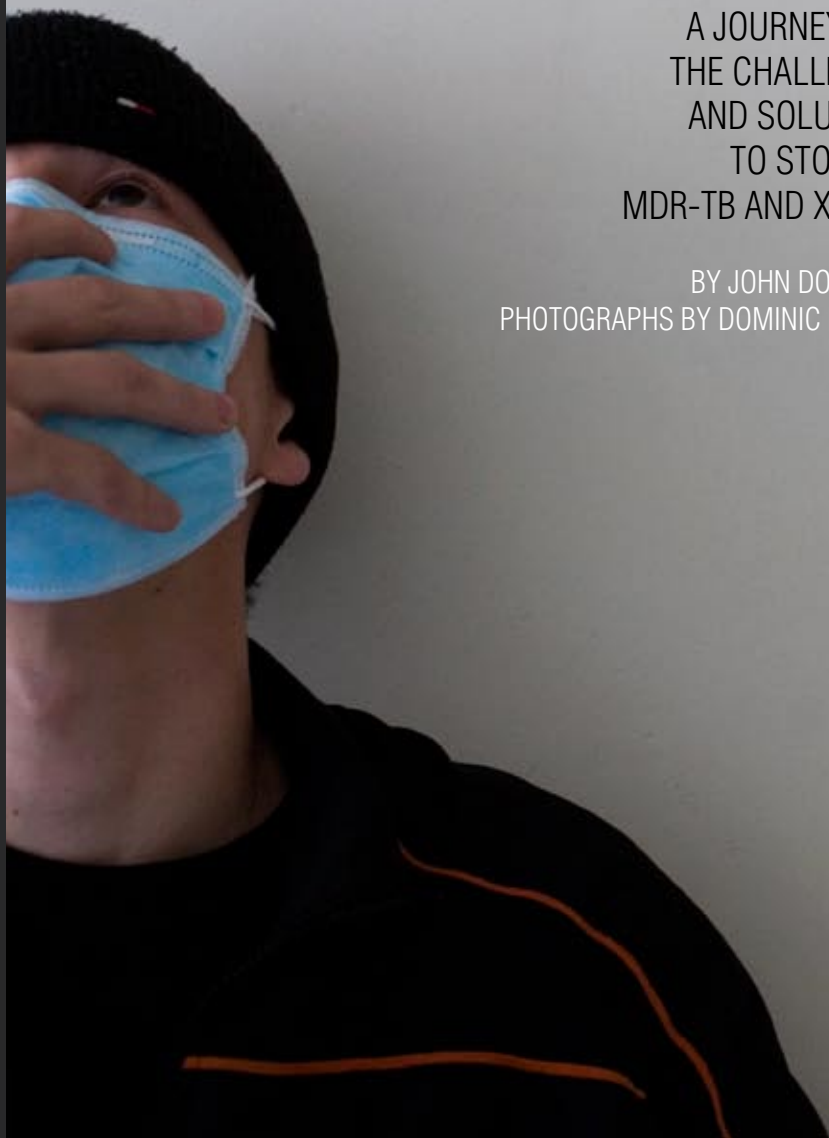
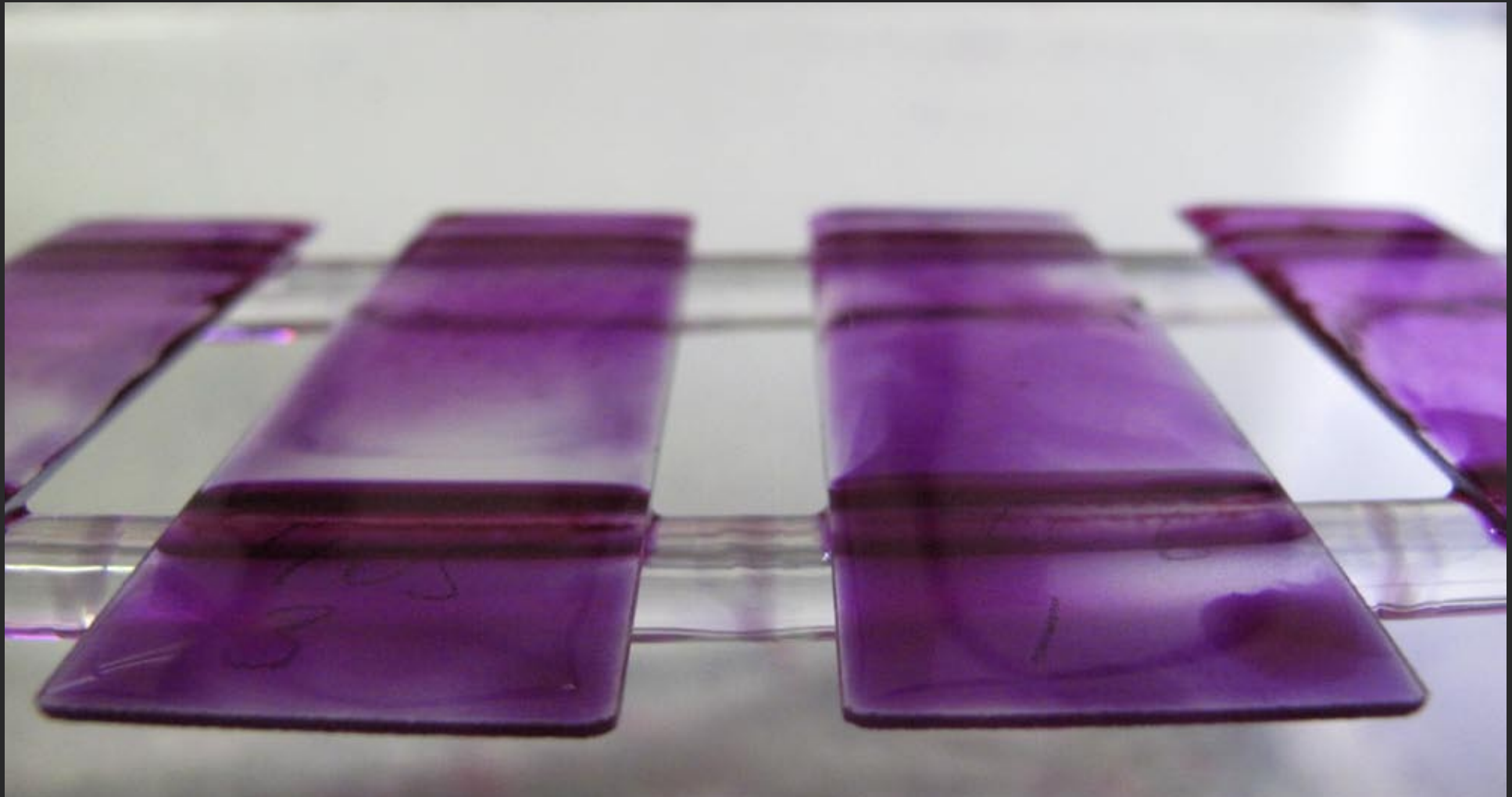


# AIRBORNE

A JOURNEY INTO  
THE CHALLENGES  
AND SOLUTIONS  
TO STOPPING  
MDR-TB AND XDR-TB

BY JOHN DONNELLY  
PHOTOGRAPHS BY DOMINIC CHAVEZ





Rows of patient sputum smears, stained and ready for microscopy examination in the Central TB Laboratory at Queen Elizabeth II Hospital in Lesotho.

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FRONT COVER PHOTO: Beibut, a former soldier, is a patient at the National TB Center in Almaty, Kazakhstan.

BACK COVER PHOTO: Masepe Lenkoe smiles at her son at their home in Sekhutlong, Lesotho.

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# FOREWORD



DR MARGARET CHAN  
DIRECTOR-GENERAL  
WORLD HEALTH ORGANIZATION

I was struck by the words, recorded in this booklet, of a teenager from Manila. She was explaining what multidrug-resistant tuberculosis has meant for her life.

"I want to be a nurse and help others who are sick," said Charlene Laguinday. "I want to give back what was given to me."

Charlene has personally experienced the toll of this airborne infectious disease that sickens and kills so many people every year. She recently lost her mother to multidrug-resistant tuberculosis, or MDR-TB. She is now undergoing treatment for the same disease, and her health is improving with every week.

Her experience demonstrates the importance of high commitment to good-quality TB control. MDR-TB, which can spread from one person to another, is a tragedy that should not happen. Properly managed, TB can be cured. Poorly managed, TB can develop into a form that resists multiple drugs, with successful treatment undermined and costs multiplied at least 100 times.

The figures are alarming. MDR-TB is now causing an estimated half a million new cases every year. The stories collected in this booklet give you an idea of the suffering behind the statistics. Even more ominous is the recent rise of extensively drug-resistant TB, or XDR-TB. This form of the disease, which is extremely difficult to diagnose and in some cases impossible to treat, is now being reported from more than 50 countries.

If the right action is not taken right now, the continuing spread of MDR-TB could transform a disease that is curable with affordable medicines into a costly and deadly epidemic. If the right action is not taken right now, the continuing rise of XDR-TB could take the world back to the era that predates the development of antibiotics, with nothing in hand to guarantee treatment success.

This would be a vastly bigger tragedy. Some countries burdened with MDR-TB are showing the way forward with commitment, leadership and good results. However, to tackle this preventable problem on an adequate scale, national TB control programmes will depend on progress on a larger health agenda that aims at universal health coverage, high-quality patient-centred care, laboratory strengthening and infection control in health facilities. That agenda must also include improved mechanisms for drug prequalification and rational use of drugs, as well as the intensive engagement of the private sector, patients and communities.

I urge you to read the personal stories collected in AIRBORNE. These are human tragedies that should never have happened. But these are also stories about the uplifting success possible when the right elements are in place.

I further urge you to accept this call to action. The microbial world has given us a clear either-or situation. Either we tackle the problem now with rational and proven approaches, or we pay later with an epidemic of an airborne disease that renders our modern-day medicines and straightforward treatment regimens obsolete. This would truly be a tragedy, on a huge and costly scale, that should not happen.



