourse surrounding ARV adherence and resistance had implications beyond the moral framing of HIV patients—it also had consequences for the symbolic framing or "signification" of the HIV virus itself and the global AIDS epidemic as a whole (Treichler 1987). Embedded within Western anxieties surrounding antiretroviral adherence and anarchic imaginaries of Africa and Africans were more subtle assumptions about the causes, lethality, transmissibility, and geography of drug-resistant HIV. Like drug-resistant tuberculosis, resistant HIV was understood to be a rapid and inevitable outcome of missed medication doses. Experts described resistant virus as signifying "doom for the individual" (Harries et al. 2001, 410) and believed that it could be easily transmitted to others, thus posing a significant risk to public health. However, drug-resistant HIV was not always imagined as such a threat. In fact, when I interviewed HIV drug resistance experts for this book, I was surprised to learn that there had initially been "huge skepticism" among clinicians and scientists that HIV drug resistance would have any significant negative impact on patients at all.

When HIV was first discovered in the 1980s, the predominant view in medicine was that viruses, once they developed drug-resistant mutations, became too weak to replicate in the body and were thus unable to cause disease. This belief was based on clinical experience treating the herpes virus with the drug acyclovir. Dr. Ron Pajaro, an American HIV clinician and nationally recognized expert on antiretroviral resistance, explained it to me as follows:

> At that point, there was huge skepticism that anti-viral resistance was at all relevant to the clinic. There was one experience with herpes simplex virus. It

> was common to find acyclovir-resistant virus, but acyclovir would still usually work. It was only in the rare case when it wouldn't work. And the reason for that, it was learned after a while, was that the acyclovir-resistant viruses didn't grow very well in the body. They didn't really replicate well enough to cause any disease. And so that was the expectation for HIV resistance.

Pajaro wanted to test this expectation, and made his mark in the field by putting together a group of doctors and virologists to study the impact of HIV drug resistance on patients. The team he organized analyzed the results of a large clinical trial of AZT, the principal antiretroviral drug available at the time. Their study, published in 1995, showed that drug-resistant HIV was in fact quite different from drug-resistant herpes. AZT-resistant HIV remained able to reproduce itself inside the body, and rendered AZT useless in a matter of months. At the time, these findings were so contrary to what was expected that prominent colleagues accused them of making a mistake in their analysis of the data.

As it would turn out, Pajaro's findings would coincide with historical events that rapidly caused the pendulum of scientific opinion about HIV drug resistance to swing from dismissal to fear. The outbreak of MDR-TB in New York in the 1990s and the alarm that it caused shifted the lens through which drug-resistant HIV was viewed. Rather than comparing HIV to drug-resistant herpes, experts likened it to multidrug-resistant TB, which was potentially lethal and carried with it a particular image of danger marked by race and class (Bangsberg, Moss, and Deeks 2004). "HIV drug resistance frighteningly recapitulates the history of antimicrobial drug resistance in bacteria with a pernicious twist," wrote one prominent HIV researcher in 2004 (Richman et al. 2004, 1398). Following the TB publicity, Pajaro told me, the discourse "was very much the broad brushstroke that resistant HIV is not going to respond to anything."

Once resistant HIV was framed as analogous MDR-TB, it was a short step to figuring potentially poorly adherent patients like William and Esther as threats to public health. However, a closer examination of the history and epidemiology of drug-resistant HIV reveals both these assumptions to be erroneous. Tuberculosis, in retrospect, was a misleading model for predicting HIV drug resistance. Moreover, the major source of drug resistant HIV strains did not turn out to be the urban poor in the United States or

Africa, but middle class (and often highly adherent) patients in North America and Europe.

