View from the Ground

Fighting a Pandemic

The World's Effort to Control Multidrug-Resistant Tuberculosis

Alex Bozzette

"Si tienes el dinero, puedas hacer maravillas." If you have the money, you can do wonders. Those were some of the first words Dr. Clara Friele, coordinator of Ecuador's National Tuberculosis (TB) Control Program, said to me last summer. The disease she and so many others are fighting is fully curable. It has been documented for millennia—recorded in the bones of Egyptian mummies, the pages of the Hindu Vedas, and the scenes of countless films, plays, and operas (from *Tombstone* to *La Traviata*).[1] TB claimed 1.4 million lives in 2010 and is the leading killer of people with AIDS.[2] It infects the lungs before spreading throughout the body and, if untreated, kills almost two-thirds of those with the severe active disease.[3] Supported by a generous travel-study grant, I spent June through August 2011 in South America, East Africa, and Southeast Asia learning from those who fight this TB pandemic firsthand.

Funding, as Dr. Friele warned, limits TB control considerably. She explained, however, that *dinero* is just one of many obstacles opposing efforts to curb the deadly disease. The major obstacle we face today is drug resistance: TB bacteria can become immune to the drugs used to fight them when treatment regimens are interrupted or poorly managed. This

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happened rapidly throughout the latter half of the twentieth century, which spawned multidrug-resistant tuberculosis (MDR-TB)—a strain immune to our two most effective TB drugs. MDR-TB now affects 650,000 individuals worldwide, and that number is growing.[4] Those people live in 114 reported countries, and that number is growing as well.[5] Worse still, its complicated laboratory diagnosis and need for rare drugs make MDR-TB more expensive and difficult to treat than its non-resistant counterpart.

Nonetheless, MDR-TB cures are almost guaranteed where laboratories exist to diagnose the disease, drugs are available to treat it, and health care providers ensure that patients stick to their prescriptions. Crucially, the international community has demonstrated that this can be done in the developing countries where MDR-TB is most common. Key initiatives are markedly improving MDR-TB control worldwide by building laboratory capacity, making MDR-TB drugs more available, and promoting best practices for treatment supervision.

But the sense I had in late 2010 was that this progress is not moving nearly fast enough. It is limited by very real challenges on the ground. As a student of global health, I wanted to learn more about those challenges directly from the health workers that face them. I wanted to walk through their hospitals, visit their laboratories, and experience their communities to see current efforts in context. How far have MDR-TB control programs come? Where are they going? What obstacles do they face? And how might they overcome those obstacles? I traveled 40,000 grant-supported miles to meet with people who had answers to those questions.

June in South America. My visit with Dr. Friele kicked off three months of interviews and site visits with twenty-nine TB professionals in six countries on three continents. I left Washington, D.C. in late May and split June between Ecuador and neighboring Peru. After Haiti, they have the second and third highest rates, respectively, of new annual MDR-TB infection in Latin America and the Caribbean, but effective control efforts have kept those rates well below those in many Asian, Eastern European, and sub-Saharan African countries. Ecuador's MDR-TB control program is up-and-coming, and Peru's is hailed as an international success story. I hoped to learn about their work and identify best practices that might fit similar countries. That happened to a degree, but my experiences mainly introduced me to a reality that must change: even relatively good MDR-TB control programs are being outpaced by the disease.

I visited my first TB-specialized hospital after leaving Dr. Friele's office at the Ecuadorian Ministry of Public Health. Ms. Christiana Fattorelli—an Italian ex-pat and field representative for the Ecuadorian Lung Health Association—guided me to Hospital Pablo Arturo Suarez in downtown Quito. The waiting room was packed. Never-ending lines filed down hallways as healthy families stood and sat alongside the ailing ill. For a disease that is spread through particulates in the air, like TB, it was a biosecurity nightmare.

Ms. Fattorelli explained her work as we waded through the crowd en route to

the hospital's TB director. She spends most of her time searching for the disease in slums and rural villages. Door to door, she asks residents if they know anyone with rapid weight loss, coughing, fever, or night sweats. When they do, she finds those people, meets them, and refers symptomatic TB suspects for diagnosis and treatment. She does all this without wearing a standard protective mask because "they make people scared to let you into their homes." For Ms. Fattorelli, the patients are more important than the risk of infection. Her incredible dedication was shared by nearly everyone I would meet over the next three months.

