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DETECTING COVERT INFECTION AHEAD OF THE FINAL DIAGNOSIS

> **Now the bulk of the deaths were boringly similar. They were the deaths of lies. We heard there was the feared AIDS pandemic stalking the homesteads. Yet no one died of it. Or anything related to it. . . . At the funerals I mourned; the dreaded four letters were never mentioned, only TB and pneumonia and diarrhea. People died of silence. Of shame. Of denial. And this conspiracy resulted in a stigma that stuck like pubic lice on both the living and the dead.**
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> —Zakes Mda, 2007

One of the pathologist 'Ṣẹgun Ojo's lifelong gripes has been the steady decline of medical laboratory science in Nigeria. Aware of the pressing need to train a generation of competent laboratory diagnosticians and researchers, he committed himself to building the expertise necessary to remedy diagnostic insufficiency. I initially encountered Dr. Ojo in graduate school, when he was a lecturer, researcher, and consultant pathologist at western Nigeria's Obafemi Awolowo Teaching Hospitals complex. Formally and informally, he mentored residents and students working in subdisciplines as diverse as clinical chemistry, biochemistry, microbiology, and pathology, and encouraged many young practitioners to pursue careers in laboratory medicine. Ojo was subsequently appointed to head the department of Morbid Anatomy and Forensic Medicine at Obafemi Awolowo University, and named professor of anatomical pathology. Several years later, I spotted an article in the Nigerian *Guardian* newspaper reporting on his inaugural address, delivered a few years after he was elevated to the chair. Ojo's lecture, "The Pathologist, the Misery, the Mystery and the Final Diagnosis—An Interminable Quest for Excellence," outlined his work on the diagnosis and epidemiology of hepatitis B.[1]

Viral hepatitis is an inflammation of the liver caused by any of six or more viruses, hepatitis A, B, C, D, E, or F. Acute viral hepatitis, which many doctors can diagnose clinically, manifests as a rapidly debilitating illness with yellowed eyes, dark urine, and severe tiredness. The more common chronic form of the disease is less dramatic, so unseen infection persists until it manifests as liver cancer. Chronic hepatitis can only be diagnosed in the precancerous stage by measuring liver enzyme concentrations in the blood (as enzymes spill from damaged liver cells) or by detecting the viruses. Ojo, with other liver experts, determined that in Nigeria the disease is commonly caused by hepatitis B virus. Preventing infection is key, and a vaccine is advocated for use by health workers and any other at-risk populations. Diagnostic resources for blood screening also reduce the threat from the disease by preventing transfusions with infected blood. According to data collected by Ojo and others, as many as 15 percent to 20 percent of Nigerians may be chronically infected with hepatitis B virus, and most of them are unaware of their infection status. The virus is responsible for 50 percent to 80 percent of all liver cancers in Nigeria, and liver cancer is one of the most common cancers in that country.[2]

Across Africa, hepatitis B is among the most important causes of death in middle age. This disease is controllable, even technically eradicable, and it can be treated—but only at a cost that most Nigerians cannot afford. As decades can pass between the time of infection and the point of diagnosis and death from liver cancer, prevention and early diagnosis are key. In his inaugural lecture, Professor Ojo enunciated the great need for control of the hepatitis B virus and explained the central role that the laboratory must play in its control, prescreening all transfusion blood and testing and vaccinating health workers and other populations at risk. He emphasized the importance of creating at least one national liver care center with up-to-date diagnostic and therapeutic equipment.

The diagnostic dilemma posed by hepatitis B is also seen in many sexually transmitted diseases, for which symptoms in at least some infected people are few or none but long-term infection can be devastating or irreversible. Bacteria that cause sexually transmitted diseases are difficult to culture or manipulate genetically, making vaccine development a real challenge. Quick identification of infected people and prompt treatment, which in most cases is cheap, effective, and easy to administer, is an important way to diminish spread. Social stigma prevents many patients from seeking care overtly and frequently. Patients that are correctly diagnosed and treated in a single health-center visit are least likely to be lost to follow-up, a persistent problem with sexually transmitted infections.