Cracks in the conventional wisdom about drug-resistant HIV were revealed in a rather dramatic fashion in February of 2005, when the cover of the *New York Post* featured a nearly full-page headline warning of the discovery of a "nightmare strain" of HIV not in Africa, but in New York City, where a gay man in his forties was found to be resistant to all three major classes of antiretrovirals. The man had only recently tested HIV-positive and had never taken any HIV drugs previously, indicating he had been infected with a virus that was *already* drug resistant. Furthermore, his CD4 count was dangerously low, meaning he met the criteria for an AIDS diagnosis even though evidence suggested he had become infected only a few months earlier.[10] This unusual combination of multi-drug resistance and seemingly aggressive disease progression proved so alarming to the New York City Department of Health and Mental Hygiene (DOHMH) that its director, Dr. Thomas Frieden,[11] took the unusual step of holding a press conference to announce the discovery and alert clinicians and hospitals to screen their patients for evidence of the virus (City of New York 2005).[12] The New York officials' alarm was echoed in a case study of the infection published a month later in *The Lancet*, in which experts (including one of the developers of HAART) asserted that the combination of multiple drug resistance and rapid progression to AIDS made the virus "unique" and warned that "the public health ramifications of such a case are great" (Markowitz et al. 2005). At a major scientific AIDS conference that was held (coincidentally) just two weeks after news of the infection was made public, last-minute

10. His CD4 count was 80 cells per cubic millimeter of blood, where normal is between 500 and 1500. AIDS is diagnosed in anyone with a count of less than 200.

11. Interestingly, Frieden was involved in the investigation and combating of the MDR-TB outbreak as a CDC Epidemiologic Intelligence Service Officer and New York City's Assistant Commissioner of Health for Tuberculosis Control during 1990s. In 2009, he became the Director of the CDC.

12. The New York health officials' concern over the virus was fueled by the patient's description of his sexual activity. In the DOHMH's press release, the infected man was described as a methamphetamine addict who regularly engaged in anonymous, unprotected anal sex with other men while high on crystal meth. Calling the case a "wake-up call to men who have sex with men" and citing rising rates of sexually transmitted disease among gay men, Commissioner Frieden urged the gay community to do more to stop the spread of HIV and methamphetamine use among its members (City of New York 2005).

changes were made to the conference schedule in order to devote an entire session to discussion of the virus (Conference on Retroviruses and Opportunistic Infections 2005). The news media jumped on the story, producing multiple articles about the arrival of the potential "AIDS superbug" (Santora and Altman 2005; Perez-Pena 2005; Edozien 2005; Honigsbaum 2005).

That such a virus would arise in New York rather than in Kampala or Gabarone should not have come as a surprise. Despite expert and policymaker anxiety over viral resistance emerging in Africa, it was well established that the bulk of HIV drug resistance occurred in Europe and North America, where treatment had been available for over a decade.[13] For example, one study of San Diego patients reported that nearly half of those on treatment had developed some degree of drug resistance during the late 1990s (Garrett 2001; Richman et al. 2004). Research also indicated that these drug-resistant viral strains were being transmitted to others. Although exact numbers are difficult to come by, a 2004 review showed that anywhere from 8 to 27 percent of newly infected (and never-treated) patients in the United States carried a virus with at least one drug-resistant mutation, and that 10 percent of people newly diagnosed with HIV in Europe showed some drug resistance (Tang and Pillay 2004). In contrast, the review included only one study of drug resistance in Africa, conducted in Côte d'Ivoire between 1997 and 2000, which found no evidence of transmitted ARV resistance.[14]

Significantly, antiretroviral resistance in the United States is most prevalent among highly adherent, well-educated, middle class, white, insured gay men, and not the homeless, mentally ill, and drug-addicted patients of color that physicians initially feared would foster viral resistance (Garrett 2001). The primary reason behind the high levels of resistance in this comparatively privileged population is not a failure to take treatment as prescribed, but rather an aggressive pursuit of effective medication in the face of near-certain death in the early years of the epidemic. Prior to the advent of HAART, it was primarily middle-class gay men and their allies who

13. Brazil and Argentina, both of which have long-standing antiretroviral treatment programs, also have significant levels of drug resistance.

