



Reversal of Misfortunes

South Africa has the world's worst HIV/TB syndemic; now it's trying to overhaul its response to both diseases

KWAZULU-NATAL PROVINCE, SOUTH AFRICA—On 4 April 2012, an 11-year-old boy named Sandile left his family in Ulundi and traveled 250 kilometers south to his new home at King George V, a hospital in Durban that specializes in the region's most complicated tuberculosis (TB) cases. Like 69% of the other 224 patients at King George V, Sandile was co-infected with HIV, which in all likelihood he acquired from his mother. Records that came with him indicated that she had died, but they did not specify the cause.

Sandile had received a full 6-month course of treatment for TB in 2009. But HIV-infected people remain especially vulnerable to *Mycobacterium tuberculosis*, and a few years later, he again developed an active case of the lung-damaging disease. The doctors here surmise that he didn't receive his medication each day during his second bout, allowing drug-resistant strains of *M. tuberculosis* to flourish. With drug-resistant TB, his treatment at King George V would require 18 months of costlier, less effective, and more toxic "second-line" pills plus painful daily shots of medication for at least 1 year.

Multidrug-resistant (MDR) TB destroyed Sandile's left lung and badly damaged his

right one. In September, Sandile was healthy enough to play outside, but Babu Sunkari, the pediatrician in charge of the children's ward, warned that Sandile had nearly died the month before: He had a severe respiratory attack and kidney failure, probably from a combination of TB drug side effects and an infection he picked up at the hospital, further compounded by his HIV infection.

Sandile urgently needed a lung transplant, Sunkari said, yet, like most South Africans without means—which is almost everyone infected with TB here—there was no transplant in the offing. "He doesn't have a hope in hell of surviving," Sunkari said.

Sunkari said he was seeing more and more of these sad cases. Sandile was one of 32 children on the pediatric ward at King George V last September who had MDR or the even more frightening extensively drug-resistant (XDR) TB. "This used to be the normal TB hospital, with one to two cases of MDR," Sunkari said. "Now we're not taking normal cases in the ward."

Children like Sandile "mirror what is happening in the community," says Nesri Padayatchi, who ran the TB program at King George V for 14 years until leaving to do clinical HIV/TB research at Durban's Cen-

tre for the AIDS Programme of Research in South Africa (CAPRISA).

South Africa has the world's worst convergence of HIV and TB. It has 5.7 million HIV-infected people, more than any country; the highest rate of TB per capita; and, after Russia, the second highest reported number of MDR TB cases. The big picture is that South Africa has less than 1% of the global population but more than 25% of people dually infected with these diseases—a particularly deadly combination. This alarming rise in coinfection has been dubbed the HIV/TB syndemic, because, for both biological and social reasons such as poverty, the two diseases have synergistic effects, with each making the other worse.

South Africa's HIV/TB syndemic has its roots in a badly broken health system and years of neglect. For TB, a cure has existed for decades, but many sick people in South Africa remain undiagnosed, and those who receive treatment often fail to take their drugs as prescribed, which in turn gives rise to drug-resistant strains. "The reason we have so much MDR and XDR TB here is because implementation of our TB program has sucked," Padayatchi says.

HIV infection cannot be cured, but drugs can effectively thwart disease for decades

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◀ **Double jeopardy.** Babu Sunkari shows the lungs of his young patient Sandile, who was infected with both HIV and *M. tuberculosis*.

and also slow the spread of the virus. But from 1999 to 2008, as the AIDS epidemic exploded in the country, then–South African President Thabo Mbeki and his health minister—who for many years questioned whether HIV even caused the disease—dragged their feet when it came to both treatment and prevention.

Now, with President Jacob Zuma at the helm and a new health minister in place, South Africa has made a dramatic turnaround and is at the forefront of efforts to combat these married diseases. “We’re trying to integrate HIV/AIDS and TB, to regard them as two sides of the same coin,” says Minister of Health Aaron Motsoaledi, who Zuma appointed when he took office in 2009. And to that end, the government has allocated more of its own money and attracted substantial international support to find everyone who needs drugs for HIV and TB, better coordinate their treatment, improve prevention efforts, and ramp up research to figure out how the diseases interact.

