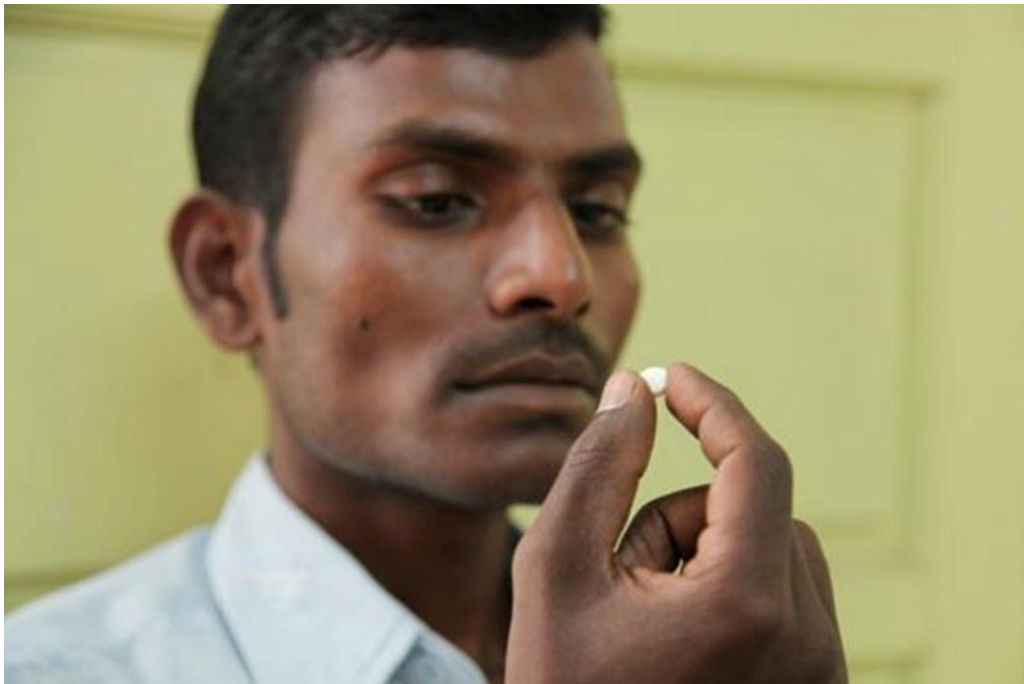


# World TB Day 2013

Recent TB News Stories





## **Los Angeles health officials concerned about TB outbreak on skid row**

February 22, 2013

(Reuters) - Los Angeles County health officials have asked for federal assistance to analyze and contain an outbreak of tuberculosis within the city's homeless population, a spokeswoman for the county agency said on Friday. Los Angeles County Health Department spokeswoman Mabel Aragon said the agency is still in the process of confirming the number and type of TB cases in the county. "The CDC is helping us with surveillance and statistic gathering," she said. CDC spokesman Scott Bryan confirmed that the federal health agency has been asked by local and state TB officials to assist with the outbreak investigation. Bryan said the CDC plans to dispatch staff to the state in the next two weeks. The Los Angeles Times reported that health workers have identified about 4,650 people who were probably exposed to a persistent outbreak of the contagious disease on downtown Los Angeles' skid row. The newspaper said that over the past five years, county officials have identified 78 cases of a unique strain of the contagious disease, including 11 deaths. Sixty of those cases were homeless individuals leaving in the skid row area.

In an interview posted on the Los Angeles health department's website, Kiren Mitruka of the U.S. Centers for Disease Control and Prevention said: "Although progress has been made toward eliminating TB in the U.S., TB outbreaks continue to occur and remain a challenging issue. "The United States had about 10,528 cases of tuberculosis in 2011 and there were 529 deaths from the disease in 2009, according to the latest full year CDC statistics. The CDC responds to TB outbreaks only when state and public health departments exceed their surge capacity to control it, Mitruka said. "We don't go in unless we're asked," she said in the online interview. Typically, the CDC will conduct an onsite investigation lasting two to three weeks, working closely with state and local public health partners, Mitruka added.

The cluster of TB cases going on in Los Angeles follows a pattern of infection. A review of 51 TB cases which the CDC investigated between 2002 and 2008 published in Emerging Infectious Diseases found substance abuse was the most common risk factor, with 58 percent of outbreak patients reporting substance abuse. Tuberculosis infection destroys lung tissue, causing patients to cough up the bacteria which then spreads through the air and can be inhaled by others. Most cases can be cured with a six-month cocktail of antibiotics, but rates of drug-resistant TB have been spreading fast, causing alarm among public health officials and prompting calls for more research into new treatments.

