NEWSLETTER

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Internationale Nachrichten

1. Today the SDGs on health needs to go beyond GDP

The UN General Assembly in New York adopted the Sustainable Development Goals, or SDGs, a long list of goals and targets supposed to make the world in 2030 a better place.

Every self-respecting leader was there and hundreds, if not thousands, of VIPs, lobbyists and activists attended the event. Let's have a look at some of the statements made yesterday.

First the Pope, who reminded us that while the SDGs continue to put all hopes of eradicating the ills of the world – from poverty to violence – on economic growth, "most of us are acutely aware of the need to dethrone GDP growth as the measure of human progress".

Economic growth is indeed playing an increasingly prominent role in discussions on development, linking a country's GDP classification to its social and health progress.

This is despite the fact that most of the world's poorest and sickest people live in countries classified as middle income. As a result, their health needs risk being ignored while the majority of international health aid is allocated elsewhere.

Linking economic growth to health funding will cripple the ability of global health initiatives to remain global and to fight diseases where they claim most victims.

Yes, India may have more billionaires than the UK, but it is also home to a large proportion of the world's unimmunised children. Many serious public health crises, such as the explosion in multidrug-resistant tuberculosis, occur in countries which fall into the middle income bracket, but which are unable to cope with the financial burden imposed by these diseases.

Without international support, struggling countries are even less likely to meet international health targets and bring the diseases under control.

Yesterday, a group of economists said, 'Our global society has a vested interest in investing in health'. It's a welcome statement for the health sector, of course. However, the economic argument raises the question of who better health makes economic sense for, and who stands to gain?

My suspicion is that the focus will be on those with the potential to contribute to economic growth, and money will be rationed to those interventions considered cost-effective.

Is a woman in need of an emergency caesarean living in a remote village in the highlands of Lesotho a good investment opportunity? What about marginalised people, such as sex workers, prisoners or migrants – will they get the same entitlement to healthcare as other people? Health and healthy lives should have a value in themselves, not just as an interesting economic opportunity.

After a welcome breathing space from 2000 to 2015, when health was seen not as a commodity to be bought with economic growth, but as a public good, we seem to be back at square one.

The SDGs seem to concur with the old premise that health and other sectors will have to wait for the trickle-down benefits of countries' economic growth.

Key international donors are reverting to the paradigm of the 1980s and 90s, when the major concern about health was "how much does it cost?" and not the cost of suffering of people with little or no access to quality health services, existing medicines or diagnostics.

Buried among 17 goals, health goal number three – "to ensure healthy lives and promote wellbeing for all at all ages" – remains conveniently vague and fails to address the vast inequalities in health provision between and within countries.
The health needs of vulnerable groups, and of people who are stigmatised, discriminated against or excluded from political and health systems, remain hardly visible within the SDG framework.
A good start for the UN meeting on the SDGs would be to go well beyond GDP classifications and economic growth aspirations. If we are serious about making progress in health, people's needs should be central from day one.
With the SDG framework now done and dusted, our hopes must rest on what happens next, and what additional resources are mobilised to achieve these ambitious goals. Without real, concrete action to reverse the current trends, the SDGs' rousing motto – 'Leave no one behind' – will pale into just another slogan.
Source: Thomson Reuters Foundation, http://tmsnrt.rs/1KKBrOI (26.09.2015)

2. Kenya: TB Cases Hit 90,000 As Survey Launched
The government has launched its first ever tuberculosis survey, as statistics show that 90,000 cases of were recorded in the country last year alone.
Of this, 4,500 cases were recorded in Mombasa, according to Dr Jane Ong'ang'o, the TB Survey Coordinator at the Ministry of Health.
The coast region has the highest number of TB infections in the country, followed by Nyanza and Nairobi regions, she added.
Dr Ong'ang'o said the survey would be used to gauge the number of TB cases and assist in planning health interventions, unlike before when hospital records, which are not representative, were used.
It will also enable them to understand the behaviour of TB patients, especially why they do not go for tests or treatment, those who use traditional medicine and so on, she added.
"Most of the times, we know people who have TB out of hospital records but there are many people who are at home and do not know that they have TB.
"Others are aware of it but are scared of visiting a health facility for tests," she said, during a field survey at the Makumba Grounds in Kisauni, Mombasa on Friday.
The health officer further said the survey had already been completed in Kiambu, Machakos and Kajiado and will also be conducted in Kilifi and Kwale next week.
She attributed the high cases of TB in Mombasa to poor environmental conditions such as stuffy rooms with poor ventilation, overcrowding, and poor nutrition, which results in weak immunity.
"TB is spread by breathing in the germs. When someone coughs out the germs, whoever is next to them easily contracts the TB bacteria," Dr Ong'ang'o said.
TB mobile field supervisor Susan Mutua said that the team had so far screened more than 150 people for TB at the site since the survey started on Wednesday.
Source: AllAfrica, http://bit.ly/1MYKIpR (28.09.2015)