But South Africa still has a long way to go, and progress often occurs more slowly than anyone would like.

HIV and TB’s disastrous marriage

In the mid-1990s, South Africa followed the lead of many other countries and introduced what’s known as DOTS—directly observed therapy, short course—to combat tuberculosis. DOTS used new drugs that led to cures more quickly, and as part of the program, observers watched people swallow their pills each day to make sure they took all of their doses. But just as TB rates began to decline, HIV infections skyrocketed, and by the turn of the century, the two diseases were climbing in parallel (see graph, p. 900).

Salim Abdool Karim, a clinical epidemiologist who heads CAPRISA, helped launch the DOTS program in Hlabisa, a rural municipality not far from Ulundi. At the time, he says, TB mainly afflicted elderly men. “In the mid ’90s, a couple of things hit us in a way that we just couldn’t grasp—overnight it caught up with us,” Karim says. Suddenly, the TB patients were predominantly young and female, a reflection of the fact that the AIDS virus was racing through that population. “All our previous efforts to improve

TB control were overwhelmed,” he says.

Pre-HIV/AIDS, South Africa’s DOTS program—which certainly had operational challenges—made the headway that it did because intact immune systems help contain both illness and spread. *M. tuberculosis*



Good news, bad news. Bonnie Davis (top) says a new diagnostic, GeneXpert, saved the life of this MDR TB patient at Hlabisa Hospital. Davis’s colleague, Martin Tshipuk (bottom), says the wards are full because many patients don’t adhere to treatments.

infects one-third of the world’s population, but it remains latent in most, typically causing disease only when HIV or other factors compromise the immune system; 90% of people who have latent TB infections never

develop active disease in their lifetime. But HIV drastically alters that equation. A person with a latent TB infection who then becomes infected with HIV has a 10% chance of developing an active case of TB each year. HIV and TB interact in a vicious cycle. HIV compromises the immune system, which allows *M. tuberculosis* to copy itself at higher rates. *M. tuberculosis*, in turn, triggers inflammatory responses and the secretion of transcription factors that directly activate HIV genes. More HIV means more immune destruction—and still more opportunities for *M. tuberculosis* to flourish. A compromised immune system has difficulty containing the infection to the lungs, which means the disease can travel around the body, damaging the brain, the spine, or joints. Diagnosing TB in HIV-infected people is also trickier, so they often do not receive treatment and spread the infection to others. Worldwide, TB is now the leading cause of death in HIV-infected people.

Joel Ernst, director of infectious diseases at New York University in New York City, says these two bugs likely aid and abet each other by several other mechanisms that scientists have yet to elucidate. “There is so much we don’t know about HIV/TB interactions,” says Ernst, co-author of “HIV and Tuberculosis: a Deadly Human Syndemic” in the April 2011 issue of *Clinical Microbiology Reviews*. “I can’t think of a better syndemic—or a worse one—than HIV/TB.”

The Mbeki administration fueled the syndemic with its pronounced skepticism about the link between HIV and AIDS and its reluctance to introduce antiretrovirals (ARVs). To the astonishment of the medical community inside and outside the country, Mbeki’s health minister, Manto Tshabalala-Msimang, went so far as to advocate treatments such as lemons, beetroot, and garlic instead of promoting ARV drugs. “It was very clear that our response to the HIV pandemic in the beginning was the wrong one,” says current Health Minister Motsoaledi (see Q&A, p. 902).

HIV prevalence in South Africa nearly doubled between 1998 and today, and many people needlessly died from AIDS. A study done by a team at the Harvard School of Public Health and published in the 1 December 2008 *Journal of Acquired Immune Defi-*

ciency Syndromes calculated that 330,000 lives could have been saved between 2000 and 2005 had Mbeki's administration launched a "feasible" ARV program. TB cases tripled during Mbeki's time in office, and in 2010, nearly half a million South Africans developed active cases—only China and India had a higher incidence—and 60% of them had HIV.

A decade ago, South Africa, like many other countries, did little systematic testing for MDR TB—which is more difficult to diagnose than drug-susceptible TB. A 2004 World Health Organization (WHO) report cited only two provinces that had repeatedly surveyed their populations for MDR TB, and the trends suggested that cases were relatively stable. But then in 2006, news of the world's first outbreak of XDR TB in KwaZulu-Natal—53 cases at the same hospital in Tugela Ferry—made clear that the mix of HIV and drug-resistant TB in South Africa had hit a flash point (*Science*, 15 February 2008, p. 894).

