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## Internationale Nachrichten

### 1. Ukraine's capital is facing an explosive TB epidemic

Kiev may be facing an unprecedented tuberculosis crisis. This is according to Larissa Kanarovskaya, the Head of the Kiev City Union of health workers. On December 1, 2014, at a press conference, she announced that on the average, 100 people die every day from tuberculosis in Ukraine's capital.

The situation, Mrs Kanarovskaya continued, is complicated by an acute shortage of doctors and nurses of TB profile, as well as a critical situation in Ukraine's health care in general. The growing workload on health workers is accompanied by more and more TB cases being detected among physicians.

As a result of a humanitarian catastrophe in south-eastern oblasts of Ukraine and in Crimea Autonomous Republic, caused by an armed conflict, significant numbers of Ukrainian citizens were forced to flee the area of conflict and leave their homes. While the ability of the government to fund the health care programmes is severely impaired because of the conflict, the rapid growth of TB rates is an anticipated outcome of such a situation. As a result, a new risk group to TB is rapidly emerging – refugees and displaced persons – left out without access to health and social care, and in disparate living conditions. They are often left without documents, financial means, and lose access to health care services. As of September 2014, UNHCR had information about 275,489 forced migrants from south-eastern Ukraine (17,794 from Crimean peninsula and 257,695 from eastern Ukraine).

Forced migrants usually do not have money to purchase quality medical care services, buy medication, etc. The numbers of people who would require medical help in connection to TB are growing in all parts of Ukraine. Likely, health and social assistance will be required by the people with Multi-Drug-Resistant TB (MDR-TB), HIV/AIDS, Hepatitis, co-infection, PWID on substitution therapy (ST), whose life has been endangered because of interrupted treatment. The situation is aggravated by a political crisis, and colossal currency devaluation. This problem requires urgent response.

Another problem is BCG vaccination. According to RT, in September 2014 Kiev maternity units have run out of the BCG vaccine that is administered to all newborns before leaving the hospital. The BCG vaccination is used in Ukraine, and in many other FSU states to prevent TB in children. The first vaccination is usually made at birth, to form the immune response to TB in a newborn baby.

According to RT, the reason for the vaccine absence was a refusal of Ukraine's government to procure Russian-made BCG vaccine. Ukrainian internet site Korrespondent on Sept 18, 2014 has informed that BCG was absent not only in maternity wards in Kiev, but across all Ukraine, and situation was like this in the previous six months. Instead, the Ministry of Health has promised to supply Ukraine's maternity wards with a vaccine made in Denmark. There is no information of what the situation with BCG vaccines is now in Ukraine.

**Source:** TB Europe Coalition, <http://www.tbcoalition.eu/2014/12/02/ukraines-capital-is-facing-an-explosive-tb-epidemic/> (09.12.2014)



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## 2. India slashes health budget, already one of the world's lowest

The Indian government has ordered a cut of nearly 20 percent in its 2014/15 healthcare budget due to fiscal strains, putting at risk key disease control initiatives in a country whose public spending on health is already among the lowest in the world. Two Health Ministry officials told Reuters on Tuesday that more than 60 billion rupees, or \$948 million, has been slashed from their budget allocation of around \$5 billion for the financial year ending on March 31.

Despite rapid economic growth over the past two decades, successive governments have kept a tight rein on healthcare expenditure. India spends about 1 percent of its gross domestic product (GDP) on public health, compared to 3 percent in China and 8.3 percent in the United States. But hopes were high that Prime Minister Narendra Modi, who was elected in May, would upgrade basic health infrastructure and make medical services more affordable for the poor. The United Nations estimates about one third of the world's 1.2 billion poorest people live in India. (...)

Dominated by private players, India's healthcare industry is growing at an annual clip of around 15 percent, but public spending has remained low and resulted in a dilapidated network of government hospitals and clinics, especially in rural areas.

The retrenchment could also derail an ambitious universal healthcare program that Modi wants to launch in April. The plan aims to provide all citizens with free drugs and diagnostic treatments, as well as insurance benefits. The cost of that program over the next four years had been estimated at 1.6 trillion Indian rupees (\$25 billion). The Health Ministry officials had been expecting a jump in their budget for the coming year, in part to pay for this extra cost. (...)