Forschung & Entwicklung

1. Effects of MVA85A vaccine on tuberculosis
A new systematic review of animal studies testing a vaccine for tuberculosis raises questions about whether the studies provided sufficient evidence to move into trials of children.
The new vaccine was a virus-expressing antigen 85A (MVA85A) designed to boost the immunity offered by the existing Bacillus Calmette-Guérin (BCG) vaccine which has little protective effect in practice. The review, published today in the *International Journal Epidemiology*, evaluates the animal evidence that contributed to the decision to conduct human studies.
LSTM's Professor Paul Garner is the senior author on the review, and coordinating editor at the Cochrane Infectious Diseases Group. Working along with colleagues at the University of Edinburgh

and South Africa, the team included data from studies where animals were given the MVA85A booster with BCG and then exposed to a TB challenge, and compared their outcome with that in animals receiving BCG alone. The team identified eight studies published up to September 2014, involving a total of 192 animals.
Different kinds of animals were used in the different studies, but overall the authors found that studies were too small, the quality was low, and details of the experimental methods used were poorly reported. Combining the findings from all studies gave no evidence to support the effectiveness of MVA85A as a BCG booster.
What surprised the review authors was the delay with publishing the largest monkey trial with the longest follow up. This trial had 5 deaths out of 6 monkeys in the new vaccine group compared to two deaths in the 6 monkeys in the control group who only got BCG. This trial only appeared in the public domain after the researchers had received funding for an experimental human trial and had recruited over half of the 2797 infants in South Africa needed.
"This is very disappointing", said Professor Garner. "Tuberculosis remains a major health challenge in many parts of the world and - as with every field of research - we all have a responsibility to work to the highest standards of scientific integrity. We need to make our findings accessible to as wide an audience as quickly as possible. You don't bury results you don't like. It can mislead other scientists, and misinforms the public".
Source: EurekAlert!, http://bit.ly/1jxLkpR (10.09.2015)

2. Radboud university medical center reveals how BCG vaccine works against tuberculosis
Not only the acquired immune system but also the innate immune system has a memory. And the BCG vaccine against tuberculosis can stimulate this memory. After a BCG vaccination the innate immune system responds better to a wide range of other infections. Mihai Netea and colleagues from Radboud university medical center discovered and described how that works. They think that the old vaccine could be useful for specific target groups, such as the elderly.
BCG, a vaccine against tuberculosis, was discovered in the 1920s and is one of the most used vaccines worldwide. In the Netherlands, the vaccine no longer falls within the national vaccination program. Now that it is known that the vaccine can give a boost to the innate immune system, Mihai Netea and his colleagues are calling for more research to determine whether the vaccine can prevent infections in certain risk groups.
During a bacterial infection, monocytes penetrate the infected tissue where they differentiate/ change into macrophages. These carry out the first line of defense: the destruction of the intruder. Monocytes and macrophages are two important white blood cells of the innate immune system. They respond quickly but attack certain pathogens less specifically. The acquired immune system responds more slowly to an unknown intruder but is specifically targeted at a specific intruder. Furthermore, the acquired immune system has a memory so that it responds faster to the same threat. For a long time it was thought that this memory was an exclusive characteristic of the acquired immune system. However research by Mihai Netea has revealed that this is not the case. The innate immune system also has a memory but this is not specific. Netea and his colleagues refer to this as 'trained immunity'.
Shortly after the introduction of the BCG vaccine it was noticed that not only tuberculosis occurred less frequently but that young children also died less due to other pathogens. On September 22, 2015 Johanneke Kleinnijenhuis from Netea's group will defend her doctoral thesis for her research into a biological explanation for the non-specific effects of BCG. In volunteers who received a BCG vaccination, she observed an increase in cytokine production (proteins that control immune cells) and in the number of receptors that play a role during the recognition of intruders. This effect was sustained until three months after vaccination. The scientists discovered that this was because the DNA required was more easily reachable. Netea: "The DNA needs to be read out for the required proteins to be produced. Prior to the vaccination the DNA was hidden so to speak and was consequently difficult to read out. Vaccination ensures that the DNA is exposed."

The researchers also examined the effect in an animal model. Mice without cells from the acquired immune system were administered a potentially lethal quantity of the fungus *Candida albicans*. One part of the group received a BCG vaccination two weeks before this and the other part received a placebo. The BCG-vaccinated animals all survived the fungal infection, whereas in the placebo group more than half of the animals died. As a result of this study the researchers concluded that the effects can be ascribed to the innate immune system.
According to the researchers, the trainability of cells from the innate immune system opens up many opportunities for applications. Netea: "I do not think it is worthwhile introducing BCG again on a large-scale but it would be useful to target it at specific groups. One such example is elderly people who are discharged from hospital and who often experience a relapse when they are back home again. Another possible use is as a booster for other vaccines." In the coming years the researchers want to investigate such applications.
Source: News-Medical.Net, http://bit.ly/1Vri4Ne (24.09.2015)

3. Big Price Increase for Tuberculosis Drug Is Rescinded
A huge overnight price increase for an important tuberculosis drug has been rescinded after the company that acquired the drug gave it back to its previous owner under pressure, it was announced on Monday. However, outrage over a gigantic price increase for another drug spread into the political sphere on Monday, causing biotechnology stocks to fall broadly as investors worried about possible government action to control pharmaceutical prices. The Nasdaq Biotechnology Index fell more than 4 percent.
“Price-gouging like this in the specialty drug market is outrageous,” Hillary Rodham Clinton, a contender for the Democratic presidential nomination, said in a tweet on Monday. She said she would announce a plan on Tuesday to deal with rising drug prices.
Ms. Clinton was referring to the actions of Turing Pharmaceuticals, which last month acquired Daraprim, a 62-year-old drug used to treat a serious parasitic infection, and raised its price to $750 per tablet, from $13.50.
The cases of Daraprim and of the tuberculosis drug, cycloserine, are examples of a relatively new business strategy — acquiring old, neglected drugs, often for rare diseases, and turning them into costly “specialty” drugs. Cycloserine was acquired last month by Rodelis Therapeutics, which promptly raised the price to $10,800 for 30 capsules, from $500.But the company agreed to return the drug to its former owner, a nonprofit organization affiliated with Purdue University, the organization said on Monday.
“We discovered literally on Thursday the strategy that had been undertaken” by Rodelis, said Dan Hasler, the president of the Purdue Research Foundation, which has oversight of the manufacturing operation. “We said this was not what we had intended.”
By Saturday, he said, Rodelis had agreed to give back the drug. Rodelis confirmed this in a brief statement on its website.
The foundation now will charge $1,050 for 30 capsules, twice what it charged before, but far less than Rodelis was charging. Mr. Hasler said the new price was needed to stem losses.
Cycloserine is used to treat multidrug-resistant tuberculosis, a serious form of the disease that does not respond to the usual drugs. There are only about 90 new cases a year in the United States, Mr. Hasler said, and about half those patients get treated with cycloserine.
Turing does not appear ready to surrender. Turing’s founder and chief executive, Martin Shkreli, a former hedge fund manager, used television interviews and also Twitter and Reddit to defend his move. Martin Shkreli, the chief executive of Turing Pharmaceuticals, explains the increase in drug prices in a CNBC interview. He said that toxoplasmosis, the infection Daraprim is used to treat, had been ignored by the pharmaceutical industry because there was little money to be made. Now that Turing can presumably make money, he said, it will be able to educate doctors about the disease, improve delivery to patients and develop better drugs for the infection.