Charlene Laguinday laughs in her two-room home in Manila. "I want to be a nurse and help others who are sick," she said.

# INTRODUCTION

INSIDE A DARK HUT, CUT INTO A REMOTE MOUNTAINSIDE IN LESOTHO, A PRIEST WEARING A LEOPARD-PRINT CAPE AND SITTING ON A THRONE-LIKE CHAIR LED HIS PARISHIONERS IN HARMONIES THAT FILLED THE ROOM.

Sweat dripped from the tip of his nose, and the still air was so warm that my cheeks burned. I wanted to escape outside for the promise of a breeze; but I stood still, almost transfixed by the sounds and images.

Then I noticed a woman sitting against a wall.

She sat apart from 20 people squeezed together on the dirt floor. I had met her the day before. Her name was Matsepe Lenkoe, and the remarkable thing about her was that for the past year she had been living a world away in the capital city Maseru receiving treatment for multidrug-resistant tuberculosis (MDR-TB). Seeing her, the thought crossed my mind that this would be an ideal place to catch MDR-TB – if an infected person coughed, any of us could be breathing in the bacterium during the hours that the priest would keep us.

I stayed in the hut. This was the beginning of a journey around the world to learn more about the global response to MDR-TB; and here, far from any town or road, in an impoverished country, I learnt my first lesson, with sweat trickling down my back: The Government of Lesotho had protected me and all the others that morning at the Jerusalem Church of Africa. Because it had decided that treating MDR-TB should be approached as an emergency; and because, in very short order, it had built a comprehensive programme designed to prevent the spread of TB and to treat those

who had drug-resistant strains, we were safe. Thanks to this political commitment, Lenkoe was not only alive – she was no longer infectious.

This was quite remarkable. Still I wondered: Was she lucky?

There is no doubt.

The World Health Organization (WHO) estimates that as few as 10% of the roughly 500,000 people who contract MDR-TB every year receive treatment. And only 3% of the half-million were receiving drugs procured through the Green Light Committee, an initiative of WHO and the Stop TB Partnership that helps countries access quality-assured drugs needed to treat MDR-TB.

It is early days in the global response to treating drug-resistant TB. For the past decade or more, many countries around the world have successfully built TB control efforts. Now they have to build on those efforts to control the more dangerous threat of drug-resistant TB – strains that cannot be cured by the most commonly used drugs.

Experts from the WHO's Stop TB Department and the Stop TB Partnership warn that if countries do not act now to stop MDR-TB, the world will face an airborne contagion that will become increasingly untreatable and increasingly global. It will stop at no border, and it will infect much greater numbers of people. The early signs are already apparent: At the beginning of 2007, 20 countries reported cases of extensively drug-resistant TB (XDR-TB); at the end of 2008, the number had jumped to 55, in part because countries had started searching for cases.

In my travels over two months, I kept thinking back to similar trips that I had made around sub-Saharan Africa in 2003, when a few countries lucky enough to have leaders acknowledging a looming AIDS catastrophe had begun to figure out how to treat AIDS patients. In 2009, the situation is much the same for MDR-TB, an awakening both to the threat and to models that can control it even in the most challenging settings.





MDR-TB patient Matsepe Lenkoe (centre) covers her eyes during church in Sekhutlong, Lesotho.



The IV is for Dmitry Gagarin at the National TB Center in Almaty, Kazakhstan.

It was fascinating to watch those attacking the MDR-TB problem put in place these plans and then tinker with them day by day. No place did it exactly the same, each adapting models to fit their epidemic, their health-care system and their history. Kazakhstan, concerned about people staying indoors and spreading infections during its long, harsh winters, expanded numbers of hospital beds available for patients, and has begun to install infection-control systems in hospitals to protect health-care workers. Lesotho has been training hundreds of community health workers (and paying them small salaries) to monitor patients in far-flung areas. And the Philippines was treating patients at open-air drop-in centres and allowing them to return to their homes instead of keeping them in hospitals.

The Philippines model, in fact, had produced an unexpected benefit – something I had rarely, if ever, seen before in covering global health for nearly two decades: communities of patients who looked out for each other.

At one MDR-TB clinic in Manila, I watched Antia Silverio, a 48-year-old who had just finished her MDR-TB treatment five months before, run errands for doctors, nurses and patients. She was one of more than a dozen ex-patients who also had become volunteers; she told me that she couldn't leave – the caregivers had given her back her life, and now she wanted to do the same for others.

From my trips, there seemed little doubt that governments could beat this disease, despite the numerous barriers and obstacles. The question is, will they? In the stories that follow, you'll learn about governments that did take actions and saved thousands of lives. They saved people such as Silverio, who spends hours every week simply sitting next to patients and encouraging them to take their medicine, even though they hated doing so.

"I tell them, 'Look at me, I'm old, I've been really sick. If I did it, you can do it, too.'"

Is a patient a metaphor for a nation? If the Philippines can do it, can others as well? Global TB experts believe so. Now they need country leaders to prove them right.

– John Donnelly  
February 2009

## DEFINITIONS

### MDR-TB

Multidrug-resistant TB (MDR-TB) is a form of TB that does not respond to the standard six month regimen using first line-drugs (i.e. resistant to isoniazid and rifampicin). It can take two years to treat with drugs that are more toxic, and 100 times more expensive. If the drugs to treat MDR-TB are mismanaged, further resistance can occur.

### XDR-TB

Extensively drug-resistant TB (XDR-TB) is a form of TB caused by bacteria resistant to all the most effective drugs (i.e. MDR-TB plus resistance to any fluoroquinolone and any of the second-line anti-TB injectable drugs: amikacin, kanamycin or capreomycin).

### STOP TB STRATEGY

The Stop TB Strategy aims to dramatically reduce the global burden of TB by 2015, and has six components: Pursue high-quality DOTS expansion and enhancement; Address TB-HIV, MDR-TB, and the needs of poor and vulnerable populations; Contribute to health system strengthening based on primary health care; Engage all care providers; Empower people with TB, and communities through partnership; Enable and promote research.

### DOTS

is the basic 5-point package that is the first component of the Stop TB Strategy: political commitment with adequate and sustained financing; early case detection and diagnosis through quality-assured bacteriology; standardized treatment with supervision and patient support; effective drug supply and management; monitoring and evaluation of performance and impact.

# MDR-TB: REACHING ALL CORNERS OF THE WORLD

In 2008, WHO released the largest survey ever carried out on drug-resistant tuberculosis with results from more than 80 countries. The Anti-Tuberculosis Drug Resistance in the World report confirmed that the spread of MDR-TB is reaching all corners of the world. But at the same time, the epidemic is far from uniform with regions and countries facing a variety of challenges. It also showed that a few countries had managed to stabilize or reverse the number of cases.

The report can be read at [www.who.int/tb/publications/2008](http://www.who.int/tb/publications/2008)

## REGION OF THE AMERICAS

The prevalence of MDR-TB is low in the region as a whole. The region has the largest number of Green Light Committee-approved projects. Many countries plan to upgrade laboratory networks due to increased demand for development of second-line testing capacity.



## EUROPEAN REGION

The proportion of MDR-TB was significantly higher in the Eastern European and Central Asian countries, with an average of 10.0% MDR-TB among new TB cases, and 37.7% among previously treated TB cases. In most of Central and Western Europe, both proportions and absolute numbers of drug-resistant cases remain low.

## EASTERN MEDITERRANEAN REGION

The extent of second-line drug resistance is not known in the region. The primary limiting factor to expanding survey coverage is the high number of countries in conflict situations. Another limiting factor is the poor laboratory infrastructure in many countries.

## WESTERN PACIFIC REGION

Information on resistance to second-line drugs is limited. The Western Pacific also faces limited capacity for culture and drug-susceptibility testing. Some countries have extensive culture networks in the public sector, but only one has a significant number of laboratories able to conduct drug susceptibility testing.

## AFRICAN REGION

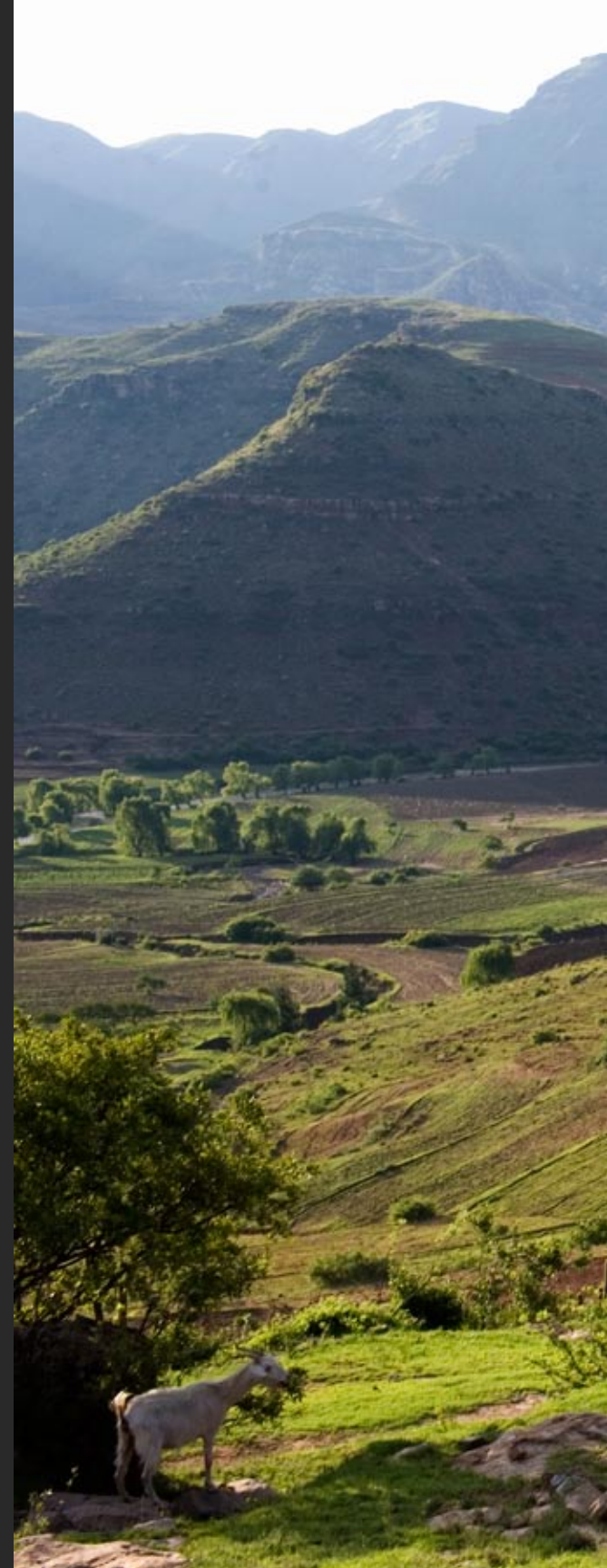
The most critical factor in addressing drug resistance in African countries is the lack of laboratory infrastructure and transport networks that can provide rapid diagnosis. It is possible that current survey methods, which are based on smear-positive cases, may underrepresent HIV coinfecting TB cases, which are more likely to be smear negative. In addition, transmission dynamics of drug-resistant TB in a heavily HIV-infected population are not well understood. A large outbreak of XDR-TB in an HIV-positive population in the province of KwaZulu-Natal, South Africa, was associated with extremely high mortality and highlighted the vulnerability of TB patients coinfecting with HIV.