14. Although rates of antiretroviral resistance in Africa have increased over the last decade as treatment has become increasingly available, the transmission of resistant viruses continues to be low (WHO 2011).

mobilized to demand access to experimental treatments for the disease that was devastating their communities. Having spent much of the previous decade fighting for gay and lesbian rights, this was a politically savvy and organized group—and despite ongoing homophobia, they were remarkably successful in getting their demands met (Epstein 1996; Altman 1988; Crimp and Rolston 1990). As a result, many of these patients were exposed to antiretroviral drugs one at a time as they first became available—a phenomenon doctors describe as "sequential monotherapy." This practice was unavoidable given the circumstances, but was later determined to be a perfect recipe for cultivating multiple drug resistance over time. As a result, those patients who survived into the era of HAART often harbored viruses that were already resistant to older drugs such as AZT, 3TC, and d4t. Thus, while the high level of drug resistance in this very adherent population might appear surprising from a purely behavioral perspective, it is less so when examined through a historical lens. The New York "superbug" was born from this history, as it turned out that the New York patient had contracted the virus from a Connecticut man who tested HIV-positive in 1993 and had been treated with both single and dual antiretroviral drugs prior to the advent of HAART (Blick et al. 2007).

Reimagining Resistance

The New York City case served as a reality check on the geography and epidemiology of drug-resistant HIV. But it also unleashed a scientific backlash that ultimately challenged commonly held ideas about the lethality and transmissibility of resistant virus. Even as some experts defended the decision to hold a special press conference to warn the public about the New York virus, other equally prominent AIDS scientists accused them of fear mongering, and described the case as "not a discovery", "not a surprise", "hardly unique", "not a novel finding" and "common" (Brower 2005; Cohen 2005; Smith 2005; Volberding 2005; Piller 2005; Jeffreys 2005). As time passed, it became evident that although the virus did contain multiple drug resistant mutations, it was not accurate—as the press release had reported—that it "did not respond to three classes of anti-retroviral medication." In fact, several months after the press conference the patient was doing well on

therapy, though his treatment consisted of a combination of six drugs rather than a more typical three or four drug regimen. In addition, the DOHMH's claim that the patient had progressed rapidly to AIDS—perhaps "within two to three months" of becoming infected—turned out to be incorrect (Volberding 2005). Furthermore, a number of researchers expressed doubt that the virus was highly transmissible, and argued that even if it were to be transmitted to others it would likely behave differently in different patients or "hosts." They noted that similar cases of HIV had been documented in Vancouver in 2003, and that these viruses had not been passed on to others, suggesting that they were not easily spread.

This downplaying of the significance of the New York case was supported by growing evidence that drug-resistant HIV was, in fact, a little bit more like herpes and less like tuberculosis after all. For example, in the early 2000s, physicians studying the management of U.S. patients with resistance to multiple HIV drugs published data showing that many of these patients continued to do well clinically despite their mutated viruses (Deeks et al. 2000). In other words, even though testing showed them to be "resistant" to the drugs they were on, the medicines were continuing preserve their health. The reason behind these paradoxical findings, researchers argued, was that resistance mutations weakened the virus, making it less able to replicate efficiently (Barbour et al. 2002). Furthermore, these weaker viruses appeared to be more difficult to transmit to others (Leigh Brown et al. 2003; Booth and Geretti 2007), suggesting that drug-resistant HIV might also be less of a public health threat than had been initially thought. This reduced "replicative capacity" or "viral fitness" was an unexpected benefit of many drug-resistance mutations—a sort of a silver lining to an otherwise dark cloud.