Infectious disease specialists, who have protested the price increase, question the need for new drugs for toxoplasmosis and say that if Turing wants to develop such drugs, it should use money from investors. They say the price increase will raise the cost of treating some adult patients with toxoplasmosis to hundreds of thousands of dollars a year.

Senator Bernie Sanders of Vermont, who is also vying for the Democratic presidential nomination, sent Turing a letter on Monday demanding information on the price increase.

"Without fast access to this drug, used to treat a very serious parasitic infection, patients may experience organ failure, blindness or death," Mr. Sanders said in a statement issued with Representative Elijah Cummings, Democrat of Maryland. The two lawmakers have been investigating sharp price increases in drugs, many of them old generics.

Rodelis, which increased the price of the tuberculosis drug, said last week it needed to invest to make sure the supply of the drug remained reliable. Rodelis reveals almost no information about itself, such as the names of its executives, directors or investors, on its web page.

Cycloserine, which went on sale in 1955 and is also known by the brand name Seromycin, was long produced by Eli Lilly and Company, which around 2000 decided to drop the drug, in part because the company was getting out of antibiotics.

Starting in 2003, as part of a philanthropic initiative on TB, Lilly transferred rights and manufacturing skill to generic drug companies in India, China, South Africa and elsewhere to supply the regions most affected. In 2007 it gave the rights for the United States and Canada to the Chao Center for Industrial Pharmacy and Contract Manufacturing, which is under the auspices of the Purdue Research Foundation.

Mr. Hasler, a former Lilly executive, said the Chao Center had lost about $10 million on the drug since 2007 because of the small number of patients and high regulatory costs. So the Chao Center was interested when it was approached by Rodelis. "They found us," Mr. Hasler said.

A patient with multidrug-resistant tuberculosis might take two capsules a day of cycloserine, along with other drugs, for 18 to 24 months, according to the Centers for Disease Control and Prevention. Under the price Rodelis planned to charge, a full course of treatment would have cost more than $500,000 for cycloserine alone. With the new price from the Chao Center, it will be closer to $50,000. The drug made by generic companies abroad costs only about $20 for 100 capsules.

Amir Attaran, an expert on pharmaceutical access issues at the University of Ottawa, said it would have made much more sense to just import the drug from abroad, rather than have it produced in America for so few patients at such high cost.

Mr. Hasler said this was probably not done because foreign manufacturers were not willing to bear the expense of applying for regulatory approval in the United States.

Dr. Attaran said Lilly should have kept more control over pricing. "There's an obligation on their part, having transferred this, to ensure that the objective of the philanthropic initiative continues to be met," he said.

Lilly said that to comply with antitrust rules it retained no control over pricing once it transferred the rights to the Chao Center and had no say when Chao transferred the rights to Rodelis.

Source: NYT, http://nyti.ms/1QWG6PE (22.09.2015)

Reportage

1. Drug-Resistant Tuberculosis Is a Global Crisis. Why Are We Doing So Little to Fight It?

Here in the waiting room of Helen Joseph Hospital, a cough never sounds like just a cough. It's more like the audio accompaniment for a glimpse at what may be the most sustained medical catastrophe of our time. A throng of new patients are spectral figures, the latest victims of what public-health officials dub a "co-epidemic" of tuberculosis and HIV. The patients' off-white masks flutter whenever they break into that distinctive guttural bark, followed by a raspy rattle in the throat. Linger long enough in this room and you'll hear prayers offered: "Please, Jesus, let this be a case of *ordinary*

tuberculosis." Rising numbers of patients are infected with strains of *Mycobacterium tuberculosis* resistant to commonly used medications. Treatment, then, will be longer, more punishing, and less effective.

Although largely unnoticed by the public in the United States and Western Europe, where TB and HIV are relatively well-controlled, the co-epidemic rages on across great swaths of Asia, Eastern Europe, Latin America, and Africa. In 2013 alone, these twin scourges took the lives of an estimated 2.6 million people, who died of one infection, or the other, or both.

Nine million people contracted TB in 2013 (1.1 million of them also HIV-positive), and nearly half a million new infections that year involved drug-resistant strains, according to the World Health Organization. The ongoing, uncontrolled spread of multidrug-resistant tuberculosis (MDR TB) also threatens to upend the public-health systems in South Africa and 21 other counties.

Against this grim backdrop, there's a $1.7 billion shortfall worldwide in funds needed for the prevention, diagnosis, and treatment of TB. Investment in research on vaccines and new treatments remains at paltry levels. The scale of suffering and dying is alarming enough, but public-health advocates worry about the potential for wider consequences, since one in three of us hosts a latent, or inactive, form of tuberculosis, and 37 million are HIV-positive.