## SOUTH-EAST ASIA REGION

Though resistance in the region is moderate, the overall burden of MDR-TB is considerable. Important progress has been made throughout the region in initiating plans for MDR-TB treatment, and almost all countries have Green Light Committee applications approved or in the pipeline. Virtually, all countries have identified laboratory capacity as the primary bottleneck to scaling up diagnosis and treatment. Also, many countries in the region have growing private sectors that are currently managing most of the MDR-TB cases, and second-line drugs are widely available through the private sector.

# TO THE ENDS OF THE EARTH

SEKHUTLONG, LESOTHO — SHE LEFT THIS VILLAGE IN THE MOUNTAINS GAUNT AND WEAK, TAKING TINY STEPS ALONG A THIN RIBBON OF A PATH, THE COMMUNITY'S ONLY LINK TO THE OUTSIDE WORLD. MATSEPE LENKOE'S FIVE CHILDREN TEARFULLY SAID THEIR GOODBYES — GOODBYES, THEY FEARED, FOR GOOD.





For three hours she walked with great difficulty, supported by her elderly mother, until she reached a town named Ketane. There, a small aeroplane flew her and her mother to the capital city Maseru – less than 160 km away, but a journey that takes more than six hours by road.

Lenkoe's body harboured a grim cocktail of two deadly infections – HIV and TB – which was later diagnosed as multidrug-resistant TB. But she was fortunate in one important respect: her government had only months earlier started fighting the spread of TB with everything it could muster.

This was no simple task, especially in Lesotho, a small mountainous kingdom landlocked by South Africa. Its population of approximately 2 million inhabits mostly rural areas – some living near treacherous roads that are sometimes obliterated by floods or blanketed by heavy snows. Others live far from roads, tucked into the folds of mountains that can be a day's ride by horse to the nearest town. Cell phones do not work here; foot messengers bring news.

When it came to mounting a national response to multidrug-resistant TB, or MDR-TB, Lesotho faced other obstacles. It had no laboratory capacity to process sputum samples for TB diagnosis; it shipped all samples to South Africa. It had no pharmaceutical system through which to order the proper drugs for patients such as Lenkoe. It had almost no doctors or nurses trained in treating MDR-TB. It had no hospital with the proper infection control measures to protect health-care workers. And most frighteningly, its TB epidemic was being fuelled by the explosive number of HIV and AIDS cases: an estimated 23% of adults aged 15 to 49 years were infected with HIV, the third highest rate in the world, unknown thousands of whom were coinfecting with TB.

But the country did respond, acting almost immediately in 2006 when, in the words of Health and Social Welfare Minister Dr Mphu K. Ramatlapeng, “we had the scare from South Africa”.

The scare was an outbreak of extensively drug-resistant TB (XDR-TB) in Tegula Ferry, a town in South Africa's KwaZulu Natal province, just beyond Lesotho's eastern border. Of the first 53 patients, 52 had died.

From that moment, Lesotho treated drug-resistant TB as an emergency. It created a national plan of action, and from the start sought outside experts.

The Ministry of Health and Social Welfare asked the World Health Organization (WHO) for ideas, which led to an application to the Green Light Committee, a WHO initiative that oversees distribution of quality-assured drugs used to treat MDR-TB; the committee approved, with money from UNITAID, the release of drugs for up to 400 MDR-TB patients.

The Ministry also asked for help from two knowledgeable outside groups: Partners In Health, which has experience in treating drug-resistant TB in the developing world, and the Foundation for Innovative New Diagnostics (FIND), which has experience in setting up laboratory systems for a range of diseases, including for TB diagnosis.

In April 2007, FIND renovated the country's main laboratory in two months, reconfiguring the facility from six to four rooms, installing a negative air system with air locks on rooms to protect workers from infection, and introducing a MGIT machine that could complete a number of tests to determine the drug-resistance patterns of TB cases. For the first time, Lesotho would do its own MDR-TB laboratory tests.

Meanwhile, Partners In Health trained doctors, nurses and community health workers to treat patients coinfecting with HIV and TB. It began renting several one or two-room homes for TB patients who lived far from Maseru but would need to live there during their treatment in case of emergency. And on the outskirts of Maseru, the Government identified an underused health centre for leprosy patients and turned it into a 20-bed TB hospital that also had a negative air pressure system to lessen the risk to health workers. The renovations, and other work on the MDR-TB project, were paid for with a US\$ 3 million grant from the Open Society Institute. The Ministry of Health and Social Welfare also made available its in-house air service – the Lesotho Flying Doctor Service – which picked up TB patients at three remote locations and flew them to Maseru for treatment.



By June 2007, the laboratory was operating.

By July, health workers were treating the first MDR-TB patients.

By September, the hospital was open.

And by October, the hospital was full; one of the patients was Lenkoe, the woman from faraway Sekhutlong.

Since then, the Government's effort has continued to expand, although the response has not yet covered the entire county. One of the most important developments came in late 2008, when the laboratory began using state-of-the-art DNA-amplification techniques to identify drug resistances in a TB sputum within two days – a huge technological leap in controlling TB. Earlier tests, involving growing cultures from sputum samples, would take between three and four months, which meant that TB patients received the most common drugs; for anyone with MDR-TB or XDR-TB, that was the wrong treatment and months wasted.

Managing and treating MDR-TB are never simple, not even in the most advanced medical settings, and the programme has wrestled with several complications. Dr Hind Satti, Director of Partners In Health Lesotho's MDR-TB programme, said it appears that patients there have experienced more serious side-effects from anti-TB drugs than in other countries, likely related to HIV-TB coinfection and severe malnutrition. That has complicated efforts to return patients to their communities as quickly as possible; one side-effect, renal or kidney failure, "could create an emergency situation that has to be managed in a few hours or the patient could die."

She said one major unmet need is economic support to families of patients; in many cases, the patient had been earning wages and the loss of that money often is devastating.

In addition, there's the worry of undetected MDR-TB outbreaks because the effort does not cover the entire country.

"We have fear about cases in the mountains that we don't know about," said Archie Ayeh, Partners In Health's programme manager in Lesotho. "Unless they present in a clinic or a health worker reports their illness, we have no way of knowing whether they have MDR-TB. It could go on until a whole village is infected."

The Government's efforts to control MDR-TB have already resulted in many benefits. One has been to bolster the country's entire response to TB. "The place to start preventing MDR-TB is to strengthen all TB services," Satti said.

A key strategy towards that end was training hundreds of community health workers in the basics of TB control, including making sure patients adhered to their treatment. One such worker was Lenkoe's mother, Malenkoe Lenkoe, aged 67 years. The mother had moved with her daughter to Maseru; after Lenkoe's stay in the new MDR-TB hospital, the two lived in a rented house provided by Partners In Health. "It was a long effort," the mother said in 2008, after returning home to Sekhutlong. "My daughter sometimes didn't want to take the drugs – they were making her confused and angry. I had to talk to her a long time about the benefits."

Along with other nearby community health workers, the elder Lenkoe walks to the Nohana Health Clinic in Ketane once a month for training updates. Each worker is paid 300 rand a month, or roughly US\$ 30. It is enough to buy many food staples.

The path to Sekhutlong hugs hillsides, dropping to riverbeds, and climbing to villages. On a late summer afternoon, the elder Lenkoe walked to her village with Lesole Mokele, a 35-year-old counsellor with Partners In Health. Above them, on a steep slope, a sheep herder sang to his sheep. Nearby, a bent-over young girl picked *moroho* shoots – wild green vegetables. This was a slower pace of life, and travelling long distances was an accepted part of living here.



Matsepe Lenkoe smiles outside her house in Sekhutlong, Lesotho. She returned home having been cured of MDR-TB.

Mokele said the Ketane-based project alone serves 75 villages, many of which were more remote than Sekhutlong.

“We have patients beyond the mountains,” he said. “Sometimes the patients are so sick they cannot walk or stay atop a horse. So people carry them on a stretcher. Last month, men from a faraway village carried a patient coinfecting with HIV and TB. When one got tired, another took over. It took them six hours.”

When they arrived in Sekhutlong, waiting for them was a thin woman wearing a red wool cap, a purple shirt, a white skirt, black socks and pink plastic sandals. It was Matsepe Lenkoe, and she was smiling broadly. She had returned to her village on 27 October 2008 – a year after she had left seeking help. On the day of her return, when she crossed the crest of the hill leading into Sekhutlong, her five children ran to her, one after the other, hugging her.

Her middle child, 12-year-old Palamang, wept at her side. He said nothing, he just clutched her. He thought he would never see her again.

Matsepe Lenkoe solemnly looked back at that moment. “I wasn’t sure I would live,” she said, sitting on a stool that overlooked a broad valley and mountains beyond. “If it weren’t for my mother, if it weren’t for the government, if it weren’t for my doctors and nurses, I wouldn’t be alive.”