Diagnosis is the lynchpin for disease control. Women infected with *Treponema pallidum,* the corkscrew-shaped bacterium that causes syphilis, can remain oblivious to their status until they bear a child that acquires the disease during delivery. A woman with syphilis can be easily treated with a single, inexpensive dose of penicillin, even while she is pregnant, so no child should have to begin life battling congenital syphilis. Testing and penicillin are cheap and assure the health of the mother and child; therefore, testing every pregnant woman is worthwhile, even where syphilis is rare. For gonorrhea and chlamydial infections, infected women, again usually asymptomatic, can become sterile or end up with dangerous ectopic pregnancies if their fallopian tubes become blocked by the disease. Babies born to women with these infections can catch them and in some cases are rendered blind. Again, usually irreversible damage can be prevented by timely diagnosis and treatment with effective medicine but most Africans with a sexually transmitted disease cannot access testing.

Underutilization of diagnostics for sexually transmitted diseases exacerbates gender disparities in health. Men with sexually transmitted diseases are more likely to have symptoms, and therefore symptom-based diagnosis can be effective. Women rarely show symptoms, and are more likely to suffer irreversible damage if not diagnosed with an appropriate test. Many existing tests do not serve women well. Urethral discharge from a man with gonorrhea can be fixed to a slide, stained directly and examined microscopically to reveal red pairs of spherical *Neisseria gonorrheae* bacteria. Results are available in minutes and all that is required for the test are the stains, slides, and a microscope. Swabs and discharge from women, however, even from symptomatic women, rarely detect *Neisseria* when they are present. Tests that will detect these bacteria in vaginal swabs are expensive and often too sophisticated or too unreliable to be used at regional health facilities in Africa.

Collecting samples and sending them to a reference lab means that some will be damaged during shipment, and that patients, who often have no symptoms and therefore little motivation, must return later for test results. When they do not return, the costs incurred in specimen transport and testing are wasted, and patients can continue to spread the disease. Therefore, rapid, point-of-care tests for syphilis, gonorrhea, and chlamydial disease are sorely needed. The impact that these tests could have goes beyond controlling these diseases and the irreversible damage they can cause. Lesions produced by these devastating but non-lethal sexually transmitted pathogens create portals for the AIDS virus.[3]

Surveillance and Denial of HIV/AIDS

The human immunodeficiency virus (HIV), the etiologic agent of AIDS, has come to emblematize present-day discourse on disease in Africa. In some circles, the mere mention of Africa conjures up images of emaciated people in their last ebb of life. Some foreigners have a vision of an entire continent's adult population passing away, leaving only helpless and neglected orphans, many of whom carry the virus themselves. Visitors with this vision of the continent who arrive in an African city and find citizens going about their daily lives with alacrity and ease are astounded. Depending on the country and the city, a visit to the local hospital could also contradict this highly publicized portrait of a dying continent. The disparity between the situation on the ground and the picture that has been so commonly projected is a baffling reality for many Africans as well. How could a wasting and ultimately fatal disease be endemic, yet so few persons be visibly ill? This disparity has led to skepticism about the nature, etiology, and epidemiology of AIDS. The skeptics, such as South Africa's former president Thabo Mbeki and his health minister, Dr. Manto Tshabalala-Msimang, appear almost ridiculous to the medical mainstream, and those directly affected by the disease find their skepticism incomprehensible and their inaction outrageous.[4] In other circles, particularly those with close ties to certain parts of West Africa, skeptics are heroes.

For far too long, and in too many critical instances, Africa has been considered as a continuous whole, with each African a unitized part of that whole. Because thousands upon thousands of people were dying of AIDS in parts of East Africa and southern Africa, many outsiders assumed that the disease was taking the same toll in towns and villages in Mali, Ghana, Nigeria, and Sudan. Data derived from relatively small and biased studies in the places where HIV infection was prevalent and AIDS appeared first were extrapolated to apply to those countries and then to the whole continent. Many of the figures and images suggested that every African must have a loved one who had perished from the disease, even if he or she was not ill or infected. In fact, in 2002 much of the population of Africa had not yet seen a case of full-blown AIDS. Whereas many people in Uganda and Botswana found the reports of HIV overtaking their continent perfectly consistent with the rising number of sick people, burials, and orphaned children, many West Africans who listened to the figures regarded them as what Benjamin Disraeli might have catalogued as "lies, damned lies, and statistics."[5]