"You know, Ebola is only a plane ride away," one of the doctors at the hospital told me shortly after I arrived for a visit on a cool autumn morning. "Like Ebola, untreatable TB is only a plane ride away, too. So I'm quite surprised by the apparent lack of a sense of urgency about this everywhere but here."

In a corridor that links the hospital's HIV clinic to its TB treatment center, I met a patient who has been fighting both illnesses for the past six years. "This sickness has been *hunting* me," Babsy Raphoto told me. "TB, you know, it eats your strength." She's a 45-year-old black woman with a pleasant, oval-shaped face, dressed in a bright pink-and-blue blouse. "And there's been so many TBs!" Raphoto exclaimed. "I've had it three times so far."

Investment in research on vaccines and new treatments remains at paltry levels.

The hospital itself is a sprawling public-health facility perched on the edge of South Africa's largest city and named for an icon in the struggle against apartheid. TB infection control had a history of struggle, too. That history included mass dormitory-style housing for mine workers, high rates of incarceration, and scant healthcare for the black majority. Those conditions fueled elevated rates of infection for generations. When the postapartheid government fumbled its early response to a burgeoning HIV epidemic, tuberculosis also boomed.

"I used to think: 'What have I done wrong?'" Raphoto confided, and I knew from talking to other patients that it was common for those who'd contracted these diseases to blame themselves. The short answer to her question is that it was merely geography and chance—having had the bad luck to come of age amid the intersection and burgeoning spread of two infectious diseases.

Raphoto's first two bouts with TB were extrapulmonary cases: the first time an attack on her stomach, the second on her lymphatic system (tuberculosis often strikes in organs besides the lungs). Then, in a stunning double whammy, she tested positive for HIV, which was how she discovered that her longtime partner (now an ex-boyfriend) had other romantic attachments. "When I got sick, he didn't want me," she said.

Between illnesses, Raphoto always returned to work—she had a teenage daughter to raise, school fees to pay, and unfulfilled ambitions of her own. After apartheid fell, she'd seized the new opportunities suddenly open to blacks, working for a prominent media company and then landing a job as assistant to the CEO of the country's largest bank. As with millions of her contemporaries, however, the drive for political liberation and economic advancement was blunted by the need to engage in a different kind of struggle—the fight for freedom from disease.

At the end of 2011, tuberculosis "gave me a break!" Raphoto said, speaking of the disease as if it had a mind of its own. Two years later, with her life and career finally back on track, she contracted TB again. This time, she was infected with a more pernicious strain, one resistant to the two drugs most commonly used against it.

The treatment for multidrug-resistant TB proved orders of magnitude more difficult. Her doctor estimates that patients who complete the two-year course of treatment have to swallow up to 14,600 pills and endure daily intramuscular injections for six months. “Aw, if you could only know that pain!” Raphoto said. “Every day you touched your bum and asked yourself, ‘Where is there even a little spot left to be injected?’”

The pain from injectable medications helps explain the high dropout rate worldwide from treatment for MDR TB. So do the severe side effects, including high levels of psychotic reaction and loss of hearing.

Raphoto credited three people with her survival through this travail: her daughter and her sister, both of whom ferried her back and forth to the hospital for years, and her doctor. “I am alive today because of Dr. Berhanu,” she told me. On this fall morning, she had arrived early for her appointment to learn whether she’d been cured once again, this time of MDR TB.

When I visited the clinic last May, the doctor in charge was gathering data for a report on how her patients had fared. Dr. Rebecca Berhanu is a 36-year-old internist who manages research and treatment at TB Focal Point, an innovative collaboration with the Health Ministry managed by the NGO Right to Care and funded by the US government. “It’s patients like Babsy who keep me going,” Berhanu said. Then we were interrupted by a phone call; Berhanu took down a batch of statistics and looked pretty grim as she set down the phone. “The data is just so bad—*really* disappointing,” the doctor said.

The latest survey revealed that only 40 percent of patients treated for drug-resistant tuberculosis at TB Focal Point had completed a full course of the treatment. This made survivors a distinct minority, in spite of the intensive effort mounted by nurses, counselors, and doctors. About one in four patients—26 percent—had died during the course of treatment, and another 30 percent were “lost to follow-up,” which meant nobody in the clinic knew what happened to them. This is how drug-resistant strains of infection spread across the country, and also across borders.

The results were doubly disappointing because South African health officials had responded to the crisis with a high sense of urgency, unlike their counterparts in Russia and India, for example. “South Africa is actually moving faster than anybody else,” Berhanu pointed out. She thought the health minister, Dr. Aaron Motsoaledi, had demonstrated visionary leadership by embracing the diagnostic tool known as GeneXpert, which allows for speedier and more accurate diagnosis, and moving toward a system of decentralized care, which had worked in places like Peru. The national government pledged to end the co-epidemic altogether by 2035.

These ambitions butted up against sobering realities. In 2015, the waiting room here, like those of so many clinics and hospitals around the country, was filled with patients complaining of psychotic breaks, balance disorders, and deafness from medications being used in the scaled-up campaign against TB.

Continued use of these drugs has placed doctors in a precarious position with their own patients. “We have to tell them, ‘OK, you might go deaf and the odds are it won’t work, but otherwise you’re certain to die of TB.’ So which would you choose?” Berhanu said, raising her eyes to the ceiling. Then, looking at me dead on, as if I were one of her patients: “Well, would *you* rather go deaf—or die?”

A relatively new drug called bedaquiline was approved by South African authorities for “compassionate use” in cases where patients suffer severe side effects under the old regimen. For doctors in the clinic, however, bedaquiline’s regulatory approval was mainly an advance in theory, since few doses actually arrived. “It’s so discouraging and so frustrating—we need to move a lot faster in getting new drugs to these patients,” Berhanu said.