“I am very happy,” she said. “I can go collect water. I can clean the home, I can prepare food for dinner, and I can be with my children.” She started preparing dinner – rice, greens, and other vegetables. Palamang watched.

The night of her return, he said, he crawled into his mother’s bed. “I slept the whole night with her,” he said. He had never done this before. He did it the next night as well, and the night after that – and every night since.

“I just want to be near her,” he said, and he rose to help his mother with dinner.

## TOP 10 COUNTRIES WITH TB PATIENTS

**India**  
**China**  
**Indonesia**  
**Nigeria**  
**South Africa**  
**Bangladesh**  
**Ethiopia**  
**Pakistan**  
**Philippines**  
**DR Congo**

SOURCE: WORLD HEALTH ORGANIZATION, 2007



## DR MPHU K. RAMATLAPENG HEALTH AND SOCIAL WELFARE MINISTER

Ramatlapeng, who has been Lesotho's top health official since 2007, was once a doctor practicing general medicine. She headed the Clinton Foundation's office in Lesotho. She talked about the spread of MDR-TB in her ministry office.

### Q: What motivated you to accelerate the response to the MDR-TB threat?

A: It was when we had the scare from South Africa, with their cases of XDR-TB (extensively drug-resistant TB). The cases were very near the border of Lesotho. We became aware from this that we, too, might have the same problem, and might find some XDR-TB cases.

### Q: What was the initial goal?

A: Find out who has it – MDR- and XDR-TB. The problem of treatment failure was evident throughout our country.

### Q: So what did you do?

A: We went into an emergency mode. In six months, this is what we did: put a new lab in place (actually that took two months); trained staff; refurbished a hospital and turned it into a MDR-TB hospital. You have to deal with this problem in the immediate moment. Our reaction was not typical to the way that most governments or organizations work.

### Q: Lesotho now is dealing with many cases of HIV-TB co-infection. What are you doing about it?

A: It's a huge challenge for us. The two epidemics

are treated almost as one entity. When you have HIV, we immediately test them for TB – we almost expect that they will have it. Even if they are negative with TB, we tell them that they can expect to have it, and they should look for any warning signs.

### Q: What is your advice to other Ministers of Health regarding tackling MDR-TB?

A: They have to act really fast. . . If you have a problem with MDR-TB, admit you have a problem. If your people are dying from this, don't put this behind closed doors. Go save them. That means not only saving the people with MDR-TB but also the general population. You have to protect the population. You've got to stop it.

# OPEN BORDERS

MASERU BORDER POST, LESOTHO – SOUTH AFRICA COMPLETELY SURROUNDS LESOTHO, AND THE FLOW OF PEOPLE BETWEEN THE TWO COUNTRIES ALMOST NEVER STOPS.

And that poses huge challenges in stopping the flow of drug-resistant TB as well. “One of the main problems here is that if someone gets TB in South Africa and then they move back to Lesotho, they don’t often continue treatment, meaning that TB develops into MDR-TB,” said Health and Social Welfare Minister Dr Mphu K. Ramatlapeng.

She said that health ministers in the region have started to talk about ways to share information in TB control, but acknowledged, “we have not made much advancement so far. Until we do, if one country has a problem with TB, all the countries will have a problem.”

Lesotho, meanwhile, has taken one small step on its own, hiring the country’s first two border officers to monitor environmental health issues.

But by late 2008, two months into the job, the officers said they had not stopped a single person on health grounds – and didn’t know how they would do so. “It’s not so practical,” said Bonang Ntsoale, 23, standing in an office shared with a customs officer who performs livestock checks.

Ntsoale said he and his assistant, Keneude Senoko, have no equipment to test for diseases, nor a laboratory to carry out the tests. They have asked for a nurse, mini-clinic, vehicle, protective clothing, gloves, and masks. So far, they have none of them.

They also want to work in collaboration with South African border health officials. But those officials are based an hour away, and come to the border just twice a week. And they themselves work eight hours a day, five days a week. The border is open 24/7.

“People are just coming in and going out,” Ntsoale said, “and there’s nothing we can do about it.”



## FACT BOX

ESTIMATED PERCENTAGE OF TB PATIENTS ALSO HIV-POSITIVE IN 2008: **80%**

PERCENTAGE OF NEW TB PATIENTS WITH MDR-TB: **0.9%**

PERCENTAGE OF TB PATIENTS CURED: **73%**

» For more information, see [www.who.int/tb/country/](http://www.who.int/tb/country/)

# UNCOMMON CARE

MANILA, PHILIPPINES — DR MARIA TARCELA GLER LOOKED OUT OVER THE ROOM OF REVELLERS — MOST OF THEM HER MULTIDRUG-RESISTANT TB (MDR-TB) PATIENTS. MORE THAN 80 WERE CELEBRATING CHRISTMAS, PLAYING GAMES, SINGING AND ENJOYING A HOLIDAY LUNCH. THESE WERE HER “SMEAR-NEGATIVE” PATIENTS — NO LONGER INFECTIOUS AFTER WEEKS OR MONTHS OF TREATMENT.





For Gler, this was her work in full view – a range of outcomes, mostly positive ones, but not all.

In the middle of the open room, five stories up in a downtown building, one of her patients, a skinny 14-year-old girl, Charlene Laguinday, was handing out plates of food. She had been doing well on her drug therapy, and her fellow patients took to her as if she were their little sister.

Next to Gler stood Catherine Del Rosario, a 27-year-old interior designer who had TB meningitis. Against Gler's recommendation, she stopped taking the powerful medications after 15 months – just three months before her scheduled stop – because she said she couldn't take it anymore.

And in the back of the room, leaning against a wall of glass that looked out at the skyscrapers of central Manila, was an elegant woman dressed in black. Tears ran down her face. She was Delia Yao. She never had TB. But her daughter did.

"Her daughter died a few months ago," Gler said quietly. "The patients are very close to her, and they were very close to her daughter. Her daughter was just 16. She had a very bad TB infection. It got to a point where I didn't know what to do anymore. We did everything, but the disease just kept coming back."

Someone called Gler to the front. Several patients surrounded Yao, their hands on her shoulders and arms. The mother brushed away her tears, but they kept coming, a stream she couldn't stop.

Later, Gler stopped Yao outside the room. "How are you doing?" the doctor asked.

Yao told her she felt she had to come; the community of patients meant the world to her daughter, Dianne Peebles. "I wanted to see everybody – I wanted to remember what was her life," Yao said.

In the Philippines, such bonds are common among MDR-TB patients,

relatives and health-care workers. They are natural outcomes from using a community-based model to try to stem the transmission of the deadly infection.

This approach means most of the patients never go to a hospital; they are outpatients, cared for at their homes, with detailed instructions, and masks, to protect others from infection. It means the patients arrive six days a week (Sunday is their holiday) at drug-distribution points – sometimes outside under tents and next to hospitals – to receive their medication. And it means they get to know each other, and then start to care for one another.

The community-based model, which is being used in varying degrees in other places such as Peru, was built atop a system in disarray. In the late 1990s, most TB patients avoided the free-of-charge public health system and used private doctors. Fearing that this mishmash of care strategies would generate huge problems, the Government took a firm step to strengthen its national TB control programme, including entering into partnership with the Tropical Disease Foundation (TDF) and other private groups. It was based on DOTS [the basic package that underpins the Stop TB Strategy]. In five years, the national programme had expanded DOTS across the country. In 10 years, it had overseen training of 5000 private doctors to correctly administer DOTS.

But it didn't stamp out drug-resistant TB: for previously treated patients, fewer than half were cured, and many died. Further tests revealed those who failed treatment had MDR-TB; officials realized they had an epidemic of these cases. TDF, with the Government's blessing, applied to the Green Light Committee – an initiative of the World Health Organization (WHO) –



for enough second-line medication to treat 200 MDR-TB patients. The committee made the Philippines its first approved project.

The start of a MDR-TB treatment programme was extraordinarily difficult. Money was scarce; for several years, TDF paid for the drugs through fund-raising. But an infusion of funding from the Global Fund to Fight AIDS, Tuberculosis and Malaria, starting in 2003, helped substantially expand treatment coverage. By the end of 2008, the MDR-TB project had treated 1316 patients in all.

Gler, known to her friends as Maricelle, has treated several hundred of them. The 40-year-old doctor, once a serious mountain climber who had more recently started scuba diving – both outdoor escape valves – didn't come to her work through traditional avenues. She first worked in rural areas helping the poor, joining development programmes in far-away islands during her pre-med studies at the University of the Philippines and later before her hospital residency.

A fellowship training in infectious diseases had deepened her interest in public health. In 2005, she joined TDF as a clinic physician and was later appointed head of its MDR-TB clinic in the central part of Manila – first housed inside the Makati Medical Center and then across the street from the hospital in an open-air section on the first floor of TDF's new building. "The work is difficult, but it's also very rewarding when people do well and get cured," she said one morning in the clinic, where she, like everyone else, wore a mask.

The scene around her was astounding to the uninitiated, showing the powerful adverse effects of the medication, which included decades-old classes of antibiotics that had been once all but abandoned because of their toxicity. Almost all patients carried a plastic bag wrapped around their wrist. After taking the drugs from a nurse or volunteer, most patients quietly, and with as much dignity as possible, lowered their heads between their knees and threw up into the bags. They repeated this process again and again, some staying for two hours in all, retreating to the corners of the clinic before feeling well enough to leave. Some shivered in the midday heat. Others whispered words of comfort in their ears.



TOP: Catherine Del Rosario, a 27-year-old interior designer in Manila, stopped her treatment for TB meningitis three months before it was finished.  
BOTTOM: Charlene Laguinday (left), an MDR-TB patient, laughs with Maria Antoniette De La Cruz and Antia Silverio (right) at Maria's house. Charlene and Antia are volunteers at International Center for Tuberculosis in Manila.

For some, the worst adverse effects came later, when they felt depressed – even to the extent of thinking about ending their life. One was Del Rosario, the interior designer who stopped taking the drugs three months before her end date.