Patients with XDR TB don't respond to the first-line drugs or several second-line treatments. Cases of XDR TB had been reported elsewhere before the Tugela Ferry outbreak occurred: Between 2000 and 2004, public health officials had documented 347 sporadic cases worldwide. But no one had seen a cluster of cases, which indicated that an extremely difficult to treat strain of *M. tuberculosis* was likely spreading quickly from person to person. As researchers described at the 2006 International AIDS conference, of the 53 people who had XDR strains at Church of Scotland Hospital in Tugela Ferry, 52 died a median of 16 days after being diagnosed with TB. Although HIV status was not known for nine of the patients, everyone else was infected with the virus.

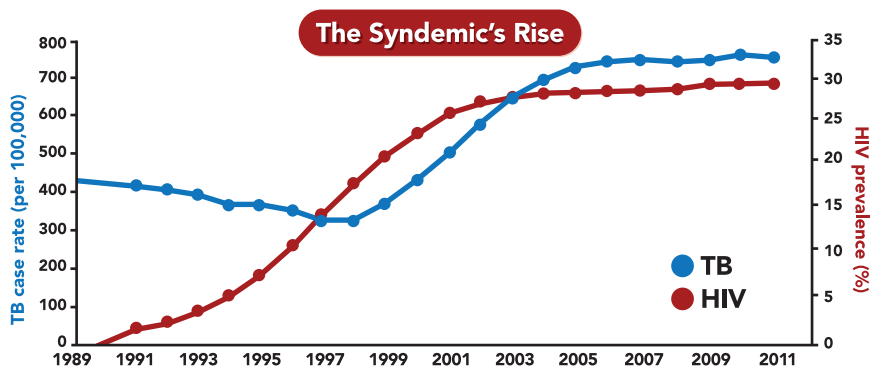
The Tugela Ferry outbreak set off alarm bells globally, sparking fears of a pandemic of XDR TB and intensifying attempts to find other cases. Last year, WHO said 84 countries had reported cases of similarly difficult to treat *M. tuberculosis* strains; it also estimated that of the world's 650,000 or so cases of MDR TB, 9% were XDR TB.

Within South Africa, the Tugela Ferry outbreak led to extensive studies to determine why it happened and what relation it had to HIV. As it turns out, XDR TB had been bubbling beneath the surface in KwaZulu-Natal for several years, driven by a sharp increase in

MDR TB cases that had gone unnoticed. A team led by epidemiologist Kristina Wallengren of the KwaZulu-Natal Research Institute for Tuberculosis and HIV (K-RITH) in Durban reviewed laboratory records for all TB patients who had their *M. tuberculosis* analyzed for drug resistance. In the October 2011 issue of *Emerging Infectious Diseases*, the team reported that between 2001 and 2007, MDR TB cases jumped from 216 to



Early warning. Nesri Padayatchi says the rise in drug-resistant TB in kids reflects the exploding problem in adults.



Feeding the fire. The rise in HIV infections fueled South Africa's explosion of TB cases.

2799, and XDR cases had a startling 45-fold increase from six to 270.

Several of the researchers who first described the Tugela Ferry outbreak published compelling evidence in the 1 January issue of *The Journal of Infectious Diseases* that most people became infected with XDR TB at the Church of Scotland Hospital. The researchers looked at 148 people—a larger group than the one originally described in

the outbreak—who had XDR TB between January 2005 and December 2006. Genetic analyses of the *M. tuberculosis* isolates from the patients showed that all but 4% closely matched each other, and 82% of the people had overlapping hospital stays at Church of Scotland. Although 98% of the patients were HIV-infected, only 31% of them were receiving anti-HIV drugs. All had extremely low levels of CD4 white blood cells, leaving them vulnerable to TB.