Her very next patient exemplified the point. Frans Ndou, a construction worker, was a slight man of medium height who’d been diagnosed with MDR TB six months earlier. Placed on the standard treatment that Raphoto had already described to me, he’d swiftly suffered debilitating side effects, including excruciating pains in his legs and feet, a psychotic break, and deafness. “My ears used to work, but because of the medicine—which they said would cure me—these ears won’t work. While you are talking, I have to follow your lips to see what you’re saying,” he told me. The doctor stopped

the injections and applied right away for the new drug. For half a year, both patient and doctor were left hanging. Berhanu was anxious to get her hands on the new treatment, because a few weeks later she was scheduled to begin a one-year leave after receiving a fellowship in infectious disease at the University of North Carolina. The experience had left her patient suspicious of the entire enterprise of modern medicine: Why couldn't they cure the disease in a way that would prevent it from coming back? "I don't want to admit it, but I might run away," he said when the doctor left the room. (He was later placed on bedaquiline and reported marked improvement.)

Berhanu was born in ethiopia and went to colleges and medical school in the United States, so she's no stranger to the global class divide in medicine. Still, she found it infuriating that it would be so hard to get her hands on a few new drugs easily available to her colleagues in the United States, Western Europe, Japan, and South Korea. In cities like Chicago, where I live, the drug is stocked but rarely used because there are so few cases of MDR TB. There were only 96 such cases nationwide in 2013, compared to more than 14,000 in South Africa the same year (and 6,242 cases of extremely drug-resistant tuberculosis, or XDR TB, from 2004 to 2012).

"It's the haves and the have-nots, right there!" Berhanu said. It also seemed unconscionable that doctors had to rely on archaic treatments in the first place: The two most commonly used drugs in first-line treatment were developed in the 1950s. Few new medications have been developed for a disease that afflicts tens of millions.

Part of the reason, she thought, had to do with the fact that nearly all the suffering and dying occurs in poor and middle-income countries. This means prices on newly introduced drugs are likely to be negotiated downward, as they had been in the case of HIV drugs. Besides, there's a much higher profit margin for drugs that treat chronic conditions.

"So the problem with producing new treatments for tuberculosis…?" I started to ask. "Is that it's curable," Berhanu replied before I could finish. "Nobody's interested in treating a curable disease anymore. If you're developing new drugs, you want to produce something for a chronic condition that everybody has in richer countries, like antidepressants for seasonal-affect disorder or remedies for insomnia." In richer markets, it's easier to charge a premium.

Global inequality reveals itself in other ways. In cities like Chicago, patients diagnosed with MDR TB are hospitalized or placed in isolation at home for at least two weeks, away from children and immune-compromised adults, like those infected with HIV. Patients are assigned social workers and nurses who visit their homes, offer support, and give injections. In June, a traveler from India who flew to Chicago and was subsequently diagnosed with XDR TB was airlifted to an isolation ward in a facility operated by the National Institutes of Health and treated at a reported cost of $480,000.

In South Africa, where there are only 2,500 beds set aside for those with drug-resistant diseases, patients are often sent home with well-meaning advice tailored more to a person in Chicago than to someone in Johannesburg. "Our advice, like the medical advice anywhere, is to sleep with open windows in separate rooms," Berhanu said. "But people are living four, five, and six in one-room shacks!" Exposure to adults at their most infectious is one of the reasons so many children are dying of TB undiagnosed, untreated, and unreported.

Many of Berhanu's patients had little money for food or transport and walked long distances to and from the hospital in excruciating pain. For the first time, there was a hint of despair in the doctor's voice. "You always think, you know, 'What if it was me?'" she said.

The doctor wondered what it would take for drug manufacturers, policy-makers, and the public to register the scale of this disaster. In the middle of the 19th century, tuberculosis caused a third of all deaths in the industrialized world. Would the rest of the world wake up only if the contagion spread? From her vantage point at the heart of contagion, Berhanu thought there was still a whisper of a chance to contain it, but only if more effective, shorter-term, and less painful treatments arrived soon.

In its annual report last year, the World Health Organization (WHO) noted signal achievements: an estimated 37 million lives saved since 2000 through improved access to diagnosis and treatment for TB and declining mortality rates. These advances demonstrated that a more concerted campaign

might make more of a difference. The biggest obstacles are failure of the imagination and will on the part of national governments, including those of middle-income, high-burden countries like Brazil, Russia, India, and China. An annual budget of $8 billion was needed for detection, diagnosis, and treatment, but only $6.3 billion had been raised. Another $2 billion was desperately needed for research and development on new drugs and treatment regimens.

While the prevalence rate (the proportion of the world's population with active TB infection) fell, the world population had also grown. So, after a long incremental decline, the numbers of people affected by the co-epidemic seemed to have crept back up in recent years: More people died of TB and HIV in 2013 than in 2012. (WHO releases its latest survey, covering 2014, early in October.)

"They love to talk about all the supposed good news," Mark Harrington told me in mid-September. He's the hyperkinetic executive director of Treatment Action Group (TAG), the New York–based organization that successfully pressed for greater investment in AIDS research, speedier testing of new medications, and a more patient-centric approach to new treatments during the early years of the HIV epidemic. Now, it struck him, dozens of drugs are available for treating HIV, but only a paltry few are ready to be deployed against tuberculosis.

In 2002, when the Global Fund to Fight AIDS, Tuberculosis and Malaria was formed with seed money from the Bill and Melinda Gates Foundation (which also supported TAG), promising new research was launched into TB vaccines and cures. Then a major vaccine trial failed, and pharmaceutical conglomerates abandoned the field. "What we thought was a renaissance turned into a spark of light before a return to the dark ages," Harrington said. "It's been a massive failure of political will and a failure of science." (And a significant failure of journalism, too, because the scope of the suffering and the political implications of the burden on developing countries hasn't received adequate coverage.)