Del Rosario said the drugs threw her into a deep depression. She started having panic attacks. “I just couldn’t fight the fight anymore,” she said. “I felt like I was always high on drugs. Sometimes I didn’t think it was worth living anymore.”

Another MDR-TB patient, a doctor of internal medicine who did not want to be identified because he feared that going public “would make me a marked man,” said he had been taking the medication for one year, and the effects had steadily worsened.

“It’s the mental anguish,” he said in a private room at the clinic, where he turned off the lights because the drugs had made him extremely sensitive to many things, including overhead lighting. “I started having severe hallucinations, suicidal ideations. I’ve tried to cope with it by talking with my wife and with my family. That helps for a while; then it gets worse. I’m grounded religiously, and I know that suicide is wrong, but I have prayed to the Lord, ‘Lord, why can’t you take me now?’”

For an hour, he talked non-stop about his pain. Then he paused and drew himself up in his chair.

“It’s a personal hell,” he said slowly, in the dark room, “if the Lord will excuse me for saying it.”

The doctor had called Dr Gler frequently over the past year. He was not alone. Many calls were cries for help. Gler learnt to listen well, sometimes late into the night. Her work, she now knew, was not bound to the hours of the clinic, or to making sure patients received the correct dosages of drugs.

One late Saturday morning after the clinic had closed, Gler travelled with one of her youngest patients, the 14-year-old Charlene, to visit her home in the Belinde neighbourhood of Manila, a shantytown along the Pasig River. Charlene’s mother had died of MDR-TB, but first she had infected her daughter. Now the girl lived with three sisters, a brother and their father in a two-room shack with plywood walls. A fourth sister lived with a relative.

Gler took Charlene’s hand as they weaved through the alleys, sidestepping thin dogs, naked toddlers and men reeking of alcohol. At Charlene’s home, her three sisters, all teenagers, invited the doctor inside to talk. It had been difficult for them after their mother died, they said; they missed her terribly, and their father was rarely around. But now they said they were supporting each other as well as they could. Charlene was sitting out her second year of high school because of her illness – her father forbade it – but her sisters had been encouraging her to return next year after she was cured.

“I’m sure it will happen,” Charlene said. “I want to be a nurse and help others who are sick. I want to give back what was given to me.”

Gler smiled and encouraged her. She rose to go. Charlene took her hand and walked her back through the confusing alleyways, and then the two hugged. The doctor left in her car. She was going for an overnight to scuba dive with friends. She needed a break.

But she couldn’t yet – not after just leaving Charlene. “I worry about her – and her family support,” Gler said. “She’s a strong girl, but she’s just a girl.”

The doctor turned silent. She had so many MDR-TB patients, so much to do, so much to think about, including what would become of Charlene.



Decere Lai Jawili struggles to keep down her drugs from the International Center for Tuberculosis in Manila.



## DR THELMA E. TUPASI TROPICAL DISEASE FOUNDATION

Tupasi, an infectious disease specialist, founded the Manila-based non-profit group and remains its executive director. The group provides services free-of-charge to patients with multidrug-resistant tuberculosis (MDR-TB) at the International Center for Tuberculosis. She discussed her experiences in an interview at the foundation.

### Q: How did you get started in fighting TB?

A: I was a TB patient myself when I was in medical school. With that experience, I decided that I had to do something relevant in TB.

### Q: What do you remember from your days as a patient?

A: It happened in 1963... I had to take the drugs every day for 18 months, including six months of injections with streptomycin. It was very difficult. However, my classmates always made sure that I took my medicines, as in present-day DOTS [the basic package that underpins the Stop TB Strategy].

### Q: When did you start getting involved with MDR-TB?

A: The first cases were found in 1999. I told my younger colleagues that if we want to be relevant, we need to treat these cases. Many were against it because of the high cost of treatment. But we believe that as doctors we have an obligation to find the appropriate treatment for these patients.

### Q: What has been the most important factor in running a MDR-TB treatment programme?

A: The commitment from the people here. All these young people are fully committed to fighting TB. The other important factor was the vibrant and dynamic public-private partnership.

### Q: What concerns you about fighting MDR-TB in the future?

A: For us to make this a national programme, we need to have a lot more people participating. We should not exclude anybody. Advocacy needs to be enhanced. We also need health system strengthening. But there shouldn't be any reason not to move forward.

### Q: What's your advice to Ministers of Health who are in the process of expanding MDR-TB programmes?

A: Battle number one is engaging the private sector. Private practicing physicians contribute to the generation of new cases of MDR-TB because some TB patients are not being treated appropriately. Engage them. Make them partners. Look at me – I'm a private practitioner and I'm doing everything I can for the public health system.

# SEEKING MORE PARTNERS

THE PHILIPPINES HAS TRIED TO CONTROL MULTIDRUG-RESISTANT TB (MDR-TB) FOR NEARLY AS LONG AS ANY COUNTRY IN THE WORLD.

And yet it has only just begun.

After eight years of building up the programme, the MDR-TB treatment programme has expanded mainly to ... Metro Manila. That amounts to about 13% of the population in a country of 91 million people and 7107 islands.

Inhabitants outside the metropolitan area who have had the misfortune of contracting MDR-TB have had two choices: travel to the Manila region to get treated, or don't get proper treatment.

One figure puts the need in stark perspective: the MDR-TB programme has treated about 1300 patients in its first eight years, but the World Health Organization (WHO) estimates that about 12 000 people are infected annually with MDR-TB in the Philippines.

In response to that unmet need, the Government, in early 2009, started an ambitious three-year programme to expand MDR-TB treatment to all major regions of the country. In its first year, the programme hopes to open 10 MDR-TB treatment centres in six regions.

The scale up means identifying local partners; selecting structures for clinics and laboratories;

equipping laboratories; and training a wide range of health personnel.

"It's going to take an amazing amount of work to make this happen," said Dr Rosalind G. Vianzon, Director of the National TB Control Programme, which is part of the Department of Health. "We're not ahead of this problem. We need to get running to catch up."

Michael N. Voniatis, a WHO TB expert who works in Vianzon's office, said that the public sector in Metro Manila and private partners have proven that the country can treat MDR-TB effectively. "But the next three years will be critical in the attempts to interrupt transmission countrywide," he said.

Vianzon said her office has learnt many lessons from the experiences in Metro Manila – most notably that it needs help from all sources.

"We have learnt from our experiences in the past several years that a big problem like TB, or an even more serious problem like MDR-TB, cannot be addressed just by ourselves in Government," she said. "We need all the stakeholders involved – private and public. We need everyone."



## FACT BOX

PERCENTAGE OF TB PATIENTS CURED: 83.9%

PERCENTAGE OF MDR-TB IN NEW TB CASES: 4.0%

PERCENTAGE OF XDR-TB PATIENTS AMONG ALL DRUG-RESISTANT TB CASES: 4.6%

» For more information, see [www.who.int/tb/country/](http://www.who.int/tb/country/)



# THE FRONTLINE

A nurse gives an MDR-TB patient his dinner at the National TB Center in Almaty, Kazakhstan. Just one bulb lights the hallway in one hospital wing, where three or four MDR-TB patients share a room.



Christopher Alabado receives his daily injection of capreomycin at the International Center for Tuberculosis in Manila. A few hundred patients arrive six days a week at the center to receive their treatment. Many of the patients have formed close bonds because of the daily visits.



Dennis Atibula, an MDR-TB patient, prays during a church service in Manila. Atibula works as a Realtor in the city, selling commercial and residential properties. He says he has relied on his faith to help him take the second-line drugs for his infection and to keep his thoughts positive.





A technician washes smears of sputum samples at the Central TB Laboratory at the Queen Elizabeth II Hospital in Maseru, Lesotho. The country has added state-of-the-art laboratory equipment, including a test that can determine MDR-TB status in just two days.



Malenkoe Lenkoe, 67 years old, jumps over a small stream on the way home to her mountain village, Sekhutlong, Lesotho. For more than a year, she has taken care of her daughter who has MDR-TB, and also, as a community health worker, has looked after other villagers who have been infected with HIV, TB, or other diseases.



TOP LEFT: At Basabelo TB Hospital in Maseru, Lesotho, Dr. Askar Yedilayev inspects the mouth of a patient who is infected with MDR-TB. TOP RIGHT: Sun streams onto an X-ray at the National TB Center in Almaty, Kazakhstan. BOTTOM LEFT: Charlene Laguinday (left) walks through her neighbourhood hand in hand with Dr Maria Tarcela Gler (centre). BOTTOM RIGHT: Maretsepile Noral Khos (left) showing off her new home to M'e Likhapha Ntlamelle (right) a community nurse in Maseru, Lesotho.



Leo Vincant Jawili carries his wife, Decere Lai Jawili, to a waiting taxi outside the International Center for Tuberculosis in Manila. Every day for several months, he has carried his wife into the center where she takes her daily regimen for MDR-TB.



Arnold Sillote (left) and his mother Luzminda Sillote (centre) waits nervously for her MDR-TB test results at the International Center for Tuberculosis in Manila. If she is found to have MDR-TB, she will need to take second-drugs daily for the next 18 months.



An MDR-TB patient lies silently in her bed at Basabelo TB Hospital in Maseru, Lesotho. The building was recently renovated to treat the growing number of MDR-TB patients in Lesotho. The Government has installed negative air ventilation systems in order to protect others from infection.



Nurses assist an MDR-TB patient to walk at Basabelo TB Hospital in Maseru, Lesotho. The patient was mostly bed-ridden, but a doctor, noticing that the patient had been gaining strength, asked him to try to take some steps. The patient walked around his bed and then asked to brush his teeth – which he did. The doctor congratulated him.

# A RACE TO SAVE LIVES

ALMATY, KAZAKHSTAN – THROUGH THE CENTURIES, GREAT POWERS HAVE FOUGHT IN THIS REGION OVER INFLUENCE AND RESOURCES, SUCH AS THE MODERN SCRAMBLE FOR VAST ENERGY SUPPLIES BURIED IN CENTRAL ASIAN EARTH.