If those whom Ms. Fattorelli suspects to have TB can afford to pause their lives—which the impoverished who are most commonly infected often cannot do—and travel to a potentially distant hospital (such as Pablo Arturo Suarez in the city center), they will then be evaluated and asked for a sputum sample—a coughed-up combination of spit and mucus. During the long wait for a doctor or nurse, those who are ill risk infecting the many others stuffed in the hospital's halls. After patients are seen, their sputum is sent to a laboratory for diagnosis. The overwhelmingly most common method for diagnosing TB worldwide is microscope-based: a stain highlights any TB bacteria present in a sputum sample, and a technician manually searches for them under a microscope. That process is quick, cheap, and simple—three attributes that make it the mainstay of low-resource labs in developing countries—but it only detects 50 percent of positive cases.[6] Shooting for more accuracy means making patients wait two months for the results of more complex, expensive, and rare bacterial cultures—a process that grows bacteria from sputum samples to provide a 'TB or no TB' verdict. With Ms. Fattorelli, I visited the lab in Quito that conducts these cultures for the region's patients. It was badly understaffed and water leaked through its bowed ceiling.

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Once patients are identified as TB-positive, diagnosing suspected drug resistance tacks on another step that takes two more months and is far more complex. Most high MDR-TB burden countries have fewer than three labs sufficient for this later stage of diagnosis.[7] Ecuador has one, and it is over two hundred miles away from Quito, in the coastal city of Guayaquil. Factoring in time spent sending samples to that distant and overburdened lab, up to six months can separate a patient's hospital visit from his or her MDR-TB diagnosis. The sick spend this diagnostic limbo getting sicker, dying, and often spreading the disease to those around them (at an average rate of ten to fif-

teen others per year).[8] Shortening that limbo by securing faster diagnostics is paramount, and it is Dr. Friele's top priority as Ecuador's National TB coordinator.

Dr. Oswaldo Jave, Peru's National TB coordinator, shares that priority. Days after leaving Quito for Lima, I interviewed Dr. Jave from his office in the Peruvian Ministry of Health. In front of a wall dotted with epidemiological data, Dr. Jave spoke about his program proudly. And rightly so: Peru boasts a world-renowned TB program that helped pioneer the directly observed treatment, short-course (DOTS) strategy—the gold standard for TB treatment that has cured 46 million people since 1995.[9]

In 2006, Peru decided to catch its laboratories up to speed by beginning to universalize MDR-TB testing and purchasing faster diagnostics. Fantastic progress has been made, but not all is well with Peruvian TB control. Days after meeting Dr. Jave, I traveled to northern Lima on the local stretch of La Panamericana, the Pan-American Highway that runs from Prudoe Bay, Alaska to Patagonia, to see another side of the disease. As I neared the slums that house the city's worst MDR-TB epidemic, development deteriorated, homes turned to half-finished concrete shacks, and streets got dirtier by the mile. Nearby, I met with ASET-COMAS, the world's oldest non-profit created by and for TB patients. Its president, Ms. Luz Estrada Gonzáles, a former TB patient, like everyone else in the organization, explained that, "due to stigma, most don't talk about TB. And because of discrimination, they don't want to admit [to having] it." One of her colleagues described TB as a "disease that the government tries to hide" to preserve its image—this in a country renowned for its TB work. That stigma cripples federal support, treatment success, and community engagement, and it must end.

In Ecuador and Peru, laboratories will bottleneck treatment efforts until diagnostics are improved, but they are far from the only shoddy links in the anti-MDR-TB chain. A shortage of hospital beds, poor social support for the ill and their families, and pervasive stigma are three others. So long as those are realities, Dr. Julio Castro's often-quoted take on the Peruvian TB epidemic will ring true in both countries: "The program is good, but the disease is better."[10] Dr. Friele, Ms. Fattorelli, Dr. Jave, ASET-COMAS, and many others I met are working hard to make sure that this changes.