One under-celebrated bright spot was the creation of a nonprofit drug-development organization called TB Alliance. Formed in 2000, it became a key player in research on combination therapies that mix old and new drugs in novel ways. The alliance headed three out of six major studies under way on new drugs for the treatment of TB. It's also a pioneer in clinical trials on combinations of old, repurposed, and new drugs to develop better standards of care for TB patients, including Nix-TB, a trial to test the efficacy of bedaquiline and two other drugs in treating patients with XDR TB.

Dr. Mel Spigelman, CEO of the TB Alliance, emphasized the need for "a truly short-course, simple, affordable, and well-tolerated universal-treatment regimen." Derek Ambrosino, spokesman for the alliance, said it was the "realities of patients' experiences" that led to research on drug regimens that could be taken orally.

Back at helen joseph hospital, babsy raphoto arrived early for her appointment to review her most recent laboratory results. Finally, some good news: In the latest sample of her sputum and X-ray, there was no sign of TB infection. "Today, I'm healed!" Raphoto declared. "I'm proud to say TB can be cured!"

When the doctor reminded her that she could take off her mask in the examining room, the patient froze. The mask, it seemed, had become part of her identity. Untying it slowly, she drew the mask down into her lap. The transformation was stunning: Masked, she'd looked drawn and fidgety, her eyes narrow and darting. Now, unlike the frail new patients down the hallway, she unveiled wonderfully clear skin stretched over full cheeks. "Overall, it's six years of being sick with TB," Raphoto said. "That's why, back home, they are saying I'm the strongest woman ever!"

As she rose to leave the examining room and fetch her sister, she listed to one side because of a balance disorder from the drugs. She worried that her halting walk made her look like a drunk. Raphoto felt so eager now to do normal things again—leave the house, go into town, shop in a mall, and work. So she tried to imagine her body completely freed from her long bondage to disease. Her African name is Busisiwe, which means "lucky girl" in Zulu. "I am alive!" she announced, like a broadcaster delivering breaking news. She repeated herself even more forcefully: "Can you believe it? I am alive!"

Source: The Nation, http://bit.ly/1WwmtB8 (30.09.2015)

2. The Gendered Delay in the Diagnosis and Treatment of Tuberculosis Patients in India

On 25 June 2015, Sulabha Kadam, a health worker in Mumbai who works with the Navnirman Samaj Vikas Kendra (NSVK) —a non-governmental organisation that works with the state government to provide access to medical treatment in slums—hiked up a hillock to the house of a 35-year-old woman who was suspected of having tuberculosis. She was told that no one in the house was sick. Twenty days later, when Kadam stopped by the house as part of a regular follow-up, she found the woman lying on a cot unable to move. Kadam had the woman's sputum checked. She tested positive for tuberculosis.

"It is only after these women are so sick that they decide to do something about it. I do not understand how her husband, who works as a rickshaw driver, could ignore her condition for so long. Only when she could not move at all did he take interest. This woman possibly had TB for months before she was diagnosed," said Kadam. Kadam works as a Directly Observed Treatment (DOTS) provider for anti-tuberculosis medicines at NSVK and regularly goes into the community to ask people if someone in a family has a persistent cough, fever, or other symptoms related to the disease. These cases are then referred to a government hospital or laboratory.

The 35-year old, who weighed just 35 kilograms at the time of diagnosis, said she had been having bouts of vomiting for a long time and that the private doctors she consulted had told her that there was "nothing wrong" with her. Only after taking anti-tuberculosis medicines for about 10 days was she able to get out of the bed, and even bathe herself. During this time, the responsibility of taking care of the household chores and of her four other daughters fell on her 12-year-old daughter.

According to the 2014 World Health Organisation (WHO) Global Tuberculosis Report, India has the highest burden of tuberculosis with an estimated 2.16 million cases out of a global incidence of 9 million. Despite its prevalence, the stigma surrounding tuberculosis is such that patients often delay or deny themselves treatment even after diagnosis, rather than admit the cause of their ailment. Experts, in several studies, attribute this to a lack of knowledge regarding the disease's transmission and its infectious nature. These studies further claim that a part of this stigma is also due to the association of tuberculosis with poverty: although the disease trickles across all classes of society, the poor are at greatest risk, both because they are in greater contact with other sufferers (due to factors such as overcrowding at home, at work, during commutes and socialising), and due to their weakened immune system resulting from poor nutrition.

The stigma of tuberculosis dates back to the early nineteenth century, with the emergence of colloquial names such as "white plague", with reference to the pallor common among tuberculosis patients, and "consumption", reflecting the atrophy of an infected body. This engendered fear of the disease and those with it, according to a 2011 Lancet paper exploring the stigma of tuberculosis the world over. "When people are stigmatised for having a particular disease there is usually an implicit assumption that they have brought it upon themselves and this helps justify the stigmatisation. So, it becomes a socially constructed, self-fulfilling process," said Anna Waldstein, medical anthropologist from the University of Kent, UK, who is quoted in the Lancet paper. Of this stigma, women are the worst affected. Health workers in Mumbai and Delhi say that, when confronted with the diagnosis of tuberculosis, many women ignore it.

The stigma around the disease is so strong that women detected with or suspected of having tuberculosis have been abandoned, or even ostracised. As of 2007, over one lakh women suffering from tuberculosis in India were being abandoned by their families every year. Of the women I met, many were sent to their relatives or parents' house to recover. Marriages or engagements were called off due to the disease, and sometimes these women were even denied access to their children.

