Inhalt

Internationale Nachrichten

1. Can the BRICS bank rally global outcasts around TB treatment?

Some of global development's emerging players could fill a void in aid to the world's most isolated countries — and their citizens who desperately crave basic services.

For instance, Russia and North Korea's foreign policy decisions have alienated them from many of the world's largest aid donors. But new actors are emerging, and some experts speculate that the recently launched BRICS development bank — officially called "New Development Bank" — could take on some of the health and development challenges facing those countries like tuberculosis.

While the BRICS comprise three of the five most TB-affected countries — India, China and Russia — other countries who share the bank's status outside of the conventional aid inner circle are sending distress signals. As common interests emerge, TB seems premiere among them.

The BRICS bank, officially created at the sixth BRICS summit in July, was founded by five emerging economies — Brazil, Russia, India, China and South Africa — as an alternative to the Western-led World Bank and to focus on financing areas of mutual interest. Tuberculosis could be one of those areas, according to Gail Cassell, senior scientist for global health equity at Harvard Medical School, formerly the Institute of Medicine, who called the Delhi Communique issued last year by BRICS health ministers "a watershed for TB control."

"What they acknowledged was that [multidrug-resistant] TB is a major problem," she told Devex in a later interview. "And they said that they are going to work together to solve it. It's pretty huge to admit it publicly, but also for them to establish a framework for collaboration." The health ministers outlined a cross-sector plan for addressing the disease that includes improving infrastructure, developing a diagnostics platform and collaboration on drug trials. "That the [BRICS] bank was established only months after that suggests that they will definitely have a hand in what happens next," Cassell said, seeming to suggest that early investments of the institution's $50 billion capital might contribute to anti-TB projects in the bank's hardest-hit shareholders.

The battle against TB in North Korea — a beneficiary of loans and aid from China, the largest BRICS shareholder — is shrouded in even greater secrecy. Estimates suggest around 345 out of every 100,000 citizens in the pariah state are infected with tuberculosis, but Eugene Bell, one of only a handful of U.S. NGOs working with MDR-TB patients in the country, claims that figure is vastly understated. Given North Korea's hesitation to cooperate with the United States, the fact that the country has reached out on tuberculosis hints at the scale of the epidemic, demonstrated by a delegation of North Korean Ministry of Health officials in 2010 to Stanford University, where they sought information about new drugs, noted Anne Claiborne, a senior program officer at the Institute of Medicine. The urgency is also clear in an international communique issued by the North Korean ministry which stated that MDR-TB "is the number one, two and three biggest health emergency" in the country.

As multidrug-resistant tuberculosis evolves, the science behind a cure must evolve faster. Unfortunately, the drug pipeline for MDR-TB contains only a few contenders, without a single drug in

phase 1, the earliest phase of testing. Cassell told health professionals the need for new drugs will likely overwhelm the already underfunded research community. In the meantime, a new opportunity for collaboration waits on the horizon in another unlikely locale: Iran. Iranian officials there are organizing a TB conference in March 2015, Cassell told Devex, and Tehran is offering to fly in health experts willing to offer their knowledge about MDR-TB. According to WHO data, Iran has seen an increase in tuberculosis since 2010, around 21 per 100,000, accompanied by a startling decrease in the number of patients undergoing treatment.
Source: Devex, https://www.devex.com/news/can-the-brics-bank-rally-global-outcasts-around-tb-treatment-84733 (10.11.2014)