BUT NOW AN ECHO OF THOSE RACES IS BEING WAGED HERE ALMOST ENTIRELY OUT OF VIEW, ONE WITH THOUSANDS OF LIVES AT STAKE – THE STRUGGLE TO CONTROL BOTH MULTIDRUG-RESISTANT TUBERCULOSIS (MDR-TB) AND THE MORE SERIOUS EXTENSIVELY DRUG-RESISTANT TB, OR XDR-TB.







Nowhere in the world have drug-resistant strains of TB been known to have gained such a foothold as in the former Soviet states. And perhaps nowhere along the southern rim of former Soviet states has a country fought back like Kazakhstan, the ninth largest country in the world. Its public health system, still trying to strengthen basic TB control across varied environments and populations, is working on several fronts to stop transmission of drug-resistant strains, which can be easily spread in enclosed areas on the wings of a cough or sneeze. The tubercle bacilli is a wily opponent. It has exploited multiple opportunities – economic meltdowns, social breakdowns, even the handiwork of ghosts from Soviet times.

Inside hospital rooms, the spread of the TB bug is painfully evident: Here lay young girls infected by mothers; prisoners infected by prisoners; border guards infected by migrants; train workers by passengers; and orchestra musicians by other musicians.

“At first I cried when I heard the news,” said Zhuldyz Zhabelova, speaking in Russian through a mask and lying on one of the five beds in a room at one TB hospital in Almaty, which she shared with four other young female MDR-TB patients.

Zhabelova, a 27-year-old former soloist in the Kazakhstan Philharmonic Orchestra, used to play the two-string dombra – a slender-necked lute with an oval body first cherished by nomads along the Silk Road. In early 2008, she became ill with a fever and a wracking cough; tests determined she had TB, and further laboratory tests found it was MDR-TB. She learnt that she might have caught the disease while playing the dombra; a friend, who sat near her in the orchestra, unknowingly was infected with MDR-TB.

“After my diagnosis, a doctor explained to me that it was curable,” she said. “So I try to be calm. Sometimes it is hard.”

For TB patients, hard in Kazakhstan can be especially hard: Those who contract pulmonary TB in Almaty, the country’s largest city, have a one-in-four chance that their *Mycobacterium tuberculosis* will be resistant to at least two of the most commonly used drugs as well as some second-line medications. That means they must take a combination of harsh medication daily for 18 to 24 months in hopes of being cured.

Such rates of drug-resistant TB are an astounding five times greater than the global average. Almaty is not alone – not among some of the former republics of the Soviet Union. In 2008, the World Health Organization (WHO) and national counterparts that conducted representative surveys found sky-high rates of MDR-TB among all new TB cases across the region: 22.3% in Baku, Azerbaijan; 19% in the Republic of Moldova; and 16 in Donetsk, Ukraine, among others. Since that report, some of the other surveys in the region have shown even more alarming rates, including 27.7% of new TB cases in Kyrgyzstan’s prisons in 2007–2008; 26% in Almaty city; and 20% nationwide in Kazakhstan (up from 14%, according to a WHO estimate based on a 2004 survey).

And yet, in Kazakhstan, the numbers don’t reflect progress in the fight: The Government, showing a serious political and financial commitment to battle the disease, more than doubled the national TB control budget in five years, to US\$ 125 million in 2008 from US\$ 58.3 million in 2003. International experts are helping, and a panel in Almaty now reviews all MDR-TB cases in the city every three months. Some early results have been encouraging: One Almaty hospital, for instance, reported an 80% cure rate of MDR-TB patients in 2008.

Still, MDR-TB rages, in part because of the ghosts – the legacy of Soviet rule and especially its breakup.



Dimitry Gagarin lays his apple next to his TV after lunch at the National TB Center in Almaty, Kazakhstan. He is coinfectd with HIV and MDR-TB. "I am waiting to see which one will kill me."

Experts believe the spread of drug-resistant TB really accelerated years later, following the collapse of the Soviet Union in 1991. Health systems began to fail. Many TB patients stopped taking drugs because supplies often ran out. The TB incidence rate rose to 119 people out of every 100,000 in 1998, up from 66 per 100,000 population in 1990. Over those eight years, the country's TB death rate nearly quadrupled – a reflection, experts say, of the spread of infection but also improved data collection and diagnostic tools.

Since 1998, numbers of TB deaths have been halved; officials say the turnaround began with President Nursultan Nazarbayev's 1998 decree to follow WHO's recommendation to implement DOTS, the basic package that underpins the Stop TB Strategy. That decree, Kazakh officials claim, has helped save 30,000 lives during the past decade.

At the end of 2008, the country was treating 36,000 patients for TB and 2,000 for MDR-TB. The cost of treating MDR-TB patients was more than 10 times higher than that of treating TB, averaging more than US\$ 4,000 per patient.

Management of MDR-TB has a long way to go. Government figures showed that 1856 registered MDR-TB patients at the end of 2008 were not being treated mostly because the drugs weren't available.

That situation could improve soon. In 2008, the Global Fund to Fight AIDS, Tuberculosis and Malaria approved a US\$ 69 million, five-year grant that will fund more second-line drug treatment for MDR-TB patients, said Dr Arman Toktabayanov, project manager of the Global Fund initiatives in Kazakhstan. (The country, in 2007, also received a US\$ 9.8 million, five-year Global Fund grant to fight TB.) "We're trying to find the solutions – we're fighting," Toktabayanov said.

One troublesome area remains inside prisons, run by the Ministry of Justice, which is now starting to expand laboratory diagnostic services, train health-care workers and improve patient care services. Still, say health officials, while basic TB control has improved in prisons, it remains substandard.

Dimitriy Gagarin, aged 33, laments that. While serving time at the Chimkent prison in south Kazakhstan from 2004 to 2007 for illegal drug use, he contracted TB. Years earlier, he had been diagnosed with HIV – now he was living with two deadly infections.

In prison, Gagarin was locked in a large cell block with 127 other prisoners. "No one talked about TB in there – no one cared," he said. "It was very easy to get TB. It was like being on a crowded train or bus, all the time."

A prison doctor started treating him for TB with a four-drug regimen, but Gagarin said the prison sometimes ran out of the drugs. Only a few months after finishing his six-month treatment, Gagarin became sick again – this time with MDR-TB.

After one year of treatment at the national TB control center in Almaty, he was feeling better. "But I have two diseases – MDR-TB and HIV – that are very dangerous," he said. "It's like I have sticks of dynamite in my body. I'm waiting to see which one will kill me."

The TB wards are full of such stories of loss and fear and anger. Mukusheva Orynsheva, a 51-year-old nurse from western Kazakhstan, contracted MDR-TB from one of her patients. She railed against the poor-quality diagnostic tests; it took three months to learn she had MDR-TB, which meant that during those three months she was taking drugs that were ineffective. "It was such a waste of time," she said, tears filling her eyes. "I'm angry not only for me, but for a lot of people. Wasting three months is not fair – and it's dangerous."

But some accept what has happened to them – even in extraordinarily difficult circumstances. Zulfiya Tursunova, 20 years old, gave birth to a girl, Samera, in 2007, only to learn months later that she had TB. Since entering the hospital in mid-2008, she had seen Samera just once – and then from 30 feet away.

Her girl was inside a car, the window rolled up. Tursunova stood on her hospital balcony and waved. “She recognized me,” the mother said. “I know because her eyes lit up.”

“It is very hard to be apart,” she added, “but I know I must be really careful.”

For another patient, a former army border guard who identified himself only as Beibut, contracting the illness has had numerous ripple effects in his life. His wife divorced him, and he asked his relatives not to visit. “I’m so ashamed that I am sick,” he said.

But days later, the 29-year-old Beibut’s mood lifted. Doctors told him he was no longer infectious and that he might be discharged from the hospital in only a few months.

So he decided to do the one thing that would make him happy: for his son, Zharaz, to see him at the hospital. Zharaz had something to celebrate – his third birthday – and his father had something to celebrate as well: feeling well again. And he could finally think about getting back his old life.

## MDR-TB AMONG TB

MORE THAN 6% OF NEW TB CASES ARE MDR-TB IN THE LOCATIONS BELOW:

- 1 Azerbaijan, Baku City (22.3%)
- 2 Kazakhstan (20%)
- 3 Republic of Moldova (19.4%)
- 4 Ukraine, Donetsk (16%)
- 5 Russian Federation, Tomsk (15%)
- 6 Uzbekistan, Tashkent (14.8%)
- 7 Estonia (13.3%)
- 8 Russian Federation, Mary El (12.5%)
- 9 Latvia (10.8%)
- 10 Lithuania (9.8%)
- 11 Armenia (9.4%)
- 12 Russian Federation, Orel (8.8%)
- 13 China, Inner Mongolia (7.3%)
- 14 China, Heilongjiang (7.2%)
- 15 Georgia (6.8%)

*ANTITUBERCULOSIS DRUG RESISTANCE IN THE WORLD.  
FOURTH GLOBAL REPORT. GENEVA, WORLD HEALTH  
ORGANIZATION, 2008 (WHO/HTM/TB/2008.394).*

## ABYLGAZY NAGMADIN MDR-TB PATIENT

Nagmadin, a 28-year-old, talked about how he contracted TB and what has happened to him since.



**Q: How did you react to your initial diagnosis of TB?**

**A:** It was very scary. I was really surprised – I didn't even know about TB. And then when I was diagnosed with MDR-TB several months later, I was even more scared. I didn't know if I could be treated.

**Q: How did you get infected?**

**A:** I work at a train station, and every month they test their workers. One day I learnt I had it. I must have got it from someone I work with, or a passenger.

**Q: What have you missed?**

**A:** Well, when I was first diagnosed, my wife was pregnant. On 12 August, she gave birth to our son, Nurlan. I still haven't seen him.

**Q: How did you hear the news?**

**A:** My wife called me on the cell phone.

**Q: What was your reaction?**

**A:** I was very happy.

**Q: How about the next day?**

**A:** Of course, I was very sad. I couldn't be with my wife and child. I'm still very sad that I haven't seen him yet. The only thing I want is to get back to my family.

