# A Woman's Drug-Resistant TB Echoes Around the World

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MUMBAI—As dawn broke on July 16, a tiny woman pushed a metal trunk aboard a train, pausing a moment to cough into the green-and-black-print scarf around her head. Her husband carried a comically large water jug.

"You've decided to travel with Powai Lake," Rahima Sheikh quipped to her husband, referring to a lake near the city of Mumbai. She helped him stow the jug under their seat.

Then, promptly at 6:35 a.m., the Gorakhpur Express heaved out of the station, carrying Mrs. Sheikh on a 1,000-mile journey home, where she expected to die.

Over the past six years, Mrs. Sheikh, 40 years old, mortgaged her family's rice fields, spent her father's and brother's life savings, and crisscrossed India in search of a cure for tuberculosis. But instead of getting healthier, Mrs. Sheikh grew increasingly resistant to medication with each failed treatment. This year, Mrs. Sheikh became one of India's first documented cases of TB that is resistant to virtually all the medicines approved to treat it.

In recent decades, tuberculosis, a fatal infection characterized by the coughing of blood, was generally treatable. The Wall Street Journal reviewed years of Mrs. Sheikh's medical records, interviewed her doctors and TB workers across India and traveled with her as she pursued treatment.

Her six-year journey to all-but-incurable TB exposes a blind spot in an Indian medical bureaucracy

that, for decades, neglected to implement widespread testing or treatment for drug-resistant strains. As a result, a curable disease has mutated into a killer.

The global community is worried about the danger. Health officials have urged India and other countries with increasing drug resistance to take stronger action. And this year the U.K. added India to the list of countries whose citizens must be tested for TB to obtain a visa of six months or more.

India has no national count of patients resistant to one or all of 12 commonly used TB drugs. The government cites a study in the state of Gujarat showing less than 3% of patients there are resistant to at least the two most-powerful ones.

Experts say these figures far understate the problem. For example, the Mumbai hospital that reported four fully drug-resistant patients this past December, had counted 15 by May. Since then, the hospital has stopped counting because of the controversy created by the bad publicity, according to the head of the lab.

Smaller studies in Mumbai and in Uttar Pradesh, India's most-populous state, show 13% or more newly diagnosed TB patients are infected with multi-drug-resistant strains.

Mrs. Sheikh "is not a rare case—I've seen thousands of cases" of patients who, like her, develop resistance to increasing numbers of drugs, said Amita Jain, a microbiology professor at King George Medical University. "India is sitting on an atom bomb about to explode."

Tuberculosis is generally transmitted by being in proximity to coughing patients. The World Health Organization, concerned about the spread of drug resistance, began warning in recent years about the risk of contagion, "in confined spaces, such as aircraft cabins," advising people with infectious TB not to board flights.

But even extended exposure doesn't always result in infection. Mrs. Sheikh's husband and three children are all TB-free, despite years of close contact.

India in 2000 pledged as part of a United Nations initiative that it would halve TB prevalence and deaths by 2015. But despite setting up 13,000 diagnostic centers nationwide, it is still far from these goals. The disease is on the decline, but still afflicts 2.3 million Indians annually. It kills more Indians than any other infection.

Treating a patient who is multi-drug resistant or worse in India costs more than $2,000 over a period that lasts at least two years, compared with $10 to treat regular TB for six months. And while regular TB is virtually curable, studies show that between 30% and 50% of patients who are resistant to multiple drugs don't ever get cured, even on treatment.

Mrs. Sheikh, one of six children of a high-school teacher and his homemaker wife, grew up in the village of Rampur, amid rice and wheat farms near Nepal. Her family was relatively prosperous, as her father owned an acre-and-a-half of farmland.

As a child, she got an elementary-school education, but then was kept home to help her mother to cook and sew traditional garments for family members—salwar kameezes for the women, kurta-pajamas for the men. She was the "fairest" daughter, her father said, and the most capable. "She was so light-skinned, just like her mother," he said proudly.

Slight in stature, she stood just an inch over five feet tall, with nimble fingers that made her a gifted seamstress. "My brothers would always say that I could make them an entire kurta-pajama in the time it took them to take a bath," she said, speaking in Hindi during one of many hours of interviews in recent months.

At 21, Rahima married Tabarak Sheikh from a farming family nearby. Mr. Sheikh didn't have much

land or education. “I didn’t pay attention in school back then,” he said, laughing. “I just used to run here and there.”

He found a job as a garment worker in Mumbai, India’s largest city, making men’s pants, for 200 rupees a day, or $4. He sent money home to support Mrs. Sheikh and their three children.