Forschung & Entwicklung

1. PI-Based HIV Regimen Succeeds; Short TB Treatment Fails
An investigational single-pill regimen for HIV -- the first to be based on a protease inhibitor -- was less toxic than a similar regimen using separate drugs, researchers said. But a trial of shorter treatment for tuberculosis was disappointing, other investigators reported at the recent Interscience Conference on Antimicrobial Agents and Chemotherapy in Washington, D.C.
The two illnesses are tightly linked -- in many places, TB is a leading cause of death among people with HIV. New therapies for TB have been difficult to find, but the situation is much different in HIV, where many new drugs and drug combinations have become available in recent years.
Meanwhile, approaches to TB therapy that promised to shorten treatment by a third have failed to make the grade, researchers reported. In a randomized double-blind trial, 4-month regimens based on the fluoroquinolone antibiotic moxifloxacin (Avelox) could not be shown to be better than or even equivalent to a standard 6-month TB regimen, according to Stephen Gillespie, MD, DSc, of the University of St. Andrews Medical School in St. Andrews, Scotland. The bottom line is that the moxifloxacin regimens can't be recommended to replace standard 6-month regimens, Gillespie reported at the DC conference. The results of the trial were published simultaneously online in the New England Journal of Medicine. Shorter TB regimens are needed in order to reduce costs, cut adverse effects, and improve treatment adherence, the researchers noted.
Preclinical and some early human data had suggested that substituting moxifloxacin for either isoniazid or ethambutol in a standard regimen would cure drug-sensitive TB more quickly, Gillespie and colleagues noted. The suggestion was that the fluoroquinolone would kill TB bacteria more quickly, leading to a faster cure, Gillespie told MedPage Today. The REMoxTB (Rapid Evaluation of Moxifloxacin in Tuberculosis) trial actually "confirmed what we thought in the beginning," Gillespie said -- that moxifloxacin is more bactericidal than either of the other drugs. "It just isn't bactericidal enough to shorten treatment from 6 months to 4 months," he said.
While the study was negative, it gave a clear answer, Gillespie said, adding that subsequent trials, now under way, may come closer to finding an acceptable short TB regimen. "We didn't make the grade," he said, but "I expect we'll get to a treatment-shortening regimen quite soon."
Source: MedPage Today, http://www.medpagetoday.com/InfectiousDisease/HIVAIDS/48671 (19.11.2014)

2. How much is tuberculosis screening worth? Estimating the value of active case finding for tuberculosis in South Africa, China, and India
Recent World Health Organization (WHO) guidelines recom- mend, for the first time, routine TB screening of certain high-risk groups (e.g., people living with HIV), and active TB case finding is increasingly becoming part of an essential package of TB prevention and care. However, with limited resources available to improve health world- wide, it is critical to implement those interventions likely to provide greatest impact and value for money.

Although passive (symptom-driven) diagnosis and treatment of sputum smear-positive TB is among the most cost-effective health interventions available, most economic evaluations of TB interventions have not, to date, included active TB case finding. As such, the potential impact and cost-effectiveness of active case finding (ACF) remains largely unknown.
Here, we use combined transmission- economic models of TB epidemics in China, India, and South Africa to estimate the most likely medium-term epidemiologic impact and cost-effective- ness of feasible case-finding approaches. By modeling generic interventions, we create a tool for converting data that are easily estimable by people considering specific case-finding programs (i.e., program costs and number of additional TB cases detected from ACF campaigns using a specific approach) into data that are important for decision making (i.e., cost per disability adjusted life year (DALY) averted). We use these results to provide guidance as to how much donors and in- country TB control programs should be willing to pay to find one additional case of active TB.
In summary, our results suggest that ACF for TB, both short-term and sustained, may have important impact and are likely to be highly cost-effective within 10 years, even for campaigns costing $1,000 or more per case detected and linked to care. Since most gains in incidence are real- ized in subsequent years, evaluations over a shorter time span may grossly underestimate the full benefits of ACF. Both longer-term follow-up of existing campaigns and rapid evaluations of highly intensive interventions are needed to fully assess the potential of active TB case find- ing to avert TB incidence and mortality. In the interim, our "best available evidence" estimates suggest that, if we are to undertake a serious effort to meet TB control tar- gets by 2035, active TB case finding deserves a prominent place on the global health agenda.
Source: BMC Medicine, http://www.biomedcentral.com/1741-7015/12/216 (27.11.2014)