July in Africa. One month into the whirlwind summer, three flights took me from Lima to São Paolo to Johannesburg to Dar es Salaam, where I stayed with a Tanzanian friend from the Jane Goodall Institute and learned about MDR-TB control in the first of two East African countries I would visit. The same challenges I encountered in South America were comparable or worse in Tanzania and Ethiopia, with one major complication: rampant HIV/AIDS.

Tanzanian MDR-TB control benefits from a well-organized public health network but suffers from terrible diagnostic delays. A few days into my stay in Dar es Salaam, I hopped on the local *dala-dala* network—a web of impossibly crowded mini-buses with unposted

routes and signs in Swahili—and headed for Tanzania's central TB reference lab at Muhimbili National Hospital. Ms. Basra Doulla, the lab's director, referenced the *dala-dalas* that my foreigner self barely managed to navigate (with hand signals and lots of laughs) while discussing her country's biggest MDR-TB challenges. Like Ecuador's reference lab in Guayaquil, Ms. Doulla's lab is the only one in Tanzania that can diagnose MDR-TB. Without a more organized transportation system, regional health workers must use unreliable *dala-dalas* to get sputum samples into the capital for analysis. And they are only permitted to do it one quarter per year because Ms. Doulla's lab is so overwhelmed; in other words, if a patient contracts MDR-TB during his or her region's three off quarters, he or she will not be diagnosed.

Days after visiting the central reference lab, I learned that Tanzania's horribly high HIV/AIDS rate (one in twenty has it nationwide) affects MDR-TB control in more ways than one.[11] Dr. Jacob Kayombo, Director of a non-governmental organization (NGO) called the Tanzanian Public Health Initiative, believes that Tanzania's dearth of MDR-TB diagnostics, among its other TB challenges, would be best addressed through HIV/AIDS-caliber advocacy, awareness, and engagement. Dr. Kayombo explained that Tanzanian HIV/AIDS policies have made the disease a "central issue"—one that is discussed in "any government office, workplace, or community." He stressed that "we need to make TB a social problem whereby everyone should take part [in the solution]. That is what the HIV community has managed to do in the country." Doing the same for TB would improve funding, community-based case detection, and patient care. It would also boost MDR-TB awareness and educate patients about the risk of developing resistance by straying from their prescriptions.

In Ethiopia, my interviews focused on the double-edged link between the two pandemics: HIV/AIDS as fuel for spreading TB and TB as the leading killer of those with HIV/AIDS. For internist Dr. Yoseph Mamo of UCSD-Ethiopia, UC San Diego's satellite HIV/AIDS project in Addis Ababa, the two diseases are "evil collaborators." TB flourishes in the weak immune systems of the HIV-positive; they are twenty to thirty-seven times more likely to contract TB than those without HIV.[12] Co-infection is a massive problem in Ethiopia because 70-80 percent of the country has latent TB—a dormant and non-contagious infection that healthy individuals easily suppress. HIV strips the body of its ability to keep latent TB from turning into active TB disease—the deadly condition we simply call "tuberculosis." Picture a large river being unleashed as a dam crumbles; that is what HIV is doing to Ethiopia's TB epidemic.

Ties between TB and HIV/AIDS are far from limited to Tanzania and Ethiopia or even Africa at large. The "evil collaborators" are at work globally; in 2009, 24 percent of those who died from TB worldwide had also been living with HIV.[13] We cannot address one pandemic without fighting the other.

August in Asia. Two months and four countries into my trip, I made for India and Vietnam—two countries

with raging MDR-TB epidemics. Their similarities with one another and with my previous stops conveyed how truly global MDR-TB is. But their stark differences made it clear that fighting this international crisis requires unique domestic solutions.

Days into my stay in Delhi, rickshaws and an extensive metro network took me to meet Dr. R.V. Asokan, a senior TB expert with the Indian Medical Association. He began by illustrating the horrible magnitude of India's MDR-TB epidemic. The country of 1.2 billion people generates a staggering 2.3 million *new* TB cases every year, one hundred thousand of which are estimated to be MDR.[14] India takes the limited labs challenge to an entirely different level: it diagnoses fewer than 2 percent of its MDR-TB cases and is treating fewer than three thousand of them nationwide.[15]

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Limited funding and technical expertise slow India's ongoing laboratory expansion, but part of its MDR-TB epidemic is owed to the way existing resources are used. The most sophisticated lab I visited all summer was in the heart of Delhi, but many poor Delhi residents who need its diagnoses cannot access them. TB thrives in weak immune systems (exacerbated by HIV/AIDS, malnutrition, and poor sanitation), spreads quickly in densely populated areas with poorly ventilated housing, and takes root where limited health care means the sick stay sick. In other words, it affects the urban and rural poor, who cannot pause their tough lives to seek out potentially distant diagnosis or treatment.