It is unclear how Mrs. Sheikh got TB, but she recalls when she learned. She was in the village during monsoon, July 2006, when the telltale sign emerged—a cough that wouldn’t go away.

On Sept. 8 that year, she began treatment in a government clinic. She started the standard six-month regimen.

A month in, she coughed up blood. “I got really scared,” she recalled. “I thought, ‘This is really serious. These medicines aren’t working. I better go somewhere where they have very good treatment.’” She made the 35-hour train trip to Mumbai, where her husband promised to take her to “VIP doctors.”

But once there, she was told India’s TB program offered the same treatment everywhere. So she returned to her village.

Meantime, she missed a month of treatment, because the program required patients to visit the clinic and take their medications in front of a TB worker. Stopping and starting TB medicines can breed drug-resistant strains of the bacteria that cause the disease.

Wealthier Western nations first test patients for drug resistance before prescribing medicines. This way, treatment can be tailored to combat resistance.

India’s government has been slow to start nationwide testing for resistance. When India built its TB program in the 1990s, with WHO help, it was thought to have little resistant TB.

Even though Mrs. Sheikh took her medicines, she kept testing positive. In November 2006, when she

restarted the program, she registered a level of 3+ on the scale of 1 to 4. Nine months later it was down at 2+, but far from gone, records show.

"She kept coming back, and her disease was positive and positive and positive," said Ramdayal Tiwari, a local TB worker. "We didn't know what to do." Mr. Tiwari and his team sent her to a chest physician at a nearby hospital—a broad-shouldered, mustachioed doctor named M.P. Singh.

Mrs. Sheikh stood out among his patients, Dr. Singh said. "She'd come laughing into my office," he said. "Most people just give up and go home to die."

The government still doesn't pay for the testing or treatment of drug-resistant TB in most of India. Mrs. Sheikh was poor, but she had an older brother, Abidula Siddiqui, with the means and desire to help. "She was very loving to him, and he was very close to her," Dr. Singh recalled.

With her husband in Mumbai, Mrs. Sheikh leaned heavily on her brother, a schoolteacher. "He saw the troubles I faced," she said. Often, he would pick her up with his motorbike and take her to doctor's appointments.

Dr. Singh ordered a drug-resistance test, Mrs. Sheikh's first. She had already been in treatment for nearly a year.

The results came back worse than expected. She was resistant to nine medicines tested.

There are 17 drugs recommended by the WHO for TB treatment, but not all are equal. "First-line" drugs are the most effective and least toxic. Lower on the list, second-line medicines become weaker acting and more hurtful to patients. When doctors call patients "totally resistant," they mean someone who doesn't respond to all first-line drugs and virtually all of the common second-line treatments.

Physicians and researchers reviewing Mrs. Sheikh's case for the Journal say she probably had

been infected with a tougher TB strain to begin with. Such patients can still be cured, experts say. But it requires early testing for resistance and specially tailored, aggressive treatment.

Doctors don't always know or follow these steps. Even if they do, there might not be sophisticated labs nearby to do testing.

In Mrs. Sheikh's case, these procedures weren't followed.

India's top TB officer, Ashok Kumar, insists drug resistance isn't a serious problem in India. In a three-hour interview in his Delhi office, Mr. Kumar tried to minimize the danger of TB, which he said was more curable than some other diseases. "It is better to suffer from TB than diabetes, hypertension or a psychotic problem," he said.

Still, he said, India plans to start testing sooner for resistance, and in some areas is doing so already. But testing for resistance nationally requires building new labs, which will take several more years.

Dr. Singh, who acknowledges he isn't an expert at treating drug resistance, said he did his best. Armed with her tests and the WHO's list of recommended drugs, he says he tried to follow the guidelines for treating resistance. The WHO recommends prescribing at least four drugs likely to work in the patient—meaning she hasn't tested resistant to them or gotten sicker when taking them.

Mrs. Sheikh began taking the four he prescribed. Still, her chills and coughing raged.

Specialists who reviewed her records for the Journal say the drug cocktail Dr. Singh prescribed was too weak to kill her strain. So the bacteria likely mutated further, they said. In fact, when she was tested again four years later, she had developed resistance to two of the four drugs in Dr. Singh's regimen.

Sitting behind a vast desk recently, Dr. Singh

reviewed his treatment of Mrs. Sheikh. In retrospect, he should have doubled the dose of one drug, he said. He also said he could have used stronger drugs, such as capreomycin. "But I never put her on it because it's 204 rupees a shot. That's too expensive. And it's too toxic. She was too sensitive."