The discovery that resistance mutations did, in fact, weaken the HIV virus was thus not a revolutionary finding but rather a return to earlier ideas about viral resistance. Jim Greene, one of the senior researchers who contributed to the findings about viral fitness, echoed Dr. Pajaro's comparison to herpes. "The way I think about it is: is HIV like MDR-TB, or is it like drug-resistant herpes?" he told me. "Clearly [HIV lies] somewhere in between. The latest news suggests that it's more toward the herpes side. I think more data is needed, but I think that it's more toward the herpes side." Although these findings are now widely accepted, the research was

very controversial when first presented at scientific meetings. David Capelli, a young Ph.D. involved in the research on viral fitness, told me of scientific conference sessions that ended up in "shouting matches" over data:

> I think people were very concerned about what the message of our work could be. . . . We were—I think "accused" is the right word—of saying that we thought it was okay for people to have drug resistance. And that maybe it was even good news. You know, and I think even though we tried to very carefully deliver our message onto the broadest stages in the field, I think there was still active misinterpretation of that message. We were never trying to suggest that we thought drug resistance was okay.

Dr. Capelli's account of the controversy suggests that the debate over this research was moral as much as it was scientific. By implying (however unintentionally) that drug resistance might be "okay," the research upset the standard moral framing of resistance as a form of negative payback for poor adherence, and suggested that patients might instead be rewarded for missing their drugs.

Similarly provocative findings about the causes of antiretroviral resistance were also emerging at this time, as research results began to challenge the conventional wisdom that poor antiretroviral adherence inevitably led to the rapid development of drug resistance (Bangsberg and Deeks 2002). In a study of antiretroviral treatment among U.S. HIV patients, researchers found that drug resistance was most concentrated among *highly* adherent patients—those who took nearly all of their doses as prescribed—rather than those who frequently missed their pills (Bangsberg et al. 2003). In other words, in some cases, "near perfect" adherence seemed to encourage rather than prevent antiretroviral resistance. Also surprising was the finding that patients with the worst adherence (under 65 percent) had little drug resistance, though they also had little clinical benefit from treatment. The researchers explained their paradoxical findings by arguing that the relationship between poor adherence and drug resistance had been overly simplified in the scientific literature and was, in fact, different for different types (or classes) of HIV drugs. For certain older classes of antiretrovirals, missed doses did in fact lead rapidly to drug resistance, just as most researchers and clinicians had long believed. But for the newer protease in-

hibitor[15] class of drugs, over half of all resistance appeared in patients with the best adherence to their medications (those who were 79 to 100 percent adherent in the study), and particularly among patients who took most—but not quite all—of their medicine. Though initially counterintuitive, the researchers explained these results as a factor of different drug-specific "genetic barriers" to resistance.[16] Given the common belief that it was poor adherence that caused drug resistance and "near perfect" adherence that prevented it, these findings were provocative. In addition to upsetting the conventional wisdom in HIV medicine, they also complicated the moral calculus established during the MDR-TB outbreak that linked poor adherence, "recalcitrant" patients, and dangerous, drug-resistant disease. Paradoxically—on some regimens—it was the model HIV patients who were developing drug resistance.

Although this research was conducted in the United States, these and other related findings about differences across classes of HIV drugs were very relevant to then-nascent efforts to expand antiretroviral access in Uganda and other African countries. The older antiretrovirals were chemically simpler drugs than the newer protease inhibitors, and this made it easier for generic drug companies in India and elsewhere to reverse engineer and manufacture them. They were also much cheaper. As a result,

15. It is important to note that ARV therapy has improved since the time of this study. Protease-inhibitor regimens are now routinely supplemented or "boosted" with a low dose of ritonavir, an ARV that improves the efficacy of the anchor protease inhibitor and reduces the risk of resistance. Most of the participants in this study were not on "boosted" regimens.

16. Mutation only occurs when the virus is replicating. Ideally, perfect adherence keeps drug levels in the blood high enough to prevent the virus from reproducing, thus also stopping it from mutating. However, when drug levels drop—perhaps due to missed doses—the virus may begin to replicate again. When HIV replicates in the presence of an antiretroviral drug (under what scientists call "drug pressure") the mutations that develop are likely to be resistance mutations, as it is these genetic changes that give the virus the ability to "escape" the drug. HIV can become resistant to some older ARVs by undergoing a single mutation, but it must mutate many times in order to become resistant to a protease inhibitor. In the study, patients who took less than 65 percent of their protease inhibitors had levels of medication in their blood that were simply too low to push the virus to accumulate the numerous mutations needed to develop resistance. For these patients, it was essentially as if they were taking no medication at all. But in patients who were highly—but not quite perfectly—adherent to protease inhibitor-based regimens, drug levels dipped low enough to allow viral replication but stayed high enough to force the virus to mutate in order to do so, creating the perfect pharmacokinetic conditions for the development of drug resistance.