"I think it's a wakeup call that highlights the fact that this is still a major, major problem," said Dr Mel Spigelman, chief executive of the TB Alliance, a nonprofit research group based in New York. "Even in the U.S., where we have one of the lowest rates in the world, we still have over 10,000 patients every year who get TB." Spigelman said that number pales in

comparison to the 9 million people globally who get TB. "It's still in the U.S., we just don't recognize it."

# TIME

## The Drugs Don't Work

March 4, 2013

A girl swings her legs from the examination table and glances out the small square window of the doctor's office. The breeze rolling in off Mumbai's Mahim Bay ruffles the papers on the desk, where the girl's grandmother has laid out her upturned hands imploringly. "Please help," she says to Dr. Zarir Udwadia, a chest doctor. "I don't know what to do."

Udwadia glances through the papers that document the family's months of attempts to treat the girl's virulent case of tuberculosis. A lab has just delivered the test results that explain why she's not getting better: the disease that has settled in the girl's lungs is multidrug-resistant, or MDR, tuberculosis, and most medicine is useless against it. "Ten years ago, you would have been horrified," Udwadia tells TIME, scratching out a prescription for yet another combination of TB drugs that may — or may not — work. As cases that are harder and harder to treat emerge, Udwadia says, patients who finally respond are a relief. "Now we say, At least she's only MDR."

Some of the people waiting their turn to see Udwadia won't be so lucky. Once a week, patients who have tried and failed to treat their tuberculosis line up, frustrated and frightened, outside his small office in Hinduja Hospital in India's financial capital. Hinduja is where the first Indian cases of totally drug-resistant (TDR) TB were reported in late 2011, making the hospital a key battleground in India's new war against a very old disease. What happens there concerns us all. For while the wily bacterium has been around for millennia, trade, migration, urban overcrowding and air travel mean that the disease has been able to spread like never before. And if TDR strains take hold in global populations, the resulting contagion could be catastrophic.

Doctors have been effectively fighting *M. tuberculosis* and other bacteria with antibiotics for decades. The global TB mortality rate has gone down 41% since 1990. But poor diagnosis and the misuse and mismanagement of powerful drugs have created strains that are getting harder to fight. When a TB patient is given the wrong prescription or starts but does not complete the full course of drugs, the bacterium can grow stronger. Nearly 4% of new TB patients have MDR strains of

TB; among patients who had been treated for TB before, about 20% have MDR TB, according to the World Health Organization (WHO).

A paper published last August in the Lancet reported that worldwide rates of MDR and extensively drug-resistant (XDR) tuberculosis are higher than anyone previously thought. (WHO identifies the cases that were reported at Hinduja as XDR, saying complete drug resistance in TB has not been clearly defined.) XDR TB has been found in 84 countries. East and Southeast Asia, Eastern Europe, South Africa, Russia and India have alarmingly high rates of drug resistance, and though only India, Italy and Iran have reported cases of TB that do not respond to any drugs, many experts believe that's simply because more haven't been found. "We are on the brink of another epidemic, and it has no treatment," says Dr. Shelly Batra, president of Operation ASHA, a New Delhi — based NGO that fights TB. "If TDR spreads, we will go back to the Dark Ages."

Tuberculosis — once known as consumption because of the severe weight loss it can cause — is a contagious, airborne disease that thrives in overcrowded places. It typically settles in the lungs but can attack other parts of the body as well, and its symptoms include coughing (often producing blood), fever, night sweats and chills. Malnourished people are particularly vulnerable to TB, as are those with HIV. Most TB infections are latent and asymptomatic, but once the infection becomes active, the mortality rate is high. A third of humans alive today carry TB bacteria. Only a relatively small number of them will get sick and become contagious, but it is still one of the world's deadliest diseases, killing 1.4 million people in 2011. WHO estimates there will be over 2 million new cases of MDR TB from 2011 to 2015, yet today only 10% of new MDR cases get proper treatment. The ones who don't inevitably spread the disease: a person with active TB can infect up to 15 others in a year.

India, where about two people die every three minutes from TB, is on the front line of this global battle. Some 2 million Indians develop TB each year, leaving the Indian government with the unenviable task of managing roughly a quarter of the world's TB cases. The more drug resistance, the more money must be spent on treatment, diverting funds and staff from addressing rampant but run-of-the-mill TB. That means the conditions creating drug resistance — when treatable cases go unnoticed or patients receive bad medicine — could get worse. "I've seen the resistance pattern changing," says Udwadia. "Basically, we're screwed."