Women face severe consequences of the one-sided conversation surrounding tubercolosis, even while undergoing treatment. This can be seen in a 2004 study on the impact of gender in a rural Pune district which showed that many women living in joint families suffered more than women living in nuclear families. Of the nine women living in joint families, eight were driven out by their in-laws and

were taking treatment in their parents' home. Some families even insisted on a medical certificate stating that the women were cured before allowing them back into the marital homes. The unmarried women were sent to their relatives' homes in distant places for treatment to prevent the possibility of neighbours or potential suitors coming to know of their illness.

In July, I spoke to a 25-year old woman whose husband had abandoned her seven months ago. Sitting at a DOTS centre at Tekhand village, Delhi, she told me that her life unravelled after she started getting sick with tuberculosis. Before she was detected with the disease last year, she was coughing incessantly and had high fever for about four months. She was unable to move by that point. "My husband's behaviour changed drastically after I got sick. He was upset that I wouldn't work, and would complain constantly about it." Her husband, to whom she had been married for eight years, sent her and their two children to her mother's home.

A woman from Ratnagiri district in Maharashtra also faced similar consequences. The 27-year old fell sick almost immediately after her marriage in May 2014, with constant bouts of fever and cough. However, her husband's family chose to ignore it. Her in-laws were more worried that she was not menstruating, and remarked that she might not be able to bear them a child. After nearly a year of being ill, in February this year, her mother forcibly took her to Nallasopara, a town outside Mumbai—where her brother lived—for treatment. She had shrunk to 28 kilograms by then. "When I was taken to a hospital, the doctor said that there was no guarantee I would survive. I had no blood in [sic] veins of my hand, and they had to draw blood from the veins of my neck. I was on the verge of death and was saved," she explained. When we met in August, she was receiving treatment at the Nallasopara DOTS centre run by the Maharashtra Janvikas Kendra (MJK). MJK works with the local civic authorities in case detection and treatment programmes for tuberculosis patients in Mumbai and townships close to the city. Her husband visited her in Mumbai to serve her divorce papers a few months after she began her treatment, accusing her having the disease in the past. "I am not returning till I get better. Let's see if they take me back. They keep telling me I must have had the disease in the past, and I didn't tell them," she said, shaking her head in disbelief at her situation.

In the case of the 35-year-old patient in Kandivali, the people in her neighbourhood were speculating about her disease immediately after the health workers visited her house. As the health workers stepped out, the 35-year-old patient's neighbour asked them if she had tuberculosis. A little further down, a woman asked the health workers if "there was somebody suffering from HIV in the house." Many researchers who studied the effects of stigma on tuberculosis attribute it to the disease's links with HIV, since co-infection between the two is common. An unwritten rule, which public health officials insist on, is that journalists should not reveal the identity of tuberculosis patients, precisely because of the nature of this disease.

"The information about tuberculosis is just not accessible for people, especially for women." Blessina Kumar, the chair of Global Coalition of TB Activists told me over the phone. Despite being fully curable, the myth persists that it is a death sentence. Once administered medication, a patient ceases to be infectious in two months. "Women depend on their husbands, sons, or fathers to take them to a health centre. Not knowing where to go and what they can do if they are sick only adds to the fear and leads to further stigmatisation," she said.

For instance, after suffering wracking coughs for more than three months, and having received no help for treatment from her husband or in-laws, a 24-year old woman from Lanjari village in Jalna district, Maharashtra, came to Mumbai on the pretext of meeting her sister. She finally got herself checked at a hospital and discovered that she had tuberculosis.

When I met her, she weighed barely 38 kilograms. "It was the season of wheat chaffing, and I just couldn't get out of work," she said. One private doctor who was unable to diagnose her recommended that she get an X-ray taken, but no one in her family supported her. She has two children, including a two-year-old boy. The woman added that her mother-in-law accused her of being "weak" and not used to working hard.

Having found several odd-jobs to supplement her income while taking her daily DOTS treatment from NSVK's Kandivali centre in Mumbai, she is adamant about completing her treatment, "I will go back

only after I get better. Now my husband knows I am more able, he is telling me to come back and work on the farm."

While both men and women tend to delay diagnosis to some extent, public health experts say that women tend to delay diagnosis and treatment more. Most health workers I met in Delhi and Mumbai say that women display a "higher tolerance" and ignore their symptoms while juggling multiple responsibilities—cooking, cleaning, feeding children, taking them to school, and working—all at the same time. Some women do not have the resources to go to a clinic for treatment, and some are even discouraged from going to clinics alone. Additionally, a lot of time is wasted in going to private practitioners, who are not always equipped to look for tuberculosis. A 2012 Public Library of Science study would seem to corroborate this—of the 108 people sampled, women, on an average, sought care after 6.3 months of exhibiting symptoms, compared to the 3.8 months that men took.

Unfortunately, the lack of many large-scale studies on the issue of gender and tuberculosis in India also affects the visibility of the disease. "I am not sure there is a special reason for the lack the studies on the issue of gender and TB. Just like [sic] there haven't been many studies on childhood TB," said Kumar.

Dr Yatin Dholakia, honorary secretary of the Maharashtra State *Anti*-TB Association said, "I also think that the fact that there are not big studies on this issue is a gender issue in itself." Part of this, according to the 2014 WHO multi-study, might be attributed to the recent and gradual shift in studies on tuberculosis from the context of poverty to questions of stigma and gender.

Between April and July last year, the Foundation of Medical Research (FMR)—a Mumbai-based research organisation that conducts research on tuberculosis and other diseases—conducted a study with 76 people. The study seems to indicate that women tended to delay their treatment more than men.