Still, he doesn't believe his regimen made her more drug-resistant, and he doesn't know why his treatment didn't help, except to say resistance is extremely difficult to treat. "When you become more resistant, the disease is more dangerous than AIDS," he said.

Mrs. Sheikh stayed under Dr. Singh's care for more than a year. Then, in late 2008, Dr. Singh told her brother: "Take her to a better place."

Mrs. Sheikh and her brother caught an overnight train to the city of Kanpur in northern India, and showed up at the clinic of S.K. Katiyar. So many TB patients flock to him that he has built a courtyard adjacent to his clinic with room for 100 or so patients to wait beneath a huge tree.

Dr. Katiyar, a portly man with black hair and a shiny white mustache, says he looked at Mrs. Sheikh's records and gave her less than a 50% survival chance. "All the money you spend may not prove of use," he recalled telling them.

Mrs. Sheikh recalls the meeting bitterly. "He said, whatever medicines I took, nothing would be helpful."

Mrs. Sheikh's brother told the doctor he was willing to pay anyway. And he handed over Mrs. Sheikh's drug-resistance test results.

Dr. Katiyar turned away the documents. "I don't need that," both men recall him saying.

Dr. Katiyar acknowledges ignoring Mrs. Sheikh's tests. He said the labs are so unreliable, he doesn't believe the results. "We teach that you don't always go by the lab reports. Go by clinical experience." Some Indian labs can be inaccurate and the government is

instituting an accreditation process.

He prescribed seven drugs, including three that her tests already indicated a resistance to. Over two weeks, Mrs. Sheikh's brother and father pooled their savings to pay 28,000 rupees, about $500, for her care. That exhausted the two men's savings.

Mrs. Sheikh changed doctors again, switching to one in Kanpur who worked with charities to subsidize TB drugs. For two years, she says, she stuck to the regimen. Her skin, once fair, turned darker, a drug side effect. But for the first time, her disease disappeared. In X-rays and bacteria tests, no TB could be detected.

Then, as winter 2010 approached, she developed another side effect: unbearable itching. Her doctor acknowledges telling her to go off her drugs. She had been taking them for two years, the minimum to cure resistance.

In hindsight, that was probably a mistake, he conceded in an interview in Kanpur. "I felt so badly for her. Maybe we should not have stopped the medicines," he said. "I did my best, but you always wonder if you should have continued for longer."

Four months later, in December 2010, Mrs. Sheikh began coughing again. Within days, she was coughing blood.

Her husband, still a believer that Mumbai's "VIP doctors" held the answers, persuaded her to try there again. In December 2010, they mortgaged his quarter-acre rice field for 40,000 rupees, about $800, and headed for Mumbai. Mrs. Sheikh shook so violently with chills and coughing, she said, "I didn't think I would live to finish the journey."

The afternoon they arrived, they went straight to the private clinic of the doctor that many in Mr. Sheikh's Mumbai slum raved about: 70-year-old K.C. Mohanty.

Dr. Mohanty, head of the chest-medicine

department at Somaiya Hospital, a nonprofit bordering a slum, is a slight man whose junior doctors start each day by lining up and touching his feet as a gesture of respect. Dr. Mohanty also ignored Mrs. Sheikh's resistance tests. Her records show that, in previous treatments, she had already taken all five drugs he prescribed. And, years earlier, she had tested resistant to three.

Dr. Mohanty, in an interview at Somaiya, said he disregarded her drug-sensitivity test because, like Dr. Katiyar, he worried the lab wasn't reliable. He said he chose his drug regimen based on his clinical experience.

He also said it would be "almost impossible" for him to recall today why he broke the WHO's recommendations for TB treatment—namely, patients be given at least four drugs likely to work. "How can I tell you today about a clinical judgment I made two years back?" he said.

Dr. Mohanty's regimen didn't work. After six weeks, Mrs. Sheikh's bacteria level was 4+, the highest. In that brief time, the Sheikhs burned through almost all of the $800 they got mortgaging their rice field.

Giving up on Dr. Mohanty, the Sheikhs showed up at G.T. Hospital, a government facility where they hoped for free treatment. Jaising Phadtare, head of TB treatment there, reviewed her paperwork. "You've taken all the drugs in Hindustan," he recalled telling her, using an old-fashioned name for India. He saw few paths forward, he said in an interview. He prescribed four drugs, including capreomycin, the one rejected earlier by Dr. Singh as too costly.

Mrs. Sheikh's TB didn't abate. So in July 2011, he sent her for another drug-sensitivity test.