Unfortunately for the credibility of Western medicine on the continent, the historical record is replete with instances in which European colonial officials falsely alleged that epidemics of sexually transmitted infections were occurring in Africa. Anxieties about sexually transmitted diseases were part of a colonialist mentality that regarded Africans as members of a "primitive race" who were unable to exercise rational, moral control over their bodily sexual impulses.[6] In 1897, for example, the supposed rapid and widespread dissemination of syphilis in colonial Africa caught the attention of British medical practitioners. Megan Vaughan has drawn attention to a series of papers published in London about a syphilis outbreak that allegedly was ravaging the Baganda, a people of the Buganda region in present-day Uganda. The population in question was presumed to have had no previous exposure to the disease; the epidemic was said to be occurring on "virgin soil," so it spread especially rapidly. According to the initial report by army medic Colonel Lambkin, 80 percent of adults were infected, and the entire clan was perilously close to being wiped out. Lambkin's article was followed by a series of papers ascribing the epidemic to causes including the decline of traditional gender norms, resulting in an uncontrolled expression of women's "strong passions," and the failure of the people of Buganda to embrace Christian morality.[7]

This racist and sexist discourse continued in Britain's foremost medical journals for months, with contributions from clergymen as well as medics. The vast majority of the "syphilitic" Baganda presented with skin lesions, and the cure rates following administration of mercury injections were much better than has previously been documented for sexually transmitted syphilis, or the congenital form of the disease. Unfortunately, these observations, although carefully noted, did not suggest to the medics engaged in "saving" the Baganda that they were dealing with an entirely different disease. It is now clear that the Baganda rarely, if ever, had sexually transmitted syphilis; rather, they had some other form of treponemal disease, perhaps yaws, or more likely a less severe version of syphilis produced by a tradition of deliberately inoculating children with *Treponema* to produce a mild disease that would protect them from more virulent infections later in life.[8] What was never clarified to the avid readers of the *Lancet* and the *British Medical Journal* is that the basis for this stigmatizing epidemiology was clinical presentation and a positive Wassermann reaction, a serological laboratory test that cannot distinguish true venereal syphilis from treponemal diseases that are not sexually transmitted.[9]

The unfounded assumptions and unwarranted inferences that underlie the discussion of the supposed syphilis epidemic in Uganda at the turn of the twentieth century are evident in the initial reports about AIDS in Africa as well, and Africans' well-founded concerns about the invidious intent and systematic errors of colonialist medicine have shaped their responses to reports about the epidemic.

Recalling numerous instances similar to the supposed Buganda syphilis epidemic, many Africans concluded that the AIDS epidemic was a new stereotypical and subjugating Western fiction. It did not help that other subpopulations commonly associated with the disease—gay men and injection drug users—were marginalized in Western culture. Many members of Africa's intelligentsia, including physicians, familiar with earlier case studies labeling Africa "the infectious continent," stubbornly refused to accept the "myth" of AIDS. In too many cases, the very people who might have spearheaded HIV intervention programs derided them. Persons living outside regions where HIV-related deaths are commonplace have on occasion refused to be tested or to protect themselves from the virus, believing that condoms and abstinence messages are being used to curb Africa's population growth. In the 1980s, AIDS, called SIDA in French, was variously described as the "American Idea of Discouraging Sex" or "Syndrome

Imaginaire pour Dēscourager les Amoureux," the Imaginary Syndrome to Discourage Lovers.[10] Health care workers have even been reported as taking inadequate precautions to protect themselves and other patients from infection.[11]

Initial HIV antibody tests occasionally drew false positives. This is a common problem with antibody tests in general—the Widal test for typhoid fever, for example, is even more nonspecific than the earliest HIV tests. During development, diagnostic tests are typically developed and validated using samples from non-African patients so that even tests that perform well elsewhere can perform less well in Africa. The difficulty in deciphering the cause of AIDS when the disease first appeared, coupled with the urgent need for a test to diagnose the infected and screen transfusion products, meant that AIDS diagnosis was particularly prone to insufficiently specific first-generation tests. Today's tests are much more reliable than their predecessors, and at least two tests, one of which is not an antibody test, are needed to confirm each HIV infection.[12] There were unavoidable but marked social implications of using nonspecific tests for HIV in Africa, where similarly nonspecific Wasserman tests had led to overestimation of syphilis prevalence rates several decades before. Among them was the muddling of the problem of test limitations, which were rapidly resolved, with denialist hypotheses that discounted the existence of the virus altogether.

Most recent epidemiological studies adequately address the problems with HIV tests and, whether the results are required for patient care or research, it is standard practice to use more than one test to confirm the results. Therefore, people documented as HIV positive from the 1990s are indeed infected with the virus. However, the final figures presented in some reports have inflated HIV prevalence continent-wide because of sampling bias. It makes sense to start by seeking cases in a high-risk catchment group and conduct small point-prevalence studies in order to establish or disprove the presence of a disease. However, after the presence of HIV had been established, samples were still far too often drawn from antenatal clinics in urban centers, where HIV research and health delivery services were justifiably located. Research focused on HIV prevalence in young, pregnant, urban women—one of the most sexually active subpopulations, and the least able to protect themselves from sexually transmitted diseases. In malaria-endemic areas, this subpopulation is also among those most likely to receive blood transfusions, so this group is exposed to multiple risk factors for HIV.