The study concluded that the Tugela Ferry outbreak resulted from a combination of long hospital stays, poor infection control, delays in the diagnosis of TB drug resistance, and HIV infection. Although the feared pandemic never materialized, the Tugela Ferry outbreak will go down in history for prodding the world to realize that XDR TB had made more inroads across the globe than anyone had imagined. And in South Africa, it also sent a loud message to the country that the response to its HIV/TB syndemic needed a serious overhaul.

Extraordinary measures

On 1 December 2009, World AIDS Day, President Zuma announced sweeping reforms that aimed to prevent and treat infections with both HIV and *M. tuberculosis* more effectively. "We need extraordinary measures to reverse the trends we are seeing in the health profile of our people," Zuma declared.

As Zuma spelled out, the health ministry would launch a "massive campaign" to test 15 million South Africans for HIV. ARVs, until then still restricted to people who had severely damaged immune systems, would become available to HIV-infected people with TB much earlier in the course of the disease. "TB and HIV/AIDS will now be treated under one roof," he promised. Zuma also decided to make ARVs available to all HIV-infected, pregnant women and children under a year of age, regardless of their health status. Fifteen months later, on 24 March 2011—World TB Day—Motsaledi unveiled a new, equally ambitious, two-pronged approach to diagnosing active cases of tuberculosis. First, the government would ramp up efforts to test the 407,000 families that had a relative with an active case of TB. The second prong called

for a countrywide deployment of a new machine called GeneXpert, which promised to revolutionize the ability to find active TB cases.

The most common TB diagnostic is a sputum “smear” test for *M. tuberculosis* that relies on microscopy; it detects only 60% of active cases and that drops to as low as 35% in HIV-infected patients. Culturing the sputum samples gives the most accurate results, but these tests can take weeks. Drug-sensitivity tests require still more time and costs. GeneXpert, which uses PCR to amplify and detect specific *M. tuberculosis*

sequences, in contrast provides a highly accurate diagnosis within 2 hours, and can also detect MDR TB. Although GeneXpert is more expensive than sputum smears or culturing, studies suggest that it will save money in the long run by reducing transmission.

A review article in the 8 December 2012 issue of *The Lancet*, “Health in South Africa: changes and challenges since 2009,” shows how these “radical policy changes” have already produced results. Co-authored by CAPRISA head Karim and several other leading South African researchers, the article notes that government funding for TB

and HIV/AIDS nearly doubled between 2009–10 and 2010–11. The mass HIV-testing campaign still under way had reached 13 million South Africans by June 2011, up from 2 million. The country quickly developed the largest GeneXpert TB program in the world, performing nearly half a million tests by July 2012. Since April 2010, South Africa has doubled the number of people on ARVs to nearly 2 million, more than any other country. And nearly 400,000 HIV-infected people who have latent *M. tuberculosis* infections take isoniazid, a first-line TB drug that works as a preventive.

Treatment as Prevention, Real World

KWAZULU-NATAL PROVINCE, SOUTH AFRICA—In the summer of 2011, researchers for the first time began seriously discussing the possibility of ending the AIDS epidemic in certain locales. The catalyst for what to many would have seemed like wild-eyed optimism a year earlier was a remarkable finding about the power of antiretroviral (ARV) drugs:

If HIV-infected heterosexuals take their ARVs as prescribed, levels of HIV in their bodies fall so low that it reduces the chance of transmission to their long-term partners by 96%. Published in the 11 August 2011 issue of *The New England Journal of Medicine*, the study definitively proved that treatment is prevention. But it had one major weakness: It wasn't “real world,” as study participants rigorously adhered to the regimen, taking their medication as directed, which knocked down the virus in their blood to undetectable levels for several years. The cohabiting couples in the study were also more stable than seen in many sub-Saharan communities.

Now on page 966, a new study shows that widespread ARV use reduced the spread of HIV in a large population here in KwaZulu-Natal, which has one of the world's most severe HIV/AIDS epidemics—and is as real world as it gets. “We were super excited when we first saw the data because the results were so striking,” says epidemiologist Frank Tanser at the Africa Centre for Health and Population Studies in Somkhele who led the study.