**Q: Have you seen a picture of your son?**

**A:** No.

**Q: How is your treatment going?**

**A:** It was hard in the beginning, but now I'm doing very well. Sometimes I forget that I am sick.

**Q: What advice would you give someone who suspect they have TB?**

**A:** TB is a very dangerous disease. Some people are ashamed they have this problem. So they don't seek treatment. That isn't right. They shouldn't be ashamed. They should seek treatment. It will bring them back to life.

**Q: When you leave the hospital, what will you do?**

**A:** I will go straight to my family and my son. I want to hold my son in my arms.



## DR TAMARA VOSHENKOVA VICE-MINISTER OF PUBLIC HEALTH

Voshenkova is a medical doctor who rose to her current position in Kazakhstan in late 2008. She talked about the country's efforts to battle MDR-TB from her office in Astana.

**Q:** Have any specific cases of TB made a big impact on you?

**A:** Many. There was one case involving a family that really touched me. The mother, who ran a small store, came down with MDR-TB a year and a half ago. Now she's in the

hospital; unfortunately, it looks unlikely that she will be able to reverse the illness. She has a 3-year-old daughter who is also diagnosed with TB. You see this good family that was living a good life, and then all their plans are broken because of TB. It's heartbreaking.

**Q:** What's the most important part of Kazakhstan's fight against drug-resistant TB?

**A:** It's that we have shown strong political will to face the problem. The Government recognized the problem and it has taken steps to address it. One of the main efforts now is to get the most reliable information possible on MDR-TB.

**Q:** What worries you the most?

**A:** We recognize the challenges in TB control. Based on our cure rates (71%), we are not reaching WHO targets (85%). We also recognize that MDR-TB case numbers are high, and that we expect more XDR-TB cases. It will be difficult, but we are trying, along with help from international donors and technical experts, to solve this problem. We are taking a strong intersectoral approach, involving many ministries, including education, culture, internal affairs and justice. We realized that just the medical response to the problem couldn't solve it. Only an intersectoral approach will work.

Dr Tamara Voshenkova, Photo by John Donnelly.



RUSSIAN  
FEDERATION



CHINA

## FACT BOX

PERCENTAGE OF NEW TB PATIENTS WITH  
MDR-TB IN 2008: **20%**

PERCENTAGE OF NEW TB PATIENTS ALSO  
HIV-POSITIVE: **0.5%**

PERCENTAGE OF TB PATIENTS CURED: **71%**

» For more information, see  
[www.who.int/tb/country/](http://www.who.int/tb/country/)



# SCALING UP THE RESPONSE

**DR MARIO RAVIGLIONE  
WORLD HEALTH ORGANIZATION**

Raviglione, Director of the Stop TB Department since 2003, has worked on TB control issues for two decades. He talked about past and future challenges from his office in Geneva.

**Q: What is your main concern in TB control overall?**

**A:** My concern is that people don't fully understand the basics of TB control. In our enthusiasm to fight XDR-TB (extensively drug-resistant TB) and MDR-TB, many are thinking that we have to deal with these 1000 MDR cases in country X, while forgetting about the 100 000 normal TB cases in that country. Those 100 000 cases all have to be treated properly or we will get more MDR cases. We should never withdraw from the notion that MDR has to be taken care of. But we must make sure we prevent MDR cases in the first place.

**Q: In the early 1990s, WHO recommended DOTS [the basic package that underpins**

**the Stop TB Strategy] to treat TB. At the end of the decade, an argument unfolded over treatment of drug-resistant cases. What happened?**

**A:** There was a big debate between those who wanted DOTS only and those who wanted the treatment of drug-resistant TB. One side believed the basic thing had to be implementing basic TB control. Others, including Paul Farmer and Jim Kim at Partners In Health, said we had also to serve those with MDR-TB, that it was an issue of basic human rights as well as controlling these difficult-to-treat cases. You have to remember that we were talking at a time when a couple of hundred thousand dollars for TB control in a country was considered a big success, and thus the

priority was basic DOTS.

But then we held a meeting in Cambridge (MA, USA) in April 1998. It was an amazing meeting, there was a lot of enthusiasm and we reached an understanding. At the end, we had a direction. We realized the first step was to make sure we had the drugs available to treat MDR-TB patients, and so we conceived the Green Light Committee. I had no capacity to build this thing, so Partners In Health sent someone to help Marcos Espinal, then the MDR-TB team leader, and I – Raj Gupta, who was just 25 or 26 years old at the time. He was really instrumental in putting together the Green Light Committee in just six months. That, we hoped, would create a demand for the drugs, lower their price and oversee the use of the drugs.



**Q: What were the lessons learnt from that meeting?**

**A: What I learnt was if WHO doesn't pursue a solution that benefits everyone, the whole world can suffer. The strong collaboration with Harvard University and Partners In Health allowed us to move forward. At that meeting, it was just a few people that created the chain reaction that resulted in the efforts we see today. We had started a plan to treat those with drug-resistant TB.**

**Q: Why hasn't the world made greater progress in the past decade to treat MDR-TB?**

**A: We certainly have persuaded a bunch of countries to do it, including some that were very reluctant. Why is it not done everywhere? It's extremely difficult to deal with. You need a laboratory to detect it. You need access to drugs. You need money. I have to say that immediately we were supported by USAID, the Rockefeller Foundation and Lilly MDR-TB Partnership. Later, the Global Fund became a lifesaver for so many countries. More recently, UNITAID joined the call. And yet with the emergence of XDR-TB we need much, much more.**

**Q: What was the impact of the discovery of extensively drug-resistant TB, and naming it XDR-TB?**

**A: This hugely accelerated the process of making people aware of the dangers of TB. 'The X underlines the urgency of the problem.' The outbreak in Kwa-Zulu Natal (where 52 of 53 people died of XDR-TB) really shocked people. It showed how scary this could become. After it happened, we called a meeting in Geneva (Switzerland) and named the first XDR-TB Task Force. During this period there was a lot of attention around the world. Everyone now knew that this was one of the worst possible diseases you could get and named it the first XDR-TB.**

**Q: What do you hope happens next?**

**A: I want health ministers around the world to say, "My goodness, I didn't know this was so scary. I must do something". Then you hope the next day they call the national TB control programme manager and say they want them to face this thing as a top priority. I want them to put more money in their budget towards this and to apply for a grant from the Global Fund. I want them to upgrade their laboratories immediately, introduce the new technology that identifies MDR-TB**

**and XDR-TB in 24 or 48 hours, not four months. I want them to make sure the drugs are of assured quality, make sure the physicians are trained immediately on what needs to be done. They should get outside experts to come to their country and teach them how to do these things, and they should develop a national plan to fight TB.**

**Q: Couldn't the global financial crisis impede progress?**

**A: This is an emergency. There is no choice. Money can be mobilized. If people get more ambitious, they can get the money and get this done. When people decide to do things, they can do it. In Brazil, in the 1990s, they gave antiretroviral drugs to everyone who had AIDS. No one else in the developing world did it, but they showed you could do it. If there is political will, then the possibility is there.**

# A “TO DO” LIST ON MDR-TB

GLOBAL EXPERTS ON TUBERCULOSIS (TB) SAY THAT FIGHTING MULTIDRUG-RESISTANT TB (MDR-TB) IS COMPLICATED. THEY POINT OUT THE EASE WITH WHICH ONE PERSON CAN TRANSMIT THE DISEASE, AND THE DIFFICULTIES OF COUNTRIES IN STOPPING TRANSMISSION. THEY LOOK AROUND THE WORLD, ESPECIALLY AT DEVELOPING COUNTRIES, AND SEE ONLY A HANDFUL OF PLACES WHERE THE SPREAD OF THE MDR-TB EPIDEMIC ACROSS AN ENTIRE NATION HAS BEEN REVERSED. SO THEY ARE SCARED.

AND YET THESE EXPERTS ALSO STRONGLY BELIEVE THAT CONTROLLING MDR-TB CAN BE DONE.

HOW? HERE IS SOME OF THEIR ADVICE. THEIR OPINIONS COMPRISE A USEFUL POCKET GUIDE, COLLECTED THROUGH INTERVIEWS AND OBSERVATIONS. AND WHILE NUMBERS ARE ASSIGNED TO ITEMS, THESE ARE NOT RANKED IN ORDER OF IMPORTANCE. COLLECTIVELY, THESE ITEMS SHOULD CONTAIN SOME COMMON SENSE, SOME ACQUIRED WISDOM AND MAYBE A FEW KERNELS OF INSIGHT.

## 1. TURN OFF THE TAP

Dr. Mario Raviglione, Director of the Stop TB Department at the World Health Organization (WHO), has been saying this for years, and it bears repeating. The only way to stop MDR-TB is to build a strong basic TB control programme so that those who become ill with TB do not develop MDR-TB. And at the same time, officials also need to build strong MDR-TB treatment programmes so that those infected do not spread the infection and that their infection doesn't turn into extensively drug-resistant TB (XDR-TB).

## 2. HELP IS NEAR – PARTNERS, TOO

WHO and its partners have scores of experts who can offer technical assistance to countries as they build their response to MDR-TB. In 2000, they also initiated the Green Light Committee, which allows access to high-quality second-line drugs to treat MDR-TB. Since 2003, the Global Fund to Fight AIDS, Tuberculosis and Malaria has committed US\$ 2.4 billion to TB control programmes. Still, funding gaps persist. The 22 high-burden TB countries had a combined **funding gap of hundreds of millions of dollars in 2008**. Dr Raviglione said the organizations are “aware of those gaps and working closely with governments, the Global Fund, UNITAID and other funding agencies to mobilize needed funds.”

Finally, several nongovernmental organizations have years of experience in building MDR-TB programmes. Two examples are the Foundation for Innovative New Diagnostics (FIND), who are experts in setting up laboratories; and Partners In Health, who are experts in initiating treatment programmes.