Other overestimations arose from HIV tests performed only on patients with symptoms that suggested they might have opportunistic infections, again the product of convenience sampling. One study in Nigeria recorded a 25 percent prevalence of HIV in this subpopulation.[13] This figure appears low given the test population, but if viewed outside its original context it can be misinterpreted to mean that HIV prevalence is extraordinarily high. At the regional level, more data comes from countries with high HIV prevalence than from those with fewer patients with full-blown AIDS. Researchers did not always assume that data based on antenatal testing or other skewed samples accurately reflected prevalence rates in the general population, but, in the absence of sentinel surveillance or the kinds of generalized testing programs that were established in Europe and North America, these were the only data available when public officials made projections and reporters needed a sound bite.[14] When testing is uncommon, data used to inform health policy or by the media is more likely to be inaccurate.

Obtaining unbiased data is extremely difficult in the case of a pathogen as biologically and socially complex as HIV. Drawing data from people who volunteer to be tested could show higher prevalence rates than the general population because people with risk factors or symptoms may be more likely to request a test. In places where AIDS is heavily stigmatized, volunteer testing could underestimate prevalence. Nonetheless, even this type of data, which can be procured from health systems in countries where appropriate laboratory tests routinely accompany diagnosis, is a preferable substitute when population-based data is unavailable.

Making unwarranted generalizations from data collected in high-prevalence parts of Africa may have done as much harm as good. A more region-specific and precise mode of data collection might have provided information that locals could reconcile with their own environments, giving them a realistic view of their actual risk. In Senegal, where testing at four sentinel sites began in 1989 and was coupled with aggressive AIDS education and intervention programs, HIV prevalence rates may have been held down.[15] The failure to rapidly provide adequate and accurate support for the then hypothesis that HIV was present and spreading in some parts of Africa helped alternate hypotheses gain dangerous ground. Among the most popular are denialists who claim that AIDS is not caused by HIV and therefore cannot be managed with antiretroviral drugs or contained by limiting viral transmission. (Any reader still swayed by denialist claims that HIV does not cause AIDS or that antiretrovirals do not prolong the lives of AIDS patients should read the article by Pride Chigwedere and Myron Essex, which systematically and directly addresses these and other denialist arguments[16]).

Although we must acknowledge holes in surveillance, the present state of HIV diagnosis is perhaps the best example of diagnostic development on the continent. In contrast to other common infectious diseases of which less than 5 percent of the infected are diagnosed with a test, laboratory diagnosis now occurs in the majority of patients who are told they are HIV positive. Nonetheless, the diagnostic resources for HIV in most parts of Africa are insufficient to catalog the demographic and socioeconomic effects of the disease, or even to ensure that apparently healthy people can easily be made aware of their infection status. Diagnostic support for treating HIV-positive people is grossly inadequate, and HIV surveillance remains suboptimal. Some commentators have argued that gathering precise figures would be a merely academic exercise. They contend that if the line is too long to be reasonably attended to, it really does not matter how long it is. However, a recent theoretical model suggests otherwise: universal testing and access to antiretrovirals would lower transmission rates.[17] Moreover, exaggerations of the state of the HIV epidemic in both directions—underestimates and overestimates—have been extreme, and they remain dangerous because they undermine intervention programs, which today are necessarily largely focused on changing behaviors. Inadequate surveillance data are fostered by continuing diagnostic insufficiency and adversely affect prevention and treatment of the disease, irrespective of how widespread it is at different localities.

Death Emerges from Its Pouch

The presence of HIV-infected persons throughout Africa is indisputable, although the extent to which the documented prevalence of AIDS reflects actual epidemiology is open to debate. Awareness of risk has come quite belatedly, an unfortunate result of the skepticism that attended early reports. As recently as 1996, health workers in Nigerian primary, secondary, and even tertiary care institutions were not taking sufficient precautions to protect themselves from HIV and other blood-borne diseases. Although some information suggested that local people were becoming infected with the virus, most West Africans did not encounter anyone with the disease until 2002 or even beyond. The average Nigerian remained ignorant of the threat from HIV/AIDS; too many were denialists. The images of emaciated patients projected from several countries in East Africa and southern Africa were attributed to greater tourism in those areas, as AIDS was seen as a Western import associated with the "foreign" cultures of homosexuality and intravenous drug use. Just as the United States received its belated kick in the pants from actor Rock Hudson's HIV infection, Nigeria's first AIDS reality check came not from the health ministry but from popular music. Most Lagosians can recall exactly where they were on August 3, 1997, when the world was told that Fela Anikulapo-Kuti was dead.