when HAART started to become more widely available in Uganda—first through the importation and sale of generics (primarily Cipla's Triomune), and later through international aid programs—regimens were almost exclusively comprised of combinations of the older medications. While equally effective, these combinations were much less "forgiving" of missed doses (Crane 2007; Thompson et al. 2010).

The pitfalls of this reliance on older combinations were not lost on African doctors and experts. In 2005 I sat in on an HIV-medicine training course held in Kampala. The course was intended to help prepare doctors from Uganda and other nearby countries for the increasing numbers of patients on antiretroviral drugs under their care.[17] During one presentation on drug resistance, a visiting Canadian lecturer described how different antiretrovirals had different thresholds for resistance, and pointed out that HIV could become resistant to the drugs nevirapine and lamivudine (commonly called 3TC) following a single viral mutation. "So," he told the class, "you'll realize immediately—what's the most common drug in Africa?" *Triomune*, the class answered—the Indian-manufactured combination pill containing both lamivudine and nevirapine, as well as a third drug. "So, two drugs with very little genetic barrier. Why?" he asked the class. *Because it's cheap*, they accurately responded. At this point the doctor seated behind me noted to herself, "Uh-oh. We're in trouble." One Ugandan expert I spoke with later described HIV treatment in his country as "a question of money"—in other words, what people and programs could afford to buy. The older drugs in Triomune had been rendered affordable by generic manufacturers, whereas protease inhibitors (which remained largely under the control of branded pharmaceutical companies) had not. As a result, despite earlier Western anxieties about drug resistance in Africa, the antiretrovirals that eventually made it to the continent first were often those most likely to cause resistance the quickest if doses were missed.[18]

Although epidemiologic data on the emergence and development of HIV drug resistance in Africa remains limited, the extremely low availability of

17. The course was organized by the Infectious Disease Institute at Makerere University, which I describe in chapter 3.

18. This disadvantage is somewhat offset by the comparative simplicity of the older combinations, which generally contain fewer pills than protease-inhibitor regimens, and are thus sometimes easier to adhere to. Both kinds of regimens are considered HAART.

antiretrovirals in Africa prior to 2005 means that drug resistance on the continent is low (Sendagire et al. 2009). The resistance that does exist can often be linked to "triage"—drug pricing decisions, health policies, and acts of desperation, like medication sharing—that have resulted in incomplete and interrupted treatment. For example, during the decade following the discovery of HAART, treatment in most of Africa was limited to those with sufficient money to buy medication, connections to procure drugs from abroad, or who were lucky enough to gain enrollment in a research study (Whyte et al. 2004; Nguyen 2010; Epstein 2003).[19] But these sources of drugs were often unreliable or unsustainable. In 2005, Dr. Gregory Odong, a physician from northern Uganda, described the problem to me:

> People started getting the drugs many years ago. But not from Uganda. People in Uganda initially had the benefit of going out [of the country]. Some went out on asylum. Now as they made contacts outside, they also got into contacts with people who could provide the drugs. So there we have briefcase drugs, which were being siphoned into Uganda.

Dr. Odong told me that these people either took the drugs themselves or gave them to relatives in need, but usually with little to no medical supervision or advice. As a result, they did not know which drug combinations to take. These were "the most difficult lot of people" for HIV physicians such as himself, as they were the ones who showed up at major referral hospitals like his, suffering from drug resistance. "They already tried almost every kind of drug combination," he continued, "and some have run out of options now." Later, as generic and discounted drugs became available, additional pathways to viral resistance arose in Africa, as patients bought ARVs when they could afford to do so but, like Esther, missed doses when they could not (Weidle et al. 2003; Adje-Toure et al. 2003; Byakika-Tusiime et al. 2005).