By we, he means all of us.

## Ground Zero

Mumbai is a crucible of bacterial opportunism. Perched on India's west coast, it is one of the fastest-growing cities in the world, with Greater Mumbai's population already at some 18 million. As more and more people pour into Mumbai, its edges have become a shifting horizon of rising and falling slums housing the migrant workers who make the city tick. In Ambujwadi, a cluster of some 8,000 people in north Mumbai, residents live like they do in most slums: in stiflingly close quarters, without running water or clean food. It's just the kind of crowded, hardscrabble place where *M. tuberculosis* thrives — and where drug resistance is increasing.

Since 2006, India's government has provided free TB medication nationwide, but to get it, patients need to go to a clinic, hospital or government drug provider three times a week. For day laborers, that means less money and less food. In India's urban slums, as many as a third of TB patients stop taking their drugs before the standard six-month treatment is complete, according to Operation ASHA. New TB patients are prescribed six months of a combination of four medications, with two months of intensive treatment followed by four months of continuing care. Following the regimen is crucial. If patients don't respond to that treatment, or if they test positive for drug resistance, they are given other, more powerful second-line drugs, which can be highly toxic and are part of a grueling two-year program. If a patient stops that, the bacterium gets stronger still.

On one sweltering June morning, health worker Shilpa Kamble winds her way through Ambujwadi's labyrinthine dirt lanes, past goats picking over garbage and open-air stalls hawking cookies and Coke. She stops outside a piece of cloth that serves as the front door of a lean-to home. In Mumbai and other parts of the country, the government has teamed up with NGOs like Navnirman Samaj Vikas Kendra, where Kamble works, to keep track of patients and to make sure they stick to their drug regimens. Inside the hot, airless hovel, a man named Nasim Mohammed rests on a dirt floor. He weakly props himself up to talk to Kamble, wiping away the fluid that seeps from his eyes. Mohammed has been taking government TB drugs for five months, but he isn't getting better. "He doesn't move around much," says his wife Hasibunissa Shekh. "He sleeps most of the time." Neighbors have been helping feed the couple since Mohammed has been too weak to work, but both husband and wife are alarmingly thin. Now they're waiting for the test results to find out whether Mohammed's TB is drug-resistant. That will take weeks; in the meantime, Shekh and anybody else Mohammed comes into close contact with could become infected.

When doctors at Hinduja first reported TDR cases in late 2011, the central government groused at them for being alarmist. But eventually New Delhi nearly doubled the budget of the national TB program. Now 529 of the nation's 662 health districts are, at least on paper, equipped to treat drug-resistant cases, and last

summer the government said the whole country would be covered by March. Says Dr. Minni Khetarpal, Mumbai's deputy health executive officer: "After a year, I am confident the numbers will go down."

## **If You Build It, Will They Come?**

At least in Mumbai there are options. Between the newly robust network of government clinics, NGOs, hospitals and labs, there is a reasonable chance that sufferers will get scooped into the system. But in rural areas — in other words, most of India — that possibility is worryingly remote. In Patna, the capital of Bihar state, which has one of India's highest TB rates, 30 spartan beds are lined up in a new drug-resistant-TB ward. This is one of three facilities in Bihar where patients go to start government treatment for drug-resistant TB. Anil Kumar, a shy 18-year-old, sits on one of the beds with his father hovering over him. Kumar has been diagnosed with MDR TB. He was only tested after his sister, who had floated from private doctor to private doctor for years, finally died. Ajay Kumar Singh, the doctor on duty, says the boy almost certainly contracted the drug-resistant strain from his sister, and for that, he's lucky. "His diagnosis was made at her sacrifice," Singh says.

Thousands of families might not know to do the same. Finding a way to bring patients into the system is tricky in a place where mistrust of government services runs deep. Once bedeviled by insurgents, bandits and some of the worst infrastructure in the country, Bihar is still trying to shake its reputation as the nation's basket case. Things have improved, but years of official neglect are hard to undo in far-flung villages that are waiting to catch up with a shinier India. "There's [not enough] staff in the local hospital," says Mohammed Ishaque, a villager whose wife has TB. "They just tell patients to go to private doctors."

And that's exactly what most people in Bihar — and indeed most of India — do. Today there are about 57 doctors per 100,000 people, a number that the government says falls far short of what's needed. The vast and unwieldy sector of private practitioners ranges from qualified professionals to unskilled entrepreneurs who sniff an opportunity to siphon off customers from crowded and generally loathed government facilities. Even patients with almost no money prefer to drop into a private neighborhood clinic than wait in line for hours at a public hospital. Thus, untold numbers of hole-in-the-wall providers are often the first point of contact in India's battle against TB.