In the 1970s, in spite of their English teachers' best intentions, Nigerian elementary school children acquired their first words in creole or pidgin English, a fashionable lingua franca of unschooled and urban professionals alike, by singing Fela's smash hit "Suffering and Smiling." In the face of back-to-back repressive military regimes, many of these children later gained political awareness by interpreting its lyrics. Fela's life and work were shaped by a striking mix of talent, energy, obstinacy, and scandalous behavior that in some eyes branded him a scoundrel. Devising his own genre of music, Afrobeat, he rapidly achieved international fame. Fela set up a music studio within his self-proclaimed "independent" Kalakuta republic, which was destroyed by Nigerian soldiers in 1977. He was repeatedly harassed by successive Nigerian military governments, and once convicted, but he would not be silenced. Fela's best music was political satire, and Nigeria's tumultuous postindependence regimes gave him much to make music about. Even more entertaining than his many recordings were the works he performed live at his Lagos Shrine, as well as on tour with his Africa 70 and then Egypt 80 bands. The Afrobeat king is also famed for his numerous concubines and wives; he married twenty-seven of them in a single day to commemorate Kalakuta's destruction.

Fela was born into the illustrious and multitalented Ransome-Kuti family in 1938. His father, Reverend Ransome-Kuti, was a minister and high school principal in Abeokuta. His mother, 'Funmi Ransome-Kuti, was the first Nigerian woman to secure a driver's license and one of her country's earliest and best known feminist activists. His two brothers, Beko and Olikoye, were internationally renowned physicians.[18] Beko remained a popular left-wing political critic until his death in 2006. Olikoye, a public health specialist, pioneered primary care initiatives in Nigeria and remained, until his death, one of the few incorruptible Nigerian public officials.

Claiming that the first part of his hyphenated surname had slave origins, Fela changed it from Ransome to Anikulapo, that is, one who carries death sealed in a pouch. It was a huge shock to all who knew of him when, in 1997, before his fiftieth birthday, the seemingly invincible Fela died. In a clear departure from the typical obituary following death at an early age, Fela's demise was not attributed to an unnamed "brief illness." His brother Olikoye publicly announced that Fela Anikulapo-Kuti, the world-renowned musician and sociopolitical critic, had died of complications from AIDS. In a cultural climate in which AIDS was considered foreign and heavily stigmatized, the family's statement was uncharacteristically open. Nigerians received the news with profound shock. Fela himself, like most Nigerians of that time, was a well-known denialist,[19] but his death from AIDS made it increasingly difficult not to believe that HIV might lurk in Lagos. Lest anyone remain of the opinion that the HIV virus was completely absent from Nigeria or that the medical community had the epidemic under control, a decade later Adewunmi Eniola was projected from obscurity when he became the much-publicized, not-so-proud father of an HIV positive baby. The case garnered more publicity than most because Eniola claimed that he and his wife were HIV negative and that the baby must have been infected at the Lagos University Teaching Hospital.[20]

By the end of 2004, although the reported prevalence rate had started to level off (a drop from 5.8% to 5.0% had been reported), the statistics were grim and the Nigerian media had begun a campaign to encourage people to believe them. This report from the Nigerian United Nation's Development Program office was published in *This Day,* a Lagos newspaper:

> According to official statistics, 3.5 million Nigerians already live with HIV and AIDS, which is more than the entire population of some countries. About 300,000 Nigerians die annually of AIDS-related diseases and 1.5 million Nigerian children have been made orphans as a result of these deaths. The fact that Nigeria's prevalence rate is in single digit [*sic*] can be misleading and can give a false sense of security. In real fact, Nigeria has the second highest number of infection [*sic*] in Africa, going by the actual figures, not the percentages. Also, the 3.5 million Nigerians living with HIV and AIDS account for about 10% of the 40 million people infected worldwide and 20% of those affected in Africa, the world's most affected continent.[21]

Other estimates place HIV prevalence in Nigeria at between 3 percent and 4 percent.[22] Nonetheless, all but a dwindling number of denialists concur that a large number of people are at risk in Africa's most populous country. Regardless of how low prevalence rates might be, in the face of continued diagnostic insufficiency they translate into large numbers of incognizant infected people who could spread the disease and have limited access to preventive interventions and treatment.