3. Using a diabetes drug to treat TB shows promise
Thanks to metformin, a drug that is commonly prescribed for type 2 diabetes patients, treating TB — both the drug-sensitive and drug-resistant types — may become far more effective if clinical trials in humans produce the same results as laboratory and animal studies.
According to a study published today (November 20) in the journal *Science Translational Medicine,* metformin was found to "inhibit intracellular growth of TB bacteria, restrict disease immunopathology and enhance the efficacy of anti-TB drugs." "These data suggest that metformin could be used as an adjuvant therapy to treat TB infection," says the note from the journal Editor. Besides the higher effectiveness, the biggest advantage is that metformin offers little chance for the TB bacilli to develop resistance against the drug. The reason: unlike the age-old practice of developing new drugs that directly target the TB bacteria, the focus now is to choose drugs that are already being used in humans and investigate their ability to ramp up the body's responses to the pathogen's ravaging attack in several ways. Besides the ease with which the pathogen can be eradicated and the disease cured, the novel route has other advantages. As the drug does not directly target the TB bacteria, the chances of the bacteria developing drug resistance are slim. Currently, drug resistance is one of the biggest problems in TB treatment. Since the drugs being investigated are already in use by humans, there is less likelihood of them being dumped on safety grounds when used for treating TB. Of the 13 drugs tested using human monocytic cell lines, the team of researchers led by Amit Singhal of the Singapore Immunology Network Agency for Science, Technology and Research, Singapore, chose metformin for detailed studies. They found that the diabetes drug was capable of inhibiting the growth of intracellular BCG within one day and also "restricted" the replication of multi-drug resistant TB strains (MDR-TB). The growth inhibition of TB bacteria was achieved by prompting the body's innate immune response to produce reactive oxygen species. If TB bacteria have an inherent mechanism of suppressing the synthesis of reactive oxygen species, the drug not only overcame this but also enhanced ROS production. This turned out to be the critical factor by which the drug was able to control the intracellular growth of the bacteria.
Source: The Hindu, http://www.thehindu.com/sci-tech/health/using-a-diabetes-drug-to-treat-tb-shows-promise/article6615238.ece (27.11.2014)

4. Unlikely Marriage Of Diseases: TB And Diabetes Form A 'Co-Epidemic'

The world is facing a double-barreled pandemic reminiscent of the dual epidemic of tuberculosis and HIV that emerged in the 1980s – only potentially much bigger. It's a "co-epidemic" of TB and diabetes that's beginning to affect many countries around the globe — poor, middle-income and even rich nations.

The problem is that people with diabetes – a galloping global epidemic in itself – are two to three times more likely to get active TB. And one-third of the world's population harbors the TB germ, making them vulnerable if they get diabetes. Researchers say that diabetes suppresses the immune system, giving latent TB germs the chance to multiply and cause disease.

The TB/diabetes double-whammy has at least two important differences from the TB/HIV co-epidemic: It involves the interaction of an infectious disease (TB is the world's second-deadliest, next to HIV/AIDS) and a non-communicable chronic disease, rather than two infections. It has potentially more global impact. The TB/HIV co-epidemic was concentrated in sub-Saharan Africa, where 18 countries saw TB rates quadruple because of HIV. Many more countries have high rates of TB and, increasingly, of diabetes. And while low- and middle-income countries with most of the world's population is at risk for the TB/diabetes problem, wealthy countries such as the United States are hardly immune in an increasingly mobile world. India, which has a high incidence of both TB and diabetes, has recently set up a system to provide free diabetes testing. But newly diagnosed patients have to pay for their own diabetes drugs, which are beyond the means of many Indians.

Source: NPR, http://www.npr.org/blogs/goatsandsoda/2014/10/30/360125323/unlikely-marriage-of-diseases-tb-and-diabetes-form-a-co-epidemic, (27.11.2014)

5. MSF: Innovating to fight tuberculosis in Papua New Guinea

Tuberculosis (TB) prevalence in Papua New Guinea (PNG) is among the highest in the world, 541 cases/100,000 population/year, with some pockets reported to be three times higher, prompting Médecins Sans Frontières (MSF) to respond and reach the most affected communities.

After analysing where the greatest needs are, MSF decided to focus on the Gulf Province. This region is estimated to have very high rates of TB and possibly, a concerning rise in drug-resistant TB, along with many remote communities that have limited access to healthcare. The team then set to work on rehabilitating some services in the Kerema general hospital, with new laboratory equipment including the GeneXpert machine to cut TB test result delays down from weeks to just 2 hours. “The objective is to improve considerably the diagnostic capacity in order to be able to start treatment very quickly.” said Benjamin Gaudin, Head of Mission.