In addition to the healthcare budget, the finance ministry has also ordered a spending cut for India's HIV/AIDS program by about 30 percent to 13 billion rupees (\$205.4 million). India had the third-largest number of people living with HIV in the world at the end of 2013, according to the U.N. AIDS program, and it accounts for more than half of all AIDS-related deaths in the Asia-Pacific. (...)

**Source:** Reuters, <http://in.reuters.com/article/2014/12/23/india-health-budget-idINKBN0K10Y020141223> (29.12.2014)

## 3. Tuberculosis post-2015: looking to the future with optimism

The Millennium Development Goal for tuberculosis—to halt and reverse its incidence by 2015—has been achieved globally, in all six WHO regions, and in most of the 22 high-burden countries. It is too early to say whether we will see the 50% reductions in mortality and prevalence relative to 1990 levels, as targeted by the Stop TB Partnership. But if the targets are missed, it will not be by much: by the end of 2013, mortality had fallen by 45% and prevalence by 41%. WHO's *Global Tuberculosis Report 2014*, from which the above statistics were taken, notes that “between 2000 and 2013, an estimated 37 million lives were saved through effective diagnosis and treatment”. Now, with the advent of the Sustainable Development Goals, the third of which is aimed towards the end of the tuberculosis epidemic by 2030, and the expiration of the Stop TB Strategy, a new era in control efforts is set to begin.

WHO's End TB Strategy envisages a world of “zero deaths, disease, and suffering due to tuberculosis”. The 2035 target is a 95% reduction in deaths and a 90% reduction in incidence relative to 2015 levels. It would mean that in 20 years' time, fewer than ten in 100 000 people around the world will develop tuberculosis. “Every country would be at pre-elimination levels—a grand convergence between the rich, OECD countries, and low and middle income countries”, explains WHO's Mario Raviglione. Incidence is currently on a global decline of around 1.5% per year. The new strategy foresees this decline accelerating to an average of 10% per year by 2025, facilitated by optimum use of the approaches that are currently available, and those beginning to emerge from the pipeline, and pursuance of universal health coverage and social protection.

“For the general policy to tackle tuberculosis, you have to have universal health care”, stresses Raviglione. On average, the total cost of falling sick with tuberculosis for patients in low-income and middle-income countries—medical expenses, travel costs, lost income, and so forth—is around half their annual income. If they are charged for diagnosis and treatment, they might delay attendance,



shorten their treatment course, or not attend at all. “(..) This folds into the 2020 target—no families to face catastrophic costs due to tuberculosis—and it requires the co-operation of Government departments outside of health. All of which is certainly ambitious. But post-war Europe offers a precedent, both for double-digit falls in tuberculosis incidence and the kind of social reforms that WHO is advocating. “It was a period of development, nutritional status improved, and people were given access to diagnosis, treatment, universal health coverage, and social protection”, outlines Raviglione. “It is not too much to ask that countries like China, Brazil, and India can do this 75 years later”. With these measures alone, WHO predicts a fall in incidence of around 75% by 2035. But it has bigger aspirations. After 2025, WHO hopes that incidence will decrease by an average of 17% per year, which would match the greatest recorded decline in human history, among the Inuit in the 1960s. For this to happen, new approaches would be needed: a vaccine, perhaps one of the 15 candidates in development, a new prophylaxis and treatment regimen, and a point-of-care test (more than 50 companies are currently involved in assay testing).

Needless to say, treatment remains a crucial factor. There are ten new or repurposed tuberculosis drugs in late stage development. But they are either from the same or very similar families to drugs which have already been registered for treating the disease. So while treatment could certainly be made more effective, it will not be revolutionised. And the absence of any drugs in phase 1 trials means that the outlook is unlikely to change within the next decade or so. Nonetheless, there is cause for optimism.

The REMoxTB phase 3 trial published earlier this year did not show that replacing one of the drugs with moxifloxacin in the standard 6 month regimen for tuberculosis could allow treatment time to be reduced to 4 months. But moxifloxacin did kill more bacteria, at least initially. “We were not able to show that either of the moxifloxacin regimens [substituting for isoniazid or ethambutol] were safe to use for 4 months”, said lead author Stephen Gillespie (University of St Andrews, Scotland). “But that does not mean that moxifloxacin containing regimens are not part of the way forward”. Moreover, this was an intercontinental endeavour. “Before we started the REMoxTB trial, there was only capacity for relatively small-scale academic studies”, Gillespie pointed out. “Now, we have built the capacity to deliver large-scale trials of tuberculosis drugs to regulatory standards”. He believes that a 4-month regimen for drug-sensitive tuberculosis is nearing realisation.