The research tracked health-seeking behaviour in three stages: from the onset of symptoms to visits to the first provider (any doctor, chemist, or non-allopathic doctor), then to the diagnosis of tuberculosis, and finally, treatment. Since the onset of their symptoms, two women, who were detected with multi-drug resistant tuberculosis (MDR-TB), had delayed their treatment for about 2 years and around 8 months respectively. MDR-TB is a strain of tuberculosis that is resistant to first-line tuberculosis drugs. The connotations of being diagnosed with tuberculosis also become a deterrent when it comes to the diagnosis. Dr MS Jawahar, a retired scientist from National Institute of Tuberculosis Research, Chennai said, "Stigma is a huge issue and we have to keep their confidentiality. But, confidentiality has its implications." He went on to explain that even the presence of a tuberculosis van—used for collecting samples or by advocacy programmes—could not be seen standing near the house of a suspected patient.

Even the collection of a sputum sample is stigmatised. A WHO multi-site study states that there seems to be a deep cultural issue in coughing and spitting to produce sputum for testing. "Women do not want to give their sputum samples. They say that they do not want to spit in front of others. We have to leave the bottles with them so that they give us the sample later. Sometimes even after referring them, it can take up to two months for them to get themselves tested," said Dhanashree Jadhav, a supervisor from NSVK.

Many women also hide the fact that they had tuberculosis in their childhood, making medical histories unreliable and adversely affecting diagnosis in the event of a relapse. "This is true especially when the husband is accompanying the patient. Tuberculosis is still a social stigma and is often not revealed to a partner and his family," said Dr Vishak Acharya, Professor of Pulmonary Medicine based in Mangalore, Karnataka. He added that a past infection or relapse could mean a higher possibility of the patient developing drug-resistant tuberculosis.

Some guidelines in the National Programme also make it difficult for a woman to start treatment soon. For instance, the district tuberculosis officers in some parts of the country insist on verifying addresses before they dispense medicines. "Single, young women do not want everyone to know they have tuberculosis, especially their landlords," said Kumar. The tendency to give fake or

unverifiable addresses is a common one, becoming a further deterrent to treatment. Once the women seek treatment, their compliance levels are higher than men, said Dr Jawahar.

That the stigma associated with tuberculosis is disproportionately distributed on the grounds of gender can be seen by the treatment meted out to women in recovery. In fact, a visit to the women's ward in Sewri TB Hospital at Mumbai during visiting hours made this discrepancy apparent to me. The men's ward was filled with women and other relatives plying them with food brought from home. The women's ward was starkly empty with almost no visitors. "My husband comes to see me once in 15 days," said a 30-year old woman who could barely talk because of the damage done to her vocal cords by the disease. The narrated accounts of social responses seemed to suggest that women were obliged to support their husbands with the disease, but the men did not have the same duty towards their wives.

Stigma, social discrimination, and family rejection contributed substantially to emotional and psychosocial distress from tuberculosis for women, states a 2006 paper by the WHO on the impact of gender and tuberculosis in four countries, including India. The study showed that around one-third of the women at the Chennai site reported psychosocial and emotional distress among the results of their tuberculosis. A few women who participated in the study said that they had thoughts of suicide, while some indicated that their husbands or in-laws had explicitly told them to commit suicide. The paper goes on to recommend that the health services and DOTS programmes should develop capacities to evaluate the psychosocial, emotional and social aspects of tuberculosis and provide locally relevant gender-sensitive support.

Many NGOs such as NSVK, Lok Seva Sangam are incorporating counselling for families in their programmes to reduce the impact of gender discrimination on women. For instance, the patient from Lok Seva Sangam, is now on better terms with her family after health workers counselled them on the disease.

Operation Asha—an NGO that works in India and Cambodia to bridge the gap between government medicine distribution centres and affected communities—has a protocol to deal with female patients that involves asking families to keep an eye out for obvious signs of depression, for which they could be referred to a hospital or health clinic. Explaining the process for handling tuberculosis in women, the founder and president of Operation Asha, Dr Shelly Batra said, "When a lady is detected with TB, we counsel the families. The message is that TB is curable and not a curse from the Gods. We tell them the basic facts that during the infective period of one or two months, the family has to take basic precautions of covering mouth, maintaining distance and disposing the sputum. Then, once the sputum is negative for TB, there is nothing to fear."

However, in India, there is no targeted programme to address the difficulty of diagnosing tuberculosis among women. "The information, education and communication material related to TB could include more female-centric material," said Dr Ramya Ananthakrishnan, executive director, Resource Group for Education and Advocacy for Community Health (REACH), a Chennai-based advocacy group that works with various stakeholders in the programme, including the media. One such instance of female-centric material was literature released by the WHO informing women with tuberculosis that they could breastfeed their children. She also suggested that other measures, such as involving a female celebrity in public broadcasts about the disease, would help reduce stigma of the disease.

The WHO multi-site study recommends that such a programme could recognise the gender-specific barrier against spitting, while clinics could ensure privacy and a well-ventilated space for patients to produce sputum,. The WHO study also states that it is important to recognise the importance of counselling at every stage of disease, including diagnosis, and emphasising the effectiveness of the treatment to reduce the stigma attached to the disease.

The Revised National Tuberculosis Control Programme (RNTCP) works on the system of passive case finding, a cost effective method, in which it awaits the initiative of a sick person to visit a government health centre. While the DOTS centres are not very far off in cities, in the rural areas, as recorded by this study, a patient might have to travel 15 kilometres or more. Making the centres more accessible

or having more DOTS providers in the community would also help bring more women in the programme.
"If more opportunities are created for screening, the ratio could tilt a little more towards women. Screening more women will reduce the spread of the disease in the family, especially children," said Dr Kuldeep Sachdeva, additional director general of the Central TB Division, which is responsible for rolling out the RNTCP. Until then, however, tuberculosis continues to be a national pandemic, especially for the women of India.
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