The government plans to make TB drugs free in the private as well as public sectors. If well implemented, the move could have an enormous impact on the spread of the disease and on drug resistance. If it's not done right, wider use of powerful second-line drugs in particular could make resistance worse. India has also made the reporting of TB mandatory and became the first nation in the world

to ban the import and use of an inexpensive but dangerously inaccurate TB blood test. (Without an effective system to communicate or enforce the new regulations, however, the test is still being widely used.) "More than 60% [of TB patients] are getting treated in the private sector, and it is totally unregulated," says Khetarpal. Even in a major city like Mumbai, she admits, "regulating them is beyond our ability."

## **The Long Game**

What happens in India could alter the course of one of the world's oldest and deadliest diseases, but India is not the only country in the fight. In Belarus, where some of the highest rates of MDR TB have been detected, public-health experts are trying to contain the disease among needle-drug users. In Russia and Britain, drug resistance is rampant in prisons. Studies in other countries, including India's neighbor Pakistan, show that getting the private sector involved is key to increasing the number of TB cases that get diagnosed — and therefore is key to containing the disease. "International policy has focused on the public sector," says Salmaan Keshavjee, a professor at Harvard University who studies TB. "That might work in Canada, but in most of the world, people buy care from the private sector ... If you don't engage with it, you're never going to get this disease under control."

WHO estimates that TB costs the global economy nearly \$12 billion a year in lost productivity and wages due to sickness and death, with India and China making up half that sum. Last March, the Bill & Melinda Gates Foundation gave a \$220 million grant to the U.S. nonprofit biotech firm Aeras to develop new vaccines. In the first major TB-vaccine trial in decades, an initially promising Aeras vaccine was found to be ineffective — a serious setback — but now about a dozen new vaccines are being tested in clinical trials, according to the Stop TB Partnership. In December the U.S. Food and Drug Administration approved the first new TB drug in decades, and several other drugs are also in the pipeline that could help fight resistant strains, be taken for shorter periods, decrease side effects and be more effective for HIV/AIDS patients. Faster and more accurate diagnostic tools are on the way, including GeneXpert, a machine already in use in India and other parts of the world that tests for drug-resistant TB in hours, not weeks.

For now, though, frontline staff are making do with the drugs they have. When TIME visited Udwadia's airy Mumbai office, he sat facing portraits of Dr. Robert Koch, the scientist who discovered the TB bacterium, and American jazz great Miles Davis. As desperate patients who weren't responding to drugs shuffled through his door, Udwadia appeared to take cues from the latter — by improvising treatments. Udwadia gestured to a longtime patient sitting at his desk. "At one stage, I told this man, 'Go away. We can't help you,'" he said. Owais Sheikh was one of the first patients Udwadia diagnosed as being TDR. He didn't think anything would help the young father of two, who also has HIV. It was only because of Sheikh's



determination to get treated and eventually Udwadia's willingness to try an unproven combination of drugs that Sheikh remained alive. "I'm very happy, my friend," Udwadia said that day, looking at his smiling patient. "Totally drug-resistant does not mean totally doomed."

Or perhaps it does. Because Sheikh has since suffered a relapse and Udwadia has been forced to seek yet another untried course that could leave the bacterium stronger if they don't succeed in killing it. In the fight against TDR, hope and happy endings are tragically rare.



## Doctors Struggling to Fight 'Totally Drug-Resistant' Tuberculosis in South Africa

February 11, 2013

In a patient's fight against tuberculosis—the bacterial lung disease that kills more people annually than any infectious disease besides HIV— doctors have more than 10 drugs from which to choose. Most of those didn't work for Uvistra Naidoo, a South African doctor who contracted the disease in his clinic. For those who contract the disease now, maybe none of them will.

A new paper published earlier this week in the Centers for Disease Control and Prevention's Emerging Infectious Diseases journal warns that the first cases of "totally drug-resistant" tuberculosis have been found in South Africa and that the disease is "virtually untreatable."

Like many bacterial diseases, tuberculosis has been evolving to fend off many effective antibiotics, making it more difficult to treat. But even treatable forms of the disease are particularly tricky to cure; drug sensitive strains must be treated with a six-month course of antibiotics. Tougher cases require long-term hospitalization and a regimen of harsh drugs that can last years.

Naidoo, then an avid runner, says he continued training for months with the disease, which affects more than 389,000 South Africans annually (about one fourth of Africa's cases), according to the World Health Organization. It wasn't until he went to visit his family in Durban (he had been working with TB patients in a pediatric clinic in Cape Town) that his family noticed he had lost more than 30 pounds.