Because Andrew Natsios's words about African adherence and drug resistance had been such a lightning rod for the debate over global treatment

19. Botswana is an exception to this. Through a partnership between the government of Botswana, the Gates Foundation, and Merck Pharmaceuticals, ARVs were available through Botswana's public health system somewhat earlier, beginning in 2002 (Carpenter 2008; Brada 2011a).

access,[20] I asked Ugandan doctors I interviewed for their thoughts about his assertions. Their reactions were more varied than I anticipated, and revealed ambivalence about both African adherence and African modernity. Although several doctors described his comments about Africans and "Western time" as "paternalistic" or "offensive," one young medical officer at the Immune Wellness Clinic in Mbarara told me that she thought fears about antiretroviral resistance emerging in Africa were "warranted" because "most of the Africans, especially the ones who are not educated, they're not so time-conscious." One of her colleagues at the clinic similarly argued that while studies in Uganda had "disproved" Western fears concerning adherence in Africa, "You could say they had a good reason to think about it, because [of] issues like illiteracy, poverty, and everything. When you have someone and they don't have a watch, he can't know what time to take his medicine."

In Kampala, Dr. Tabitha Byakika, a prominent expert in pediatric AIDS, told me that worries about poor adherence were "obviously a consideration for us even as African researchers and clinicians." Like her American colleagues, she cited earlier experiences with failed tuberculosis treatment as a cautionary tale. However, she did not view the risks as a reason to withhold treatment. "The issue of resistance has always been there, even in the West," she told me. "[But] the benefit of antiretrovirals is so significant . . . we couldn't say we're going to worry about a theoretical risk when people are actually dying from HIV." Dr. Byakika thus saw Western fears about adherence and resistance in Africa as a valid scientific inference based on the challenges of TB treatment, but a flawed basis for policy. Other Ugandan experts, however, disputed the scientific legitimacy of such fears on the basis that very few studies of antiretroviral adherence in Africa had actually been done at the time. For example, Dr. Joseph Muhwezi, a senior researcher in Kampala, told me that "as a scientist working here, you really get angry many, many times when people express sentiments of that nature that have no scientific or any other evidence base."

20. Even the American radio reporter who accompanied Idah Mukyala and me on our research visit in 2003 made a point of asking Esther, the patient, how she knew when it was time for her to take her HIV medications. Her response—"I just look at my clock"—was featured in the broadcast story as an explicit rebuttal to Natsios's claims.

Some Ugandan doctors dismissed the statements by Natsios and other experts as "ignorant." In interviews, they repeatedly expressed the sentiment that such ideas were misconceptions that could only be expressed by someone who had not spent time in Africa (although, in fact, Natsios had traveled there extensively). For example, one young physician and aspiring researcher in Kampala described the comments about time-telling as a "stereotype" stemming from "people who have never probably been to Africa. "These were researchers sitting on boards, making decisions, making these kind of comments," he told me. Dr. Mary Balenzi, an Mbarara physician who would later become director of Mbarara's Immune Wellness Clinic, told me "I found [the debates] quite insulting." Nonetheless, she said, "I don't blame them very much because some of them wouldn't know what is happening in Africa, when you're there and you've not been here at all."

"It was a lack of knowledge" that allowed such statements to be made, she argued, and "a perception of Africa which is like we're down, down on the globe. Like really we are down to the dogs."

Dr. Ezra Mukasa, an elderly but spry expert on pediatric AIDS, was the most outspoken regarding the ignorance of Americans. It was "clear," he insisted, "that most people who talked about Africa, and Africans not adhering to this, had never been to Africa. This is a terrible thing! You cannot judge somebody without knowing him. Their view of Africans are the American Negros, who are extremely different from Africa. Extremely different!" Here Mukasa appeared to be challenging American stereotypes of Africa by invoking his own seemingly negative assumptions about black Americans. He went on to comment on the low social position of black men in America, noting that he rarely saw them at the numerous scientific conferences he had attended in the United States. "You hardly find any African American [men] there," he told me. "These days we find a lot of women, so women are making up. And men, I don't know where they are." In this expert's words we see the same logic employed by the media reports that touted the superiority of African adherence over that of American patients. Mukasa simply made the racial component of this discourse explicit.