Diagnosis, "Cure," and Treatment of HIV/AIDS

It is not clear why the AIDS epidemic in Nigeria—just as in some neighboring West African countries—appears, by all measures, to be less extensive and/or more recent than the epidemics in such countries as Botswana, Uganda, or Zambia. A recently identified protective effect of male circumcision is likely to have contributed to some degree. Other credible hypotheses about contributing causes include religious and cultural differences, less contact with tourists, less effective health systems for documenting disease, and lower rates of contact with nonhuman primates. Still other explanations that have been proffered for the higher rates elsewhere include infection due to indigenous or allopathic surgery, blood transfusion, or sharing injection needles in health centers. What is clear from the diversity of theories is that the burden of disease attributable to AIDS varies across the continent.[23] The magnitude, causes, and implications of this variation are not well understood, mostly because they have not been studied systematically.

Because antiretroviral drugs were largely unavailable at the time AIDS emerged from partial seclusion in West Africa, the demand for anything that could help AIDS patients was insistent and unsatisfied. In response, providers stepped rapidly into the vacancy. The disease was new and frightening, patients were desperate, the ineffectiveness of many spurious treatments was not proven, and regulatory oversight was weak. Anyone courageous and foolhardy enough to claim they had a cure for AIDS was able to make such assertions with relative impunity. All over the continent, spiritual, herbal, and other cures were advertised and paid for. Although Nigeria had barely acknowledged the presence of the disease, many local "experts" claimed to know exactly how to cure it.[24]

A group of concerned researchers investigated awareness, diagnoses, and treatment modalities among indigenous medical practitioners. Their study was performed in Ile-Ife, the "cradle of the Yoruba race," the origin of Yoruba traditional religion and of the Ifa priesthood, as well as the home of one of Nigeria's most prestigious universities and its teaching hospital. Professor of pharmacy Anthony Elujoba and his colleagues interviewed fifty-one indigenous healers, most of whom claimed to have acquired their training in the management of sexually transmitted diseases and HIV/AIDS from their ancestors or during their apprenticeship—even though the disease emerged after they became healers. Twenty-two practitioners, almost half of those interviewed, stated that they had treated at least one AIDS patient.[25] Fifteen said that they typically relied on an allopathic practitioner to determine the HIV serostatus of their patients, but clinical signs and symptoms played a large part in the diagnosis of AIDS by indigenous practitioners. Five admitted that their diagnoses were based on patients' "confessions," and fourteen, including some of those who received "confessions" from some patients, had "guessed" that their patients had AIDS. Interestingly, all the practitioners claimed that their patients were cured, but verification was in most cases based on clinical observation alone, on the patient's testimony, and/or on a supernatural source. Only eight claimed to have requested that a hospital verify that the patient was cured.

Although all the practitioners interviewed claimed to have cured AIDS, most had not notified anyone about cures in specific cases. Five practitioners told other traditional practitioners, but four admitted to being unsure that their treatment was efficacious. Two-thirds (fourteen) stated simply that there was no need to advertise the feat, and two practitioners said that no one would believe them. The researchers concluded that "it is rather difficult to accept or reject traditional practitioners' claims of caring for people with HIV/AIDS as some of the diagnostic symptoms used can neither be confirmed nor rejected as being valid in the absence of confirmation of positive HIV serostatus of clients."[26]

This dilemma exists across Africa. Kenyan Arthur Obel claimed that his Pearl Omega drug could cure AIDS; the Gambian head of state has offered a spiritual cure for AIDS; and a Ghanaian herbalist was reportedly slain in connection with intellectual property disputes surrounding his therapy. Before antiretrovirals were sanctioned by its government, the most popular AIDS treatment in South Africa was a pair of herbal mixtures called uBhejane.[27] The mixtures were not evaluated in clinical trials, but the first was reputed to increase $CD4^+$ counts and the second to lower viral load. Low counts of the $CD4^+$ cells that are depleted by HIV, and increased viral loads, are laboratory indicators that are used to determine the point at which HIV-infected individuals progress to AIDS. Even though the value of many cure claims is stated in units defined by Western laboratory medicine, in far too many cases diagnostic shortfalls have made it impossible to validate or disprove them.