Hlabisa, a subdistrict in KwaZulu-Natal, provided an ideal testing ground for a community-level assessment of treatment as prevention. In 2003, the Africa Centre began a population-based survey in Hlabisa of HIV status, sexual behavior, and socioeconomic factors of residents aged 15 and older. The researchers initially hoped their door-to-door survey would help them understand the impact of the HIV/AIDS epidemic in the region and its

demographic contours. The survey coincided with a massive rollout of ARVs in KwaZulu-Natal, which the center helped coordinate, so this gave them a new opportunity to look at treatment as prevention. To date, the center's efforts have helped start more than 20,000 people on anti-HIV drugs.

The Africa Centre team identified 16,667 people who were uninfected with HIV in 2003 and agreed to have repeated tests for the AIDS virus each year. Between 2004 and 2011, 1413 of these people became infected.

Researchers at the Africa Centre had previously shown that sexual partnerships in Hlabisa have strong geographical links. In a study published by Tanser and colleagues in the 16 July 2011 issue of *The Lancet*, 67% of the participants reported having sex over a 5-year period with someone in their small Zulu community known as an *isigodi*. So for the new study, the investigators created a circle around each uninfected person's home that had a radius of 3 kilometers and then analyzed the proportion of HIV-infected people receiving ARVs in that small area. If treatment worked as prevention on a community level, then, theoretically, there should be fewer new infections in neighborhoods where a higher percentage of infected people were on ARVs.



Helping hands. Hlabisa residents participated in a study that proved treatment as prevention works in the real world.

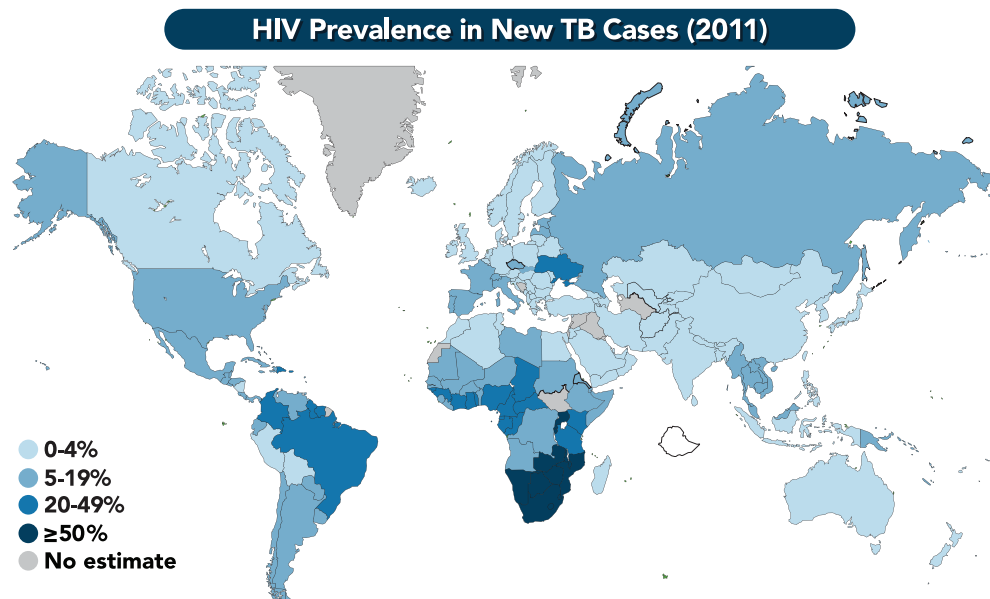
During the study, ARV coverage jumped from less than 10% of the infected population to 37%. Tanser's group found that the new infection rate was lowest in places that had the highest ARV usage: If ARV coverage was 30% to 40%, the people in those communities had 38% fewer new infections when compared with those in locales that had ARV coverage of less than 10%.

What's more, the study showed that not all infected people, and certainly not 100%, need to be on treatment to see an effect. “Once you get to 30% coverage, you get a steep decline in new infections,” Tanser says. So in the end, this is one of the rare examples in which the real world is a more forgiving place than many people imagined.

—J. C.

Tangible benefits have begun to surface, too. The proportion of deaths related to HIV/AIDS has dropped from 52.3% of the total in 2006 to 43.6% in 2011. (Death rates from TB, excluding HIV, have remained relatively constant.) As a study in this issue reports, life expectancy in KwaZulu-Natal went from 49.2 in 2003—the year before the government began providing ARVs—to 60.5 in 2011 (see p. 961). Only 2.7% of babies born to HIV-infected women in 2011 were infected after 6 weeks, down from a high of 20% to 30% a decade earlier. “Undeniably, much remains to be done,” the report concludes. “However, for the first time in two decades, this progress instills a basis for hope.”