"I had flu symptoms and chest pains, but I was still running so I didn't think anything was wrong," he says. But when he went in for an X-ray, doctors found that his entire right lung had filled with fluid. Within weeks, he was on his deathbed as his body wasn't responding to the most commonly prescribed antibiotics.

"One night I nearly passed away—it didn't look good," he says.

His father, also a physician, suggested that he may have had an emerging MDR, or a multi drug-resistant strain of TB. The emergence of MDR and its even more dangerous cousin, XDR (extremely drug-resistant TB), have pushed tuberculosis cure rates in the country from a high of 73 percent in 2008 down to 53 percent in 2010.

Naidoo survived the night and doctors eventually found a treatment regimen that worked, but he was in and out of the hospital for three years, and the drugs' side effects were almost unbearable, he says. He developed Stevens-Johnson Syndrome, a complication that

causes layers of skin to separate from each other and can be deadly. He regularly bled from his eyes. He fell into a deep depression.

"The TB doesn't feel like it's killing you, but the drugs do. I am a doctor and was informed that the drugs you take make you feel worse," he says. "My case was three years long. I don't think the average patient has that kind of patience."

At King George V hospital in Durban—one of South Africa's most popular TB clinics, which specifically treats XDR patients—the 200 beds are always full, and there's a four- to six-week waitlist for new patients.

William Bishai, of the Johns Hopkins Center for TB Research Laboratory and head of the KwaZulu-Natal Research Institute for Tuberculosis and HIV in South Africa, works with Naidoo and says his commitment to getting better is uncharacteristic in South Africa. TB is particularly easy to contract among people who have compromised immune systems due to HIV infection—a group that makes up about 12 percent of the country's population.

"There's a co-infection problem with HIV—a lot of XDR patients also have HIV and have to take eight TB drugs in addition to their HIV retrovirals," he says. "The average uneducated person would be prone to giving up. There have been a number of suicides at King George V."

Partial treatment of TB is one of the most important causes of drug resistance, says Karin Weyer, coordinator of the World Health Organization's Stop TB department on drug resistance. Any time a patient stops treatment, surviving bacteria have already been exposed to some level of antibiotics and are more likely to be resistant if the patient relapses, she says.

"The most important aspect of this is that we get the patient cured the first time around," Weyer says. "Every time a patient has to get treated again, you run the risk of amplifying resistance."

That has led to the cases of totally drug-resistant tuberculosis (TDR) described in the Emerging Infectious Diseases journal. Paul van Helden, director of South Africa's Centre of Excellence for Biomedical TB Research and one of the authors of the study, says it was only a matter of time before tuberculosis developed resistances to the last remaining effective antibiotics. TDR has previously been found in India, Iran, and Italy, but appears to be most prevalent in South Africa.

"How long it's been out there is anyone's guess. We found nine cases in one small area; obviously it's something that's been out there for a while," he says.

Patients are rarely tested for a particular strain of tuberculosis, so it's unclear how prevalent TDR is worldwide. Major health organizations have yet to even define the parameters necessary for a case of tuberculosis to be considered TDR.

Bishai says van Helden's paper suggests that "TDR is extensive in South Africa."

"It's gone relatively unrecognized," he says. "This is evidence that it's emerged and is spreading—we're playing with fire here."

Drug-resistant TB isn't just a South African problem. In the early '90s, there was an outbreak of MDR in a New York City hospital. During that outbreak, 32 patients caught MDR over the course of a few months and 29 of them died. That outbreak was eventually controlled, but more than 100 cases of MDR have been detected in the United States over the past eight years, and there have been high-profile outbreaks in Peru, Russia, and India over the past decade.

Despite the high death rate during the New York City outbreak, public health officials were able to keep MDR from escaping into the general population, a task that took a concerted effort and many millions of dollars, van Helden says. South Africa, doesn't have that luxury.

"The fact that New York City managed the outbreak suggests we can contain it, but the cost was phenomenal," van Helden says. "We don't have the same resources as the U.S. South Africa is going to go through a lot of strain trying to combat this problem."

But while tuberculosis appears to be getting more nefarious by the year, Bishai and other experts are more optimistic about humanity's chances for fighting TB than they are about some other drug-resistant bacteria. Global TB rates have been declining for years, and in the most developed countries, there are very few tuberculosis deaths. In the United States, 529 people died of TB in 2009 (the most recent year for which data is available from the CDC). About 10,000 Americans contract the disease each year.