Another widely publicized claim, perhaps second only to uBhejane, has come from a practitioner of "orthodox" allopathic medicine. In 1999, Nigerian physician Jeremiah Abalaka contended that he had devised a vaccine-based protection and cure for AIDS. Like the indigenous practitioners interviewed by Elujoba and his colleagues, he refused to disclose the nature of his medicine. Public health officials and the Nigerian media emphasized the need to validate Abalaka's claims by studying his "curative vaccine." No effort has been devoted to pre- and posttherapy testing of his bevy of patients, which would have been one way to validate or dispute his claim without his cooperation. Abalaka's case, which could easily have been verified or disputed by biomedicine was instead mediated by the courts.[28]

Abalaka has published his "Attempts to Cure and Prevent HIV/AIDS in Central Nigeria between 1997 and 2002: Opening a Way to a Vaccine-Based Solution to the Problem?"[29] In this unusual scientific paper, Dr. Abalaka was careful to state that his findings did not represent a systematic clinical trial but rather a report of his practice over five years. He noted that $CD4^+$ cell assays, which validate HIV infection and serve as a measure for the progression of AIDS and as an indicator of patients' general health, as well as all other laboratory tests, had been procured off-site, at patients' expense. Abalaka observes that "in Nigeria, there is no free laboratory investigation or medication for any person including those with HIV infection."[30] Although his critics, myself included, debate the rest of the report, the lack of access to laboratory diagnosis and appropriate treatment is undeniable. Essentially, Abalaka, his cure, and cases like this thrive because of deficits in laboratory medicine.

Diagnostic insufficiency in relation to HIV has other risks. Estimates of how many people acquire the disease following transfusion of tainted blood range from eighty thousand to 160,000 worldwide. In many parts of Africa, the need for transfusions is high because of endemic *falciparum* malaria, but 2007 estimates of banked blood tainted with HIV range from under 1 percent in South Africa, Rwanda, and Namibia to 2.5 percent in Nigeria and 7 percent in Mozambique.[31] Other blood-borne viruses, including hepatitis B, are even more likely to be transmitted. The capacity to store donated blood is often limited, so donations are often made at the point of need by family members or paid donors. A test that can verify the safety of blood within minutes is vital.

Western medicine still offers no generally applicable cure for AIDS, but HIV infection is no longer an automatic death sentence. Today, in most of Europe and North America, HIV-infected people can live relatively normally, and they survive much longer than their counterparts did two decades ago. A huge debate ensued over whether life-saving antiretrovirals should be supplied to the poor in countries that could not procure them at the high prices charged by the pharmaceutical companies that initially developed them. The lack of infrastructure and personnel for laboratory monitoring was frequently cited as a reason for withholding antiretrovirals from Africans, a claim that is becoming as irksome as the earlier insinuation that Africans could not tell time well enough to take their medications on schedule. Although it is true that laboratory services are needed to use antiretrovirals properly, they are also needed to use antimicrobials that have been available in Africa for decades. In those cases, as well as in the case of HIV, WHO director general Jim Yong Kim's criticisms of those who compare price with patients' economic means, weigh human lives against money, and enounce the prevention versus treatment "false dichotomy" all apply.[32]

The argument against providing antiretrovirals because of the absence of appropriate laboratory support for their administration became the most popular reason to deny AIDS patients in poor countries life-saving medicines. This argument could be supported by evidence, and was less unpopular because it criticized systems rather than people. The fact that this point gained so much ground in the debate illustrates that there are health policymakers who believe that the infeasibility of diagnostic development justifies the deaths of thousands. This argument has been tacitly accepted for many other infections for decades, but the antiretroviral lobby—one of the most effective in developing-country health—has been able to overcome it for HIV. It is now generally acknowledged that even though testing facilities are still scarce, they can and have been set up in the most resource-poor parts of the world, and should be expanded.

At Makerere University in Kampala, Uganda, the infrastructure had not been updated in thirty-five years until a new AIDS center was commissioned in April 2004. The center was provided with state-of-the-art diagnostic and patient management facilities through generous donations from industry and many nongovernmental organizations. The opening of the center in August 2004 was extremely timely, for it provided the facilities necessary for the conduct of clinical trials of antiretroviral drugs and AIDS vaccines. Thus, the donation of US$15 million from Pfizer, a major developer of anti-AIDS treatments, is as much a simple act of charity as a matter of self-interest. Notwithstanding, this center and others like it have greatly boosted biomedical science in Africa. Importantly, the center demonstrates that sophisticated diagnostic and treatment facilities are not out of place or unnecessary in Africa, and its success shows that it is not the white elephant that such facilities were often predicted to be.