### 3. LOOK AT THE EXAMPLES FROM OTHER COUNTRIES

Three countries are worth a look. In just four years (2002–2005), **China** greatly expanded its TB control programme, delivering treatment of ordinary TB free of charge to 1.2 billion people. It also greatly expanded surveillance of cases, which sharply increased the numbers of reported cases of TB. In 2002, China's public health system treated 170,000 TB patients; by 2005, 500,000 were enrolled in treatment programmes annually. China is now entering a new phase by turning towards control of MDR-TB and assuming global leadership on many fronts: increasing funding by millions of dollars for scientific **TB research**; and hosting a WHO ministerial meeting in Beijing of the world's high-burden MDR-TB countries.

The **Russian Federation**, in battling its high numbers of MDR-TB cases, has moved aggressively to build new laboratories, train a range of health workers and revamp health systems in prisons, including the installation of **infection-control** ventilation systems. Towards this end, the Government secured a US \$150 million loan from the World Bank and an US \$80 million grant from the Global Fund. It also has submitted multiple applications for second-line drugs with the Green Light Committee and, by the end of 2008, had more than 1,700 patients receiving drugs through the

GLC process, or roughly 40% of the global total of GLC patients.

**Peru** has mobilized a community-based response to MDR-TB countrywide, achieving cure rates as high as 83% among patients. At first, the country relied heavily on outside expertise; it now funds nearly the entire MDR-TB control programme. Now confident in its strategy, Peru offers technical assistance to other Latin American countries.

### 4. STRENGTHEN LABORATORIES

Laboratories are the backbones of any successful TB control programme, and WHO experts say many more are needed. “We need to get laboratories nearer to the patients,” said Dr Paul Nunn, Coordinator of TB/HIV and Drug Resistance at WHO's Stop TB Department. The goal, he said, will be to have one laboratory capable of growing cultures of sputum samples for every 5 million people, and one laboratory capable of detecting drug resistance strains for every 10 million. That means adding 2000 laboratories around the world. The number of laboratories, Nunn said, has not kept pace with population increases or the spread of TB. One example, Kenya, had one national referral laboratory serving 12 million people at independence in 1963; today, this same laboratory serves 35 million people. Plans are under way to build four new laboratories.

### 5. EXPAND RESEARCH

The Bill & Melinda Gates Foundation has committed roughly US\$ 500 million to date on TB research. Dr Peter M. Small, Senior Program Officer for TB, calls the lack of good diagnostic tools and anti-TB drugs **an outrage**. “We are combating a disease that

kills someone every 20 seconds, with a 125-year-old diagnostic test that fails to diagnose half the number of cases, with an 85-year-old vaccine that does not protect adults and with 40-year-old drug regimens that you have to take for six months,” he said.

Dr Jim Yong Kim, Professor of Medicine and Social Medicine at Harvard Medical School, has experience in fighting MDR-TB since 1995, when a friend had died of drug-resistant TB in a slum outside Lima, Peru. He said he hoped researchers would discover many new drugs to fight TB. “It's not just one or two new drugs, we need four or five new drugs immediately. People aren't sounding the alarm loud enough. Every time we look, the problem is worse than we thought. Now it is coming together with HIV in sub-Saharan Africa and **it could be the most frightening thing we are ever going to see,**” he said.

One hope is that emerging economies in countries such as Brazil, China, India, the Russian Federation and South Africa, start ambitious TB research programmes. “These countries all have significant research capacity, which for the most part is not turned towards TB,” said WHO's Dr Nunn.

### 6. TRAIN MORE HEALTH WORKERS

Training more health workers means ongoing training for a range of health workers – from doctors to community health workers – with limited formal education. Typical topics include MDR-TB diagnosis and treatment; case discussions; infection control; referral system plans; and, in areas with HIV-TB coinfection, the co-management of drugs for both diseases.

HIV-TB coinfection issues are highly complicated and little understood, making it difficult to train health workers. “We need more extensive training of health workers because it’s so difficult,” said Dr Hind Satti, Director of Partners In Health Lesotho’s MDR-TB control programme. “We’re finding higher rates of side-effects among patients than anywhere else in the world – and we think it is due to coinfection.”

## 7. PROTECT HEALTH WORKERS (AND EVERYONE ELSE)

Controlling TB infections in health settings is particularly important because so few hospitals in developing countries have infection-control ventilation systems. Without these systems, everyone in the hospital, from health workers to visitors, is at risk. “Virtually every health care facility in the developing world and in much of the industrialized world is in need of drastic improvement in airborne infection control,” Dr Nunn said. “It is a serious risk in many parts of the world just to go into a hospital. It almost brings you back to **the palace of diseases** of Florence Nightingale at Scutari.” [Florence Nightingale was the Superintendent of Nurses at Scutari Hospital in Turkey during the Crimean War (1854–1856), where the monthly rate of mortality among British soldiers in the first winter reached 40%. Many died from sicknesses acquired in hospitals, not from war injuries. Nurse Nightingale improved hygiene practices and, 18 months later, the mortality rate had reduced to 2%.].

## 8. ENSURE ACCESS TO HIGH-QUALITY DRUGS

In many countries, first-line and second-line anti-TB drugs can be bought over-the-counter. This concerns those who run TB control programmes because misuse of these drugs may generate further drug resistance and possibly extensively drug-resistant TB (XDR-TB). Another concern is that **counterfeit or poor-quality anti-TB drugs** are available on the open market. Ministers have three options: lobby for legislation that prohibits the sale of anti-TB drugs without a doctor’s prescription; accredit doctors who are trained to treat MDR-TB; and apply to the Green Light Committee for access to quality-assured second-line medication. “The Green Light Committee has a key role to play,” said Dr Marcos Espinal, Executive Secretary of the Stop TB Partnership, who worked on the establishment of this mechanism.

## 9. KNOW YOUR EPIDEMIC

No MDR-TB epidemic in any one country is identical. MDR-TB in eastern and southern Africa is interwoven with the AIDS epidemic, creating a raft of issues that are non-existent in regions with low HIV prevalence. In many countries of the former Soviet Union, rates of MDR-TB among new TB cases are higher than anywhere else in the world. This demands a different type of response. One of the first steps is to study a country’s MDR-TB epidemic and tailor the response to the local situation.

## 10. MAKE NO EXCUSES – COMMIT FUNDING

A common error, say many TB specialists, is that governments do not appropriate enough funds to put together a comprehensive response. Another common mistake is that countries delay starting MDR-TB programmes until the entire system is ready to go. “One example is laboratory capacity,” said Carole Mitnick, Assistant Professor of Global Health and Social Medicine at Harvard Medical School. “While I’m in complete agreement with the need to build laboratory capacity locally, I don’t agree it is a prerequisite to get treatment started. There are laboratories available elsewhere.”

The bottom line, she said, is simple: “Don’t make excuses. Start as soon as possible.”

Dr Michael E. Kimerling, former director of the Gorgas TB Initiative at the University of Alabama at Birmingham and now Senior Program Officer for TB at the Bill & Melinda Gates Foundation, said **the consequences of inaction are dire**. “If you ignore the problem, TB doesn’t go away, it gets worse,” he said. “Look at what happened after the breakup of the Soviet Union and the economic collapse then. If this current global economic crisis results in programmes falling apart, it’s very predictable what you are going to get – more drug resistance and more deaths.”



## DR PETER M. SMALL BILL & MELINDA GATES FOUNDATION

Small, Senior Program Officer for TB at the foundation, has done extensive research into the genetic variability of TB. He spoke from his office in Seattle, WA (USA).

Q: How can improved technologies help in the fight against MDR-TB?

A: Right now, the best example is the use of molecular diagnostic tests that can detect within three hours whether the patient has a drug-susceptible or drug-resistant strain.

Dr Peter Small, Photo courtesy of the Bill & Melinda Gates Foundation.

Q: Who will be using these tests in the next few years?

A: That's really the point of several international meetings [on drug-resistant TB] that will take place over the course of the next year. We need to figure out how to introduce these tests in many more countries – and quickly. Lesotho is already using them. But there's clearly a quantum leap between starting this in a small country with fairly significant external help and introducing it on a large scale in big countries. I'm optimistic about what is happening in China now. We know China is one of the global experts in going to scale with TB control. The government has also shown real leadership in hosting the Beijing meeting [in April 2009] and ensuring TB is discussed at this year's World Health Assembly [in May 2009].

Q: How would you characterize the world's response to drug-resistant TB?

A: We are pitifully behind. To be honest, even our understanding of the epidemiology is severely limited. We don't actually know where the worst situations are. Nor do we know whether in most places the situation is getting better or worse. We do know enough to get started, and there are clearly places in the world where we can fully treat the drug-resistant TB cases. We can waste no time in getting started.

## OVERCOMING

## CONSTRAINTS

FOR COUNTRIES SCALING-UP THEIR RESPONSE TO MDR-TB, THE CHALLENGE CAN OFTEN SEEM OVERWHELMING.

The WHO and TB experts from across the world have tried to make it easier by identifying some key policy constraints and ways of overcoming them:

- » Filling the gaps in basic TB control to prevent MDR-TB
- » Addressing TB ethics and human rights
- » Investing in human resources
- » Addressing laboratory needs
- » Providing care to MDR-TB and XDR-TB patients
- » Strengthening TB infection control
- » Promoting rational use of anti-TB drugs
- » Ensuring access to high-quality first and second-line anti-TB drugs
- » Promoting TB research and development
- » Financing scale up of MDR-TB and XDR-TB programmes

» For more information, see [www.who.int/tb\\_beijingmeeting/key\\_bottlenecks/](http://www.who.int/tb_beijingmeeting/key_bottlenecks/)

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– JOHN DONNELLY  
DOMINIC CHAVEZ



An MDR-TB patient puts his left hand on a frosted glass door at the International Center for Tuberculosis in Manila. This patient, like many at this center, volunteers to help with the treatment of fellow patients. He was about to enter a back room at the center to retrieve supplies.

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"IF IT WEREN'T FOR MY MOTHER, IF IT WEREN'T FOR THE GOVERNMENT, IF IT WEREN'T FOR MY DOCTORS AND NURSES, I WOULDN'T BE ALIVE." – MATSEPE LENKOE



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