That reality is the reason why Operation ASHA, "hope" in Hindi, exists. The young and growing Indian NGO's mission is to bring reliable DOTS treatment to impoverished communities. In a meeting with one of their strategy consultants, I learned that OpASHA does not maintain permanent field offices for their DOTS centers. Instead, they rent corners of existing spaces to cut operational costs, and they select sites near slum entrances so residents can access treatment on the go. When someone fails to come in for their daily dose, OpASHA finds them to ensure patients get the care they need (and therein prevent MDR-TB from developing). They can do this because they train and employ slum residents as their DOTS providers and counselors, a move that provides unprecedented access to communities that would be near impossible for government services to navigate. OpASHA's grassroots, patient-focused approach to TB control has huge potential in a world where hospitals wait for the ill to come to them.

As much as it might be needed, the OpASHA model cannot work every-

where. That became very apparent days into my stay in Vietnam. From her office in Hanoi's National Lung Hospital, Vietnam's National MDR-TB Director, Dr. Hoang Thanh Thuy, informed me that poor diagnostics and patients abandoning treatment are her biggest challenges. Vietnam generates an estimated four thousand new MDR-TB patients each year, but only three hundred of those are being treated.[16] Unfortunately, domestic NGOs like India's OpASHA cannot be part of the effort to reverse that reality because Vietnamese civil society is near non-existent.

In TB terms, India and Vietnam were at once strikingly similar and radically different. Both are in dire need of rapid MDR-TB diagnostics and better, more accessible treatment. But their disparate demographics and public sectors conveyed that international policies cannot be applied without first being adapted to unique domestic contexts.

Conclusions. Ninety days after leaving for Ecuador with only a backpack, I returned to Washington, D.C. with a mountain of memories and newfound respect for the terribly complex MDR-TB crisis. My summer left me intimidated by the spreading pandemic and inspired by those working tirelessly to control it. One of those professionals, Dr. Kumelachew Abate of UCSD-Ethiopia, left me with these words: "More can be done to fight against tuberculosis. If we believe that today is the first day of the rest of our lives, we can do a lot for the generations to come."

Support for MDR-TB control has made huge advances over the past decade, but much more must be done to realize Dr. Abate's hopeful words. Increasing the TB drug supply, redoubling TB-focused public health education, investing in TB-concerned civil society partnerships, and restructuring TB patient care to make treatment more accessible are just some of the ways governments should strive to improve MDR-TB control in their countries.

Above all, the international community must improve laboratory diagnostics by supporting efforts such as the World Health Organization's EXPAND-TB initiative—a program working hard to strengthen labs in high-burden countries. The world currently diagnoses just 7 percent of its MDR-TB cases, but epidemiologists state that we must diagnose at least 70 percent to stop MDR-TB from spreading.[17] A ten-fold expansion of this highly technical effort is a daunting goal, but we have already seen the consequences of failing to strive for it: resistance compounds with time, and India just became the third country to report cases of totally drug-resistant TB (TDR-TB), a strain that the World Health Organization has not yet officially recognized but many scientists believe is resistant to every TB drug in existence.[18]

Allowing TB to continue to affect millions and worsen is irresponsible and morally unacceptable. Fortunately, efforts to introduce new rapid diagnostics—such as the user-friendly GeneXpert system, which can do in two hours what takes two months by bacterial culture—are electrifying the anti-TB community and giving real hope to this fight. But many new tests are expensive and complex. They cannot replace cur-

rent diagnostics anywhere close to overnight on the scale that is needed, especially in the countries where epidemics are most severe. Experts I met in Ecuador, Peru, Tanzania, Ethiopia, India, and Vietnam agree: current progress in MDR-TB control is far from enough. We must work quickly and collaboratively to change that.

NOTES

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