Optimal Laboratory Testing Promotes Control

People who know their HIV infection status can be empowered to assist in containing the spread of the virus. Unfortunately, not every African who needs antiretrovirals has access to them today, and not every African who is taking antiretrovirals has access to supportive diagnostic resources. Each patient should have a positive HIV test (determined by at least two methods), a $CD4^+$ count, and, if possible, a viral load estimation before commencing antiretroviral therapy. The last two parameters need to be periodically monitored during treatment. Many patients in Africa are started on antiretrovirals based on clinical criteria alone. The lack of laboratory verification has clinical consequences because patients who are not correctly "staged" before they start antiretroviral therapy may fare worse than patients who receive a proper laboratory workup. $CD4^+$ T-cells are the immune-system cells invaded, and destroyed, by the AIDS virus. In order to determine which patients are precariously close to immune deficiency, the $CD4^+$ cells in a blood sample from the patient are labeled—to distinguish them from other white blood cells—and counted by a laser in a machine called a flow cytometer. Flow cytometry is expensive but offering this service for HIV patients is cost effective because antiretroviral drugs are essential but expensive. If patients' $CD4^+$ levels can be precisely monitored, costs associated with starting therapy too early or too late can be avoided. Laboratory monitoring is also essential to determine when the treatments of patients who are on antiretrovirals need to be updated.[33]

Globally, diagnostic requirements for HIV-infected patients have moved beyond ascertaining infection and estimating $CD4^+$ counts and viral loads. Because drug-resistant viruses have become widespread, clinicians of newly diagnosed or unresponsive patients in the West order genetic testing on viruses infecting their patients. From the DNA sequence of viral target genes, clinicians can predict which antiretrovirals a patient's virus will be susceptible to and therefore which drugs to prescribe. This type of personalized medicine, often touted as the medicine of the future, is available in Western HIV clinics today. HIV replicates rapidly and mutates quickly, but patients must receive drugs for life. Therefore, drug resistance is an inevitable consequence of antiretroviral therapy, and only by sequence typing of viruses can we be sure that every patient receives effective treatment, and that resistant viruses do not become more commonplace than susceptible ones. With so many HIV-infected people and the most difficulties in ensuring antiretroviral access, many countries in Africa are at greatest risk of being overwhelmed by resistance if diagnostic infrastructure and requirements are not strengthened.

In 1988, before the diagnostic development forced by the antiretroviral access debate, the WHO recommended that, in the absence of the necessary diagnostic testing resources, a set of standard clinical indicators be used as a surrogate for diagnosing AIDS. The clinical case definition (CCD) for AIDS includes tuberculosis, Kaposi sarcoma, and other opportunistic infections. Supra-infections in AIDS patients vary with location, so considerable local modification is essential to implement this model.[34] Even when region-specific definitions are incorporated, the effectiveness of CCD has always been questionable, but it continues to be used in some parts of Africa today. In a Tanzanian study, the CCD protocol was shown to have a very high positive predictive value and specificity (both over 90%), but an extremely low sensitivity (36.6%)—that is, almost all patients with late-stage, full-blown AIDS were readily identified, but two-thirds of those with less obvious symptoms of HIV infection were missed. Patients who fit the clinical profile recommended for diagnosing AIDS were close to death. Those whose infection might be treated and who might be enabled to avoid transmitting HIV to others were not identified. Nor were individuals coming to the end of the asymptomatic stage, whom Brandy Rapatski, Frederick Suppe, and James Yorke[35] have proposed are principal drivers of the HIV pandemic, because they have a high viral load but no symptoms.

HIV infection and the imminence of AIDS can be diagnosed with virtually 100 percent precision by detecting the virus and by measuring $CD4^+$ levels. There are very basic tests for HIV, and many can be used in resource-poor laboratories or even at the point of care. Late-stage clinical diagnosis of AIDS on the other hand places clinicians on par with laypeople, including quacks, all of whom can clinically diagnose a case of AIDS at the time of death with precision.[36] But responsive health systems need to be able to spot HIV infection before it is too late to intervene. Presently, as with hepatitis B–induced liver cancers and congenital syphilis, too many patients discover that they are HIV positive only when they develop AIDS. Diagnostic development and the distribution of antiretroviral drugs have begun, but they must be closely coordinated as well as accelerated in order to stem HIV epidemics in Africa.