Of course, this would be welcome. But it is unlikely to drastically alter the epidemiology of the disease. Raviglione reckons that cutting treatment duration by a couple of months would push up the cure rate of drug-sensitive tuberculosis, which hovers around 86%, by a few points. There would be a gain in compliance. It may also, if the regimen is mostly composed of new drugs, facilitate treatment of all forms of tuberculosis. But transmission would probably be unaffected—by the fourth month, patients are not usually infectious. The gold standard remains treatment beginning as soon as a patient becomes infectious, which requires large increases in diagnostic capacity, and finishing at roughly the same time they start feeling better—patients would tend to complete the course, and resistance would cease to flourish. “It needs an enormous amount of investment, but I can see a pathway to this kind of treatment now, whereas 10 years ago I couldn't”, Gillespie told *The Lancet Infectious Diseases*. The key scientific issue to resolve is how a fraction of mycobacteria are able to avoid being killed by the initial onslaught of the antituberculosis drugs, and instead remain latent, perhaps hiding behind biofilms, for months on end. “We do not yet have an understanding of latency that is sufficient to design a new regimen that will shorten treatment in a dramatic way. We need more investment in the basic science of tuberculosis”, concluded Raviglione. The yearly shortfall in research and development spending overall is an estimated US\$1.4 billion, while funding for national tuberculosis programmes around the world is roughly \$2 billion short of optimum. (...)

**Source:** The Lancet Infectious Diseases, <http://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2814%2971067-9/abstract> (18.12.2014)

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## **Forschung & Entwicklung**

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### **1. Neuer Schwachpunkt des Tuberkulose-Erregers**

Forscher aus Würzburg und Stony Brook haben beim Tuberkulose-Erreger eine neue verwundbare Stelle gefunden: Die spezifische Blockade eines wichtigen Enzyms im Cholesterinabbau könnte die Bakterien lahm legen.

Weltweit wurden im Jahr 2012 rund 8,6 Millionen Fälle von Tuberkulose bekannt. Wie die Weltgesundheitsorganisation WHO berichtet, starben an dieser gefährlichen Infektionskrankheit 1,3 Millionen Menschen. Dabei waren bei gut fünf Prozent der Infektionen Erreger im Spiel, die gleich gegen mehrere Medikamente resistent sind – Tendenz steigend.

Die Wissenschaft sucht darum neue Wege, um die bakteriellen Erreger der Tuberkulose auch in Zukunft wirksam bekämpfen zu können. Am Rudolf-Virchow-Zentrum der Universität Würzburg forschen Professorin Caroline Kisker und ihr Team auf diesem Gebiet: Sie fahnden in den bakteriellen Enzymen nach bislang unbekanntem Schwachstellen.

Die Würzburger Wissenschaftler nehmen unter anderem den Cholesterin-Stoffwechsel der Krankheitserreger unter die Lupe und dort besonders das Enzym FadA5 – ohne dieses haben die Erreger Schwierigkeiten, eine chronische Infektion aufrecht zu erhalten. Kiskers Gruppe hat nun in Kooperation mit Forschern von der Stony Brook University (USA) die Struktur des Enzyms genau analysiert – und einen möglichen neuen Angriffspunkt für Medikamente identifiziert.

„Wir haben in das aktive Zentrum des Enzyms ein Steroid-Molekül eingefügt und die sich ergebende Struktur analysiert“, sagt die Würzburger Professorin. Mit diesem Wissen lassen sich nun Moleküle designen, die genau ins aktive Zentrum passen und es blockieren. Mit dieser Strategie sollte sich das gewünschte Ziel erreichen lassen: der Totalausfall des Enzyms FadA5. Das berichtet ihre Forschungsgruppe in der Januarausgabe des Fachmagazins „Structure“.

Nun benutzt aber der menschliche Organismus Enzyme, die dem FadA5 aus Tuberkulose-Bakterien ähneln. Es ist also vorstellbar, dass ein neuer Wirkstoff nicht nur die Bakterien lahmlegt, sondern auch beim Menschen Schaden anrichtet. Kiskers Team analysierte deshalb auch die Enzyme des Menschen. Das Ergebnis war positiv: „Der Strukturvergleich hat