Several other recent developments illustrate how far South Africa has come in comparison to its neighbors. A study in this week’s issue of *Science* shows that widespread use of ARVs in KwaZulu-Natal reduced the spread of HIV in the community (see p. 966)—the first demonstration outside a clinical trial that treatment works as prevention in a sub-Saharan African setting. The country also has become a world leader in HIV/TB research, and now boasts its own world-class institute devoted



Hardest hit. The HIV/TB syndemic has walloped southern Africa.

to the study of these married diseases. With \$40 million from the Howard Hughes Medical Institute, in October 2012 K-RITH opened a swank 4000-square-meter, 8-story building that features several high-tech bio-safety spaces with negative air pressure that can handle dangerous pathogens, state-of-the-art DNA sequencing machines, and the fastest Internet connection avail-

able in the country. “We’re trying to put the technology where the problem is,” says K-RITH’s director, William Bishai, who maintains a lab at Johns Hopkins University in Baltimore, Maryland.

In the next 3 years, the government says in its National Strategic Plan for these diseases that it hopes to reduce new HIV and TB infections by 50%, which it will do

Pulling South Africa Back From the HIV/AIDS Brink

When Aaron Motsoaledi, the South African minister of health, spoke in Vienna at the 18th International AIDS Conference in 2010, he was largely unknown to that community, which had come to see his government as a pariah in the fight against HIV/AIDS. At the Vienna meeting, Motsoaledi, a medical doctor who was appointed to the health ministry in May 2009 shortly after President Jacob Zuma took office, announced to the audience that his country had done an about-face. Today, many of the goals that Motsoaledi spelled out in his Vienna talk have been met, as the country has aggressively expanded testing and treatment for both HIV and TB (see main story, p. 898).

Motsoaledi met with *Science* in September 2012 in the courtyard of an aging but elegant conference center atop a hill in Pretoria. The center was hosting President Zuma and other leaders attending an African National Congress (ANC) meeting. An executive member of ANC who during the anti-apartheid struggle once worked with an underground, armed wing, Motsoaledi was candid and refreshingly blunt, never sidestepping controversial issues or requesting that his thoughts be off the record.



New Rx. Health Minister Aaron Motsoaledi has reinvigorated the country’s attack on HIV/TB.

Q: The International AIDS Conference in Durban, South Africa, in 2000 was a turning point in the epidemic, as the world recognized that treatments saving lives in rich countries should be available to the poor. Yet your president at the time, Thabo Mbeki, was questioning whether HIV caused AIDS. What did you think of your country then?

A.M.: I was very confused and extremely disappointed. It was one of the lowest moments in the country. I’m a trained doctor, so I was also aware and worried, but I was not [working] within the health sector.

Q: What did you do when you came in as health minister?

A.M.: Now that I was given authority, it didn’t need rocket science for me to know exactly what it is that I need

to do, and I went out to do it. I was not the only one. We had a new chairperson of the South African National AIDS Council, the Deputy President Kgalema Motlanthe, who had similar beliefs. On top of everything else we had President Zuma, who also complained this was a wrong policy, and now that he was in charge he cannot allow it. All I had to do was to show the main figures, exactly what the scourge has done.

by ensuring that everyone in the country receives an annual HIV test and an exam for TB symptoms. It also aims to increase ARV coverage to 80% and drive mother-to-child transmission below 2%. As the strategic plan notes, achieving these aspirations depends on substantial funding increases that will have to come mainly from government coffers. K-RITH's Bishai also soon hopes to have a dozen leading HIV and TB researchers from around the world investigating how the two diseases interact. "It's a black box," says Bishai, whose own work focuses on the genetics of drug resistance. "And the fields have been siloed. There's almost no co-authorship."