Today, 22 "high burden" countries (including South Africa) account for 80 percent of the world's TB cases, according to WHO. But the organization's most recent report notes that the "global burden of TB remains enormous." The disease killed 1.4 million people in 2011. Because of that burden, pharmaceutical companies are working on new drugs to treat it—which can't be said for some more innocuous bacteria that have developed drug resistances, such as gonorrhea.

In December, the FDA approved bedaquiline, the first new class of TB drug to be developed in more than 40 years. The drug will likely be approved in South Africa sometime this year. It's unclear whether the new drug will be effective against TDR, but scientists are optimistic.

Weyer says bedaquiline is a good start, but if more new drugs aren't quickly developed, TB will develop resistance to that drug as well.

"The only game-changing effects will happen once we have enough drugs to put completely new treatment regimens into use," she says. "It's encouraging we have a few drugs in the pipeline, but we need several new ones, with new mechanisms of action, to protect against new resistances."

In the meantime, researchers are working on getting better at identifying TDR, so doctors will know what they're up against if one of their patients has a highly resistant strain of TB. A lab can easily test whether a strain is resistant to the so-called "first line" of TB drugs, but detecting more highly resistant forms of the bacteria is more difficult.

"There are not yet accepted assays for detecting resistance against second-line drugs," van Helden says. Often, doctors will have to wait months to determine whether a patient is actually responding to treatment. That's what happened in Naidoo's case: For a while, he was taking drugs that weren't having any effect on his disease.

Today, Naidoo has permanent lung scarring, but he's otherwise healthy. The scars on his skin have begun to fade, and he recently started running again. He says the experience has allowed him to become a better TB doctor because he can empathize with patients. But many of his colleagues who have been infected as a result of their work have left the field.

"Doctors and nurses are exposed so routinely to sick patients," he says. "We put our lives at risk every day."

# THE WALL STREET JOURNAL.

## **Dangerous TB Patient Detained on U.S. Border**

March 1, 2013

In medical isolation in South Texas, 100 miles or so from Mexico's border, is a man who embodies one of U.S. health officials' greatest worries: He is the first person to cross and be held in detention while infected with one of the most severe types of drug-resistant tuberculosis known today.

His three-month odyssey through 13 countries—from his homeland of Nepal through South Asia, Brazil, Mexico, and finally into Texas—shows the way in which dangerous new strains of the disease can migrate across the world unchecked.

Tuberculosis, an ancient, fatal airborne disease, has been treatable for decades with a cocktail of drugs. However, shoddy medical practices world-wide have enabled the bacteria to mutate and, in some cases, become all but untreatable. In recent months The Wall Street Journal has exposed widening TB drug resistance in hot spots like India, and shown that the U.S. is surprisingly unprepared for the growing global problem. Most U.S. cases of drug-resistant TB occur in people who were born abroad, according to the Centers for Disease Control and Prevention.

The Nepalese man detained at the U.S. border carries a particularly deadly strain—XDR, "extensively drug-resistant" TB. His TB is resistant to at least eight of the 15 or so standard drugs, according to a U.S. government description of the case reviewed by the Journal. His XDR strain has been seen only once before in the U.S., in another patient of Nepalese origin, according to the government description.

The Nepalese patient was taken into custody by the U.S. Border Patrol in late November as he tried to cross the border illegally near McAllen, Texas, according to Department of Homeland Security officials. The government declined to name him.

He was transferred five days later to an Immigration and Customs Enforcement detention facility in Los Fresnos, Texas, and put into "medical isolation" with suspected tuberculosis, according to ICE. He has since been moved to another ICE detention facility, in Pearsall, Texas, with more medical staff, ICE said. He is the first XDR-case in ICE custody.

Twelve Border Patrol agents were tested for the disease, but none contracted it from the patient, a Customs and Border Protection official said. Casual contact doesn't necessarily lead to infection, though it depends in part on how much time is spent in tight quarters with a patient, and how much the patient coughs, spreading bacteria into the air.

It remains unclear whether other people in custody with the Nepalese detainee might have been infected. By the time the Border Patrol learned of his infection, other people detained with him would have been transferred elsewhere, the CBP official said. Detainees who are suspected of being ill are placed in cells by themselves.

Given how far and wide the patient ventured—he took a flight of more than eight hours to Brazil, and also traveled by car, boat and on foot—his case was reported to the World Health Organization as having potentially widespread public-health impact. Now, officials in the 13 countries the man visited along the way must try to track down thousands of people he likely came into contact with, to see if any were infected.