A senior professor of medicine in Kampala, Dr. Mukasa originally hailed from the rural Rakai District in southwestern Uganda. Rakai is home to a long-standing HIV research project affiliated with Makerere and Johns Hopkins universities, and the research done there has been the subject of

numerous conference presentations and scientific publications. Mukasa worked and traveled in the international scientific circles where this research was presented. Raising his voice, Mukasa described his anger upon encountering what he saw as an unfair representation of his home district at an international medical conference:

> I remember, in one conference somebody showed a residence of one of the persons in the Rakai district. And I was there. And I protested. [Imitating the voice of the presenter] "Oh, this is their homestead of these people living in Rakai." I told him, "Yes, you've been to Rakai, but I was born there. Is this the real house people live in? How many houses have you visited?" He started blushing because he did not know that among the audience there were people who come from there. . . . It was too poor! It was a shack. Somebody who did not even have a door. I would not say that people even ever lived in that place at all.

It was not that Dr. Mukasa thought his country was wealthy. Earlier in our conversation, he recalled bringing American visitors to the home he had built outside of Kampala, a place he described as "a very beautiful building overlooking the city." When the visitors complemented his house, he responded by reminding them that it was "an exception."

"There are very poor people in this country who live in shacks. And there are very rich people with big houses, even bigger than where I'm living now," he said. "So you can only say that different people live differently."

Thus, the issue of African poverty was a complex one for the Ugandan doctors I spoke with, who struggled to counter Western perceptions of Africa as "down to the dogs" with the reality that they were elites living in an otherwise poor country. Even Dr. Mukasa's statements were somewhat contradictory, first denying that someone in Rakai would actually live in the "shack" depicted at the conference, but then later remarking that there were "very poor" people in Uganda who did, in fact, live in "shacks." In Mbarara, a young medical officer complained to me, "People of the West just have this general idea that Africa is still a very dark continent, that we are like monkeys basically." But her objection to this bigoted view was hardly a statement of African pride: "I think we are somewhere," she insisted. "I know we are backward, but we are somewhere."

In this way, the Ugandan experts and doctors I spoke with struggled to negotiate what Ferguson has described as Africa's "perverse" relationship to globalization, characterized by "highly selected and spatially encapsulated forms of global connection combined with widespread disconnection and exclusion" (Ferguson 2006, 14). On one hand, it is the so-called modernization of Africa in the form of urbanization, industrialization (especially mining in the south), and increased human mobility that is believed to have initially allowed AIDS to shift from a local, endemic disease in central Africa in the mid-twentieth century to the continental epidemic (and global pandemic) it would become by the turn of the millennium (Iliffe 2006). The social and demographic shifts that would eventually carry HIV along paved roads, trading corridors, migrant labor routes, battle lines, and airline flight paths developed alongside African independence and efforts to forge modern, self-governing nations out of territories of disparate polities that had been arbitrarily grouped together via colonial conquest. In addition, these changes contributed to the development of an urban, cosmopolitan elite in many African countries. In Uganda, it was this elite—and particularly its doctors—who would bear the chief political responsibility for confronting the country's AIDS epidemic (Iliffe 2002, 220). But in doing so, this elite wrestled with the formidable challenges they faced in fighting AIDS in their impoverished country, and sometimes invoked pessimistic and primitivist imaginaries of Africa not unlike those deployed by Western skeptics of treatment access.