Despite these steps forward, Hlabisa Hospital, located atop rolling hills that abut one of several game parks in KwaZulu-Natal, reveals the staggering challenges that exist today. Martin Tshipuk, the doctor in charge of HIV/AIDS at the 275-bed hospital, in September 2012 led a tour of the crowded female adult ward, where some patients slept on mat-

tresses on the floor. "Up to 80% are here for HIV, and all have complications of opportunistic infections," Tshipuk says. "Almost all patients are coming in on ARVS,



Success story. Drugs cured Nomusa Manqele's TB and have controlled her HIV infection. "People have trouble with adherence because they're not accepting their status," Manqele says. "I tell them to look at me. I'm fine. I'm healthy. I'm proud of my status. I told myself the stigma, I'd get rid of it."

but they're coming in very sick and the problem is adherence" to drug regimens.

Improved diagnostics and better use of existing drugs alone will not curb the HIV/TB syndemic. That will require even wider use of

ARVs and existing antibiotics, as well as new treatments that cure drug-sensitive *M. tuberculosis* more quickly and have more power against resistant strains. (The United States just approved a new drug, bedaquiline, that combats MDR TB [*Science*, 11 January, p. 130].) Effective vaccines against both diseases, which remain elusive, would make huge inroads, too. But South Africa clearly has more tools—and more political will—to confront HIV/AIDS and TB than ever before.

Then again, meaningful change takes time, and it ran out for Sandile on 8 October. Despite specialty care at King George V, the tag-team drubbing from HIV and *M. tuberculosis* finally proved too much for the young boy's body, leading to irreversible kidney damage and sepsis. During his entire 6 months of his hospitalization, he never had a visitor. One week passed before relatives arrived from rural KwaZulu-Natal to retrieve his body, which they took back to their village for a traditional funeral.

—JON COHEN

Q: What figures did you show?

A.M.: In this country, it's not because of a lack of research and knowledge that a wrong policy was followed. HIV/AIDS is a sort of animal, and many different groups had different parts of this animal. Nobody knew exactly what the animal looked like. I realized that if we brought these parts together, we'd start seeing whether we're dealing with a big animal or a mouse—whether it's a monster or something you can just kick and say, ay, this is nothing. I went back to 2000 and collected every piece of evidence about HIV in South Africa from internal and external organizations, and I put it together in a PowerPoint. And this started showing a clear picture of what's happening all over the country. Before I did this, some very prominent members of society were saying, "Minister, are you not exaggerating this HIV/AIDS problem? Don't we have diabetes, high blood pressure, cancer? We never hear you mention these things—every time you open your mouth it's HIV/AIDS. Don't you understand the danger of becoming the minister of HIV/AIDS instead of the minister of health?" Now these graphs balanced things.

Q: Who saw this PowerPoint?

A.M.: The first person I targeted was the president. It was October 2009, and it was half past 11 in the night when he gave me an appointment. I asked for 45 minutes with him. He was shocked. He said, "I've been knowing what we were doing was wrong but no one ever showed me in numbers and figures." He said, "Tomorrow, you are going to present this to the Cabinet." And I did. And some members of the Cabinet also said, "Oh, these figures and numbers, ay, something out of this world. We never saw them."

They might have seen them somewhere but in different parts, and putting them together, they said, "This is no ordinary animal—it's a monster." And that's why everything started.

Q: Some developing countries think South Africa has made great strides because it has more resources. Is that true?

A.M.: I don't necessarily think so. It was more of a political will. I didn't only show the PowerPoint to the Cabinet, I showed it to all the ministers, including the minister of finance. So all of the ministers are united. The public turning point happened on World AIDS Day, first of December 2009, when the president shared the platform with the executive director of UNAIDS [the Joint United Nations Programme on HIV/AIDS], Mr. Michel Sidibé, who was also very helpful. The president made far-reaching announcements about how to deal with HIV/AIDS. The budget was already completed for the full year, but he went to the minister of finance and said, You have to change the budget to suit this announcement. Other ministers had to accept budget cuts.

Q: What frustrates you and makes you think the country is not doing what you hope it could do or should do?

A.M.: You need highly skilled people to deal with this problem. We are struggling with that. There's a massive shortage of health workers around the whole world, but in sub-Saharan Africa especially. Secondly, the burden of disease is very high. And because of our wrong approach in the beginning, the program started very late, and it means we're lagging behind. We lost a decade, and that makes it very difficult to catch up.