That will be a challenge. "We will try to investigate where he was," said Martin Castellanos, director of Mexico's national TB program. But reconstructing his precise route through Mexico, or any country, will be difficult and perhaps impossible, he said.

Dr. Castellanos says he was told the man spent time in a migrant community in Reynosa, across the border from Texas. But migrants typically linger there only "for a week, two weeks," he said, before moving on. "For sure, no one who was there in November is there now," he said.

The WHO's Stop TB Department said it is working with the CDC to inform affected countries about people who may have been exposed to the man. It is also trying to get more details on potentially infected people in those countries who have been reached by local authorities.

DHS and the CDC declined to discuss details of the man's case, citing patient privacy. The man declined an interview request from the Journal made through ICE. He also declined to sign a privacy waiver allowing officials to release details of his treatment and his immigration case, ICE said.

XDR-TB is a particularly dangerous form of the disease that is resistant not only to the two most potent TB drugs, but also a handful of second-line drugs. It is rare in the U.S.: Only six cases were reported in 2011, according to the CDC.

But it is a growing threat in countries including India and South Africa, where it has been found all over the country. The risk to the world is that the disease will migrate outward from these hot spots. Treatment options for XDR-TB are limited and can themselves be toxic.

ICE officials screen patients for TB—both regular and multidrug-resistant varieties—when they arrive at a detention facility. "We prepare for it and look for it," an ICE medical official said. They find one or two cases of multidrug-resistant TB a year, the official said.

How long the man will remain in care in the U.S. is unclear. Treatment can last for years, but TB patients aren't infectious for the entire course of treatment.

Detainee patients aren't normally kept until they are completely cured. However, infectious patients aren't deported on commercial flights or by any other means that "could be a danger to anyone," the official said.

One risk, of course, is that a patient won't have enough drugs or medical expertise to complete the treatment he or she needs once deported to another country. TB strains can become increasingly drug-resistant if a patient's treatment regimen is interrupted, even briefly. This is one way that drug-resistant TB has emerged over time.

The Migrant Clinicians Network, an Austin, Texas, nongovernmental organization, helps arrange for deported patients to continue their treatment in their home countries. U.S. officials also often send patients home with a supply of the TB drugs they need, particularly to countries where supplies are uneven.

Arranging care for drug-resistant patients is complicated, said Ed Zuroweste, the Migrant Clinicians Network's chief medical officer. "XDR is hugely difficult," he said. "You really have to have experts to treat someone like that."

Nepal is known for innovative health programs, including some to fight TB. But like many countries, it has struggled with drug-resistant forms. Nepal reported more than 35,000 TB cases in 2011, and 2.9% of new and 12% of previously-treated TB cases are multidrug-resistant, according to WHO data.



# THE WALL STREET JOURNAL.

## Global TB Fight Hits a Wall

February 20, 2013

MUMBAI—Here on center stage in the global crisis of drug-resistant tuberculosis, top doctors are sounding a new alarm: India's emergency strategy to defeat the disease may be having the opposite effect—encouraging TB instead to mutate into more deadly and unstoppable strains.

In its new strategy, India is treating some, and perhaps many, drug-resistant TB patients with drugs that they are already resistant to. That can allow the bacteria to build resistance to new drugs as well.

On Friday, a prominent specialist described research to The Wall Street Journal showing that the government's treatment plan wouldn't work on fully two-thirds of the 300 patients analyzed at one major Mumbai hospital. The results suggest India's plan is "a futile exercise" that will "serve to amplify resistance," said the researcher, Dr. Zarir Udwadia. "It is morally and medically disastrous."

Shown the findings, Mario Raviglione, director of the World Health Organization's Stop TB Department, called India's approach to treating drug-resistant TB "complete nonsense."

Ashok Kumar, head of the Central TB Division of India's health ministry, declined several requests for comment.

India estimates it is home to 100,000 patients with drug-resistant TB—the most in the world—but for years it officially ignored them in favor of treating traditional TB, which is more common and curable. That policy left drug-resistant strains to spread and worsen. For countless thousands of people, it amounted to a death sentence.

Last year New Delhi made a historic policy reversal, scaling up a new strategy for treating drug-resistant patients. The change followed a Journal investigation in 2012 revealing that India, for years, had ignored evidence of increasing drug resistance and today likely has far higher rates of resistant TB than officially reported. The Journal also showed that the WHO's own policies inadvertently helped drug-resistant TB to flourish.

Drug-resistant strains are edging up in the U.S. and increasing in parts of Europe, though most cases are in India, China and Russia, the WHO says. In some Indian patients, TB is now all but incurable.