Perhaps not surprisingly, for Ugandan HIV doctors and researchers the high adherence rates documented among their patients was a source of pride. It bolstered not only their hopes for the success of antiretroviral therapy in Uganda, but also Africa's claims for inclusion in the world of global HIV medicine. The discovery that antiretroviral adherence in Uganda and other African countries actually surpassed rates in the United States challenged age-old stereotypes of Africa as a "dark continent" of "dirty water and mud roads," a place that was "down to the dogs," where people "lived like monkeys" and didn't understand "Western time." It was poor, but it was *somewhere*, and it had promise, if only given a chance. The ability to take what were seen as some of the most high-tech, cutting-edge pharmaceuticals in the world—and take them properly—thus signaled a kind of membership in the global community, and a challenge to Africa's exclusion from it.

This membership was further signaled by the long-awaited arrival of free antiretroviral therapy on the continent. United Nations Secretary General Kofi Annan's call for an AIDS "war chest" led to the founding of the Global Fund to Fight AIDS, Tuberculosis, and Malaria, which began disbursing international donations to fund antiretroviral treatment in poor countries in 2002. Even more surprising was U.S. President George W. Bush's 2003 announcement of his President's Emergency Plan for AIDS Relief, or PEPFAR, during his January State of the Union address. The plan allocated $15 billion dollars over five years to support antiretroviral therapy in some of the world's hardest-hit countries, primarily in Africa.[21] Together, these initiatives would usher in the start of Africa's "treatment era." As I describe in chapter 3, the programs would have a profound impact on HIV treatment and research in Uganda.

As antiretroviral drugs become increasingly available in Africa, drug resistance on the continent will rise (Gupta et al. 2010). This fact has much more to do with medication access than it does with medication adherence (Crane et al. 2006). The relative scarcity of antiretroviral resistance in Africa reflects the historical lack of treatment in African countries, just as the high rates of drug resistance in the United States stem from the longstanding availability of ARVs in wealthy nations. In this way, global inequalities in treatment access have become manifest as biological differences between individuals who have received full treatment, partial or inadequate treatment, and no treatment at all (Nguyen 2010, 105). Such a reading resists the framing of viral resistance as primarily a factor of individual pill-taking behavior, and instead suggests that the epidemiology of drug resistance—like the epidemiology of HIV itself—represents an embodiment of the history of treatment access and, more specifically, "the embodiment of inequality" (Fassin 2003). Like other forms of drug resistance, its emergence is rooted as much or more in politics and markets than in individual pill-taking behavior (Orzech and Nichter 2008). Understanding HIV drug resistance as

21. The politics behind the founding of PEPFAR have been the subject of much speculation, and lie beyond the purview of this book (see Behrman 2004 for one account). Possible motivations for the program's announcement include post-9/11 worries over the destabilizing effect of AIDS on African nations viewed as potential harbors for terrorism; President Bush's evangelical Christian beliefs (perhaps evident in his description of PEPFAR as "a work of mercy" in his State of the Union address); and an effort to soften the blow of his intention to initiate the war in Iraq, which was also announced in the same speech.

the embodiment of unequal treatment access requires that we reject the low prevalence of antiretroviral resistance in Africa as simply "good news." Certainly drug resistance is undesirable, and its prevention is a worthy endeavor. But the low level of drug resistance in Africa cannot be separated from the fact that the continent's epidemic went largely untreated for the first full decade of the HAART era. This lack of treatment may have prevented the development of resistant virus, but it also enabled millions of deaths from untreated AIDS. Researchers have estimated that HIV treatment saved over 3 million years of human life in the United States between 1989 and 2003 (Walensky et al. 2006). This finding suggests that many millions more years of life were lost during this period in Africa, where infection rates were much higher and treatment access much lower. Indeed, one study estimated that the lack of access to antiretrovirals in South Africa alone was responsible for the loss of 3.8 million person-years of life in that country between 2000 and 2005 (Chigwedere et al. 2008).[22] The rarity of HIV drug resistance in Africa is a reflection of this dark history.

22. This was not only due to pharmaceutical pricing, but also due to former South African President Thabo Mbeki's controversial embracing of "dissident" or "denialist" AIDS science, and his skepticism over whether HIV was the cause of AIDS (Fassin 2007; Mahajan 2006).