The difficulty in accessing the remote communities outside Kerema town led the team to think of innovative solutions. MSF and US Company Matternet trialled the use of small quadcopter Unmanned Aerial Vehicles (UAVs) to transport sputum samples of patients with suspected TB from remote health centres to Kerema general hospital for testing as well as possibly transport results and treatments back to the facilities. Currently the UAVs are capable of travelling at up to 60km/h with a maximum range of 28km in favourable conditions and can only carry a light payload. However it is predicted that their range will increase rapidly in the coming years as new lighter and longer-lasting batteries are developed. The UAV is able to be launched by a smartphone, with the goal that non-technical staff can operate them without assistance. While there is still fine-tuning of the UAV system to be done during the trial phase, initial signs indicate that this may be a useful method of connecting remote health centres to otherwise inaccessible hospitals in the future.

Source: Doctors without Borders, http://www.doctorswithoutborders.org/article/innovating-fight-tuberculosis-papua-new-guinea (17.11.2014)

6. The Union to test all-oral treatment option for multidrug-resistant TB

The International Union Against Tuberculosis and Lung Disease (The Union) announced plans for new clinical research that will evaluate the effectiveness of two new treatment regimens for

multidrug-resistant tuberculosis (MDR-TB). If successful, the study will provide robust new evidence on the effectiveness of both an all-oral and a six-month treatment regimen for MDR-TB.
The current standard treatment regimen for MDR-TB lasts up to 24 months and requires frequent injections, which pose a significant burden both for patients and for health systems tasked with administering treatment. Permanent hearing loss is a serious and tragic side effect of the injected medicines used to treat MDR-TB.
The two regimens to be tested in the study include an all-oral 9-month regimen and a 6-month regimen, which will both include bedaquiline, a new novel anti-TB medicine developed by Janssen Research & Development, LLC (Janssen). The Union and the main trial partner, the UK Medical Research Council, will enroll participants in the study from 2015 through the first quarter of 2018, as needed. Results of the study are expected in 2020. The evaluation of these new regimens comprises the second stage of a larger ongoing clinical trial called STREAM, which is testing the effectiveness of shortened treatment regimens for MDR-TB. The second stage of STREAM is the result of innovative partnerships between the United States Agency for International Development (USAID), The Union, and Janssen.
Source: TB Online, http://www.tbonline.info/posts/2014/11/6/union-test-all-oral-treatment-option-multidrug-res/ (10.11.2014)

Reportage

1. "You see yourself vanishing and you think: I`m going to die"
Andaleeb Rinquest remembers the moment she accepted, with certainty, the imminence of her own death. Lying in a state hospital ward for extensively drug resistant tuberculosis (XDR TB) patients, in the painful final throes of the disease, she looked to her left. There her friend Jolene, similarly weak and skeletal, lay. Jolene's family were too poor to travel 50 kilometres from Atlantis to Brooklyn Chest Hospital in Ysterplaat, Cape Town, for regular visits. But, on that afternoon in October 2011 Jolene's mother had come to take her daughter home – to see the family and, if it was to be, to die.
Before death, the physical decline of a patient like Jolene with an unchecked or drug resistant TB infection can be a lengthy and horrible experience, explains Professor Linda-Gail Bekker at the Desmond Tutu HIV Centre in Cape Town.
Drug-resistant TB is a slow killer, especially when such infections are not sped up by an immune system implosion associated with HIV. The feeling of general illness lasts, and worsens progressively, for months. The bacteria slowly wear away the tissue in infected organs, usually the lungs. The body replaces lost, healthy lung tissue with scars or abscesses, resulting in shortness of breath, a chronic cough and bloody mucus.
The burden of TB is particularly high in South Africa. The country accounts for the second highest rate of new TB cases in the world, owing largely to the fact that over 70% of patients are infected with HIV, making them more susceptible to illness from TB. It also has the highest rate of new drug-resistant TB cases in Africa. Government figures show that from 2004 to 2012 annual MDR TB diagnoses in South Africa more than quadrupled to 14,161 cases. Annual XDR TB diagnoses have increased 18 times to the 2012 figure of 1,545. In each case, only about half of these patients were treated for drug-resistant TB.
Rinquest knows the psychological and physical toll that treatment failure takes on the thousands of South Africans reflected in these statistics. After weeks of night sweats, nausea and weight loss, she was belatedly diagnosed with MDR TB in May 2011. Cared for by her family, she tried to manage the disease, with a prescription of 20 tablets daily, from home. By August that year she had lost a third of her body mass. The flow of pus from a swollen gland in her armpit could no longer be stalled and she began having seizures of the type which marked Jolene's death knell. So, through necessity, Rinquest