The results showed her resistance to be worse than four years earlier. She was now resistant to 12 TB drugs, constituting virtually all the ones effective in

resistant patients.

Believing Mrs. Sheikh to be doomed, Dr. Phadtare asked her husband to sign a statement that reads: "I've been explained the grave prognosis in detail. In case of untoward complication, doctor or administration won't be held responsible."

Mrs. Sheikh recalled that day, standing by her husband as junior doctors got him to sign his name to the English-language statement, explaining that it meant his wife was unlikely to live. The doctor told them, "There was nothing left he could do," Mrs. Sheikh said.

Mrs. Sheikh's drug resistance was so complete, it caught the attention of the head of the lab where the test was run. She and Zarir Udwadia, a TB specialist at Hinduja Hospital, in 2011 had noticed several patients whose disease was resistant to virtually every treatment.

They wrote a letter to a medical journal reporting four cases of "total drug resistance."

Their letter triggered a vehement government denial. India's TB office questioned the lab's credibility, and even complained about the letter's wording: There could be no "total drug resistance," the officials said, because the WHO has no category of TB called "total drug resistance."

A few months later, however, the government quietly confirmed the letter's findings.

In interviews, WHO officials acknowledge that they have resisted adopting "total drug resistance" as a TB category. But not because such patients don't exist. Rather, because lab tests confirming resistance are hard to replicate and because patients might be discouraged by such a scary-sounding definition.

Mrs. Sheikh persisted until she found a way to be seen by Dr. Udwadia, one of the top TB doctors in the world.

He, too, had scant hope—but didn't tell her that.

“To be honest, I was alarmed and horrified,” the doctor said.

He left in place the four drugs she was taking, and added two experimental ones. One is extremely toxic and painful.

This past April, for the first time in more than a year, Mrs. Sheikh tested negative for TB. “This shows that you should never give up on a patient,” said Dr. Udwadia, ecstatic at the news. “There is hope.”

Despite the welcome development, Mrs. Sheikh wasn’t in a position to share the excitement. She was often psychotic, the side effect of one drug. Her feet felt like they were on fire, the side effect of another.

She began to act violently. In June Mrs. Sheikh hit her teenage son so hard, she broke her pinkie. Another day she whacked her daughter, causing a lump to sprout on her head. “The medicines made me crazy,” she said.

She and her husband were living in a slum in the heart of Mumbai in a single, dark room with no toilet. Mr. Sheikh was forced to miss work to care for her, limiting their income. Buying food became difficult.

Mrs. Sheikh yearned to return to her village as the Muslim holy month, Ramadan, approached in July. After India’s cases of total drug resistance were publicized in January, the Mumbai city government started providing her medicines for free. She asked for a month’s supply of drugs to make the trip, but officials would give her only a day’s worth at a time, for fear she would sell them.

Mrs. Sheikh decided she would go home anyway, though it could well be a death sentence to quit treatment again. For the first time, she felt like quitting. “If they don’t give me the drugs, perhaps it’s God’s will that I give up and allow myself to die,” she said, sitting on the floor of her slum room in Mumbai, the train ride home just a few days away.

She packed her steel trunk of belongings. “What

about the medical records?" Mr. Sheikh said. Four plastic bags of paperwork hung from nails on the wall.

"Throw them out," she said.

Just two days before her departure, TB officials relented and gave her a month's medicine. But they warned she would need to return to Mumbai to get more.

The night of July 17, she arrived home in Rampur. The next few days, she lay on her mother's lap in her parents' house and stared out the door at the foot-high paddy, swaying in monsoon-flooded fields.

But as the days passed, she regained some of her equilibrium. She and her husband reopened their own house for the first time since locking it up a year-and-a-half earlier. One evening they gathered for dinner on the roof, the sky streaked pink, as calls from a nearby mosque announced the end of the daylong Ramadan fast.

Mrs. Sheikh grumbled about her darkened skin, the side effect of treatment—and the kind of thing that would have been the least of her worries a short time ago. "Everybody's been asking how I got so dark," she said to her husband. "Remember, I used to be so fair, just like Gulshan," their daughter. "Can you call the doctor tomorrow and ask what medicine I can take to get my fairness back?"

As her medicine supply dwindled, Mrs. Sheikh managed to persuade Mumbai's TB officials to courier her another month's worth. A few days ago, she looked down a dirt lane and into the distance, wondering when the courier would arrive.

"Maybe it's not in God's plan for me to die quite yet," she said. "Sometimes, I think that maybe I can get well."

*—Shreya Shah and Betsy McKay contributed to this article.*