A half-century ago, researchers discovered that tuberculosis—a fatal disease often characterized by the coughing of blood—could be cured with a cocktail of antibiotics and

chemotherapy drugs. The problem, however, is that if a patient's TB is resistant to some of those drugs, the cocktail won't work.

Instead, the bacteria can quickly mutate to become resistant to the other drugs in the cocktail. This is how a once-curable killer has, over time, become almost untreatable again. There are many strains of TB with varying resistance to the dozen or so standard drugs.

The issue with India's new program, doctors say, is that tries to be one-size-fits-all: The same six-drug cocktail is given to every drug-resistant patient, without thorough testing to see which they are resistant to.

Experts say at least four of the six drugs must work for most patients to be cured.

A top official in Mumbai's TB program said the city has greatly expanded its drug-resistance treatment this past year. She complained of a lack of accredited labs in the city for testing patients for resistance.

She said Mumbai has been "begging" the central government to change its policies so that drug-resistant patients are first tested thoroughly before being put on a particular cocktail. Despite these obstacles, she insisted Mumbai's program remained effective for many patients. "Our results are more encouraging than what we thought," she said.

The WHO's Dr. Raviglione said, "It is silly to use drugs that there is proven high resistance to, thinking they will work." The WHO recommends testing patients for drug resistance. If there aren't enough labs to do that, he said, Mumbai should conduct surveys to see which drugs its patients are most resistant to, then replace those drugs in the standard cocktail.

Dr. Alpa Dalal, a chest physician at GTB Hospital, Mumbai's main TB hospital, said she has been warning government TB officials that the standard cocktail isn't working for many of her drug-resistant cases. For these patients, time is of the essence, she said. "When you notice they are not responding, by that time you have lost the chance to treat them forever," she said. "And they have gone on spreading the disease in the community."

The world is battling an epidemic of drug-resistant TB. India has about 2.2 million of the estimated 8.7 million total TB patients world-wide, the most of any country. Last year it said it would scale up its treatment of drug-resistant TB and eventually test all TB patients for resistance at their initial diagnosis.

Several studies suggest substantial resistance here in Mumbai to many drugs in the government's treatment regimen. A preliminary analysis of one study under way showed that 28% of all TB patients tested in Mumbai were drug-resistant.

"It's a disaster on a huge magnitude," says Nerges Mistry, head of the Foundation for Medical Research, a Mumbai nonprofit that studies TB.

One basic problem: India doesn't have enough labs to test every patient for resistance, and likely won't for years. In light of that, some physicians say they are troubled by the fact that the government hasn't yet accredited one private lab in Mumbai—Hinduja Hospital, where

Dr. Udhwadia works—that they consider the most experienced in the country at testing patients for drug resistance.

"I don't understand why they don't accredit Hinduja," said Soumya Swaminathan, director of the National Institute for Research in Tuberculosis, part of the government's network of biomedical research institutions.

Last year Dr. Kumar, head of the health ministry's Central TB Division, publicly criticized Hinduja Hospital and its researchers, saying their findings of "total drug resistance" published in a medical journal would hurt Indian tourism and should have been reported to him first.

In recent interviews, Dr. Kumar said a government hospital in Mumbai would be accredited soon. He also said Hinduja's lack of accreditation was because the government's accreditation team is short-staffed and focused on processing applications from public hospitals first.

Because of Hinduja Hospital's reputation, patients flock there, often paying out of pocket for its tests to determine what drugs they might be resistant to.

On Jan. 29, 17-year-old Satish Gupta, a winsome teenager limping from severe knee pain, a side-effect of one of his TB medicines, showed up with his brother at one of the Mumbai treatment centers. They carried a report from Hinduja showing Mr. Gupta is resistant to three of the six drugs on the government's regimen, including the one causing his pain.

Despite his Hinduja report—and a note from his physician suggesting his cocktail of drugs be tweaked—the government program refused to modify his regimen. "Hinduja not accredited," a government TB official wrote on official stationery.

A senior official in Mumbai's TB program said Mr. Gupta was treated according to the recommendations of the government program as well as a team of experts consulted on all cases. In the absence of any accredited labs, she said, she has urged program doctors to be flexible and change drugs if reports from any lab indicate resistance.

Mr. Gupta is lucky in one sense. His family, which runs a tiny store on a narrow alley, has enough money to try to pay out-of-pocket for the drugs that have a chance of curing him, since the government-provided ones don't seem to work for him.

"We will pay whatever it takes for Satish to get well," said his older brother, helping Satish hobble down the steps of Hinduja Hospital.