consented to quarantine at Brooklyn Chest Hospital. Here the degradation of her body simply continued. “They weighed us each day, and every day there was less of me on the scale,” she said. “Thirty-nine-, 38-, 37 kilograms. You see yourself vanishing and you think: ‘The treatment is failing me. I am going to die.’” In October 2011, a lab diagnosis confirmed that Rinquest’s MDR TB had mutated into XDR TB. Her daily regimen was upped to 28 pills, to augment a daily injection.

The evidence on the effectiveness of drug-resistant TB regimens recommended by the WHO and used in South Africa and other poor countries is insubstantial. Yet the investment in research is far short of what is needed, warns the US-based Treatment Action Group (TAG) in its recent report on TB funding trends between 2005 and 2013. The actual global investment in developing new drugs in 2013 was only $255 million, and total worldwide TB research expenditure was less than $700 million, far short of what experts say is needed to make serious progress against the disease.

“Drug development in the pharmaceutical industry is driven more by the market than need for new and better treatments,” says Marcus Low, of the Treatment Action Campaign (TAC). “When it comes to ‘third world’ diseases – be it Ebola or drug resistant TB – there is a lack of investment, because those affected are generally poor. Pharmaceutical companies maximise profits by developing patented drugs. They are accountable to their shareholders, not to patients in need.”

The dearth of investment is coupled with a lack of urgency in fast tracking promising experimental drugs for drug-resistant TB through the stringent clinical trials generally needed for a drug to be approved. Three in particular - linezolid, delamanid and bedaquiline - have shown promise. n 2012, bedaquiline, one of the first new drugs developed for TB in over 50 years, had looked promising in preliminary clinical trials, but a final confirmatory trial had not yet started. Treatment activists pushed the MCC to allow pre-approval access to the drug, which eventually reached over 150 patients in South Africa. In October 2014, the MCC registered bedaquiline. The Department of Health has promised to roll out the drug to 3,000 MDR TB patients within a year. However, pre-approval access to delamanid is far behind. Japanese pharmaceutical company Otsuka, which has developed the drug specifically to treat MDR-TB, has refused to make delamanid available for *wide* compassionate use, even though the drug is actually further ahead in clinical trials than bedaquiline.

The lobby for pre-approved drugs inevitably enters murky water. Low warns that the needs of drug-resistant TB patients, many of whom face certain death without regimens strengthened by experimental drugs, must be balanced against the unknown risks of improperly tested drugs. The need for conclusive medical trials does not fall away, he says. This need is particularly relevant to bedaquiline. One trial suggested the drug may have serious safety concerns. A large trial that will definitively test the drug’s safety and efficacy will start in early 2015, but it is only expected to deliver results by 2022. “We don’t want to break the regulatory system, or for the potential risks of these drugs to remain unknown,” Low warns.

As far as drugs currently available go, linezolid is “the crux” in the treatment of XDR TB, says Professor Paul Wilcox, who treated Rinquest. “Linezolid has proven to have an 87% success rate of sputum culture conversion (from positive to negative) in XDR patients where state-administered regimens have previously failed,” he said. After seven months, Rinquest was healthy and discharged from hospital. But she had fallen behind on the payments and owed the hospital R450,000.

Source: GroundUp, http://groundup.org.za/article/the_need_for_medicines_for_drug_resistant_tb_2475 (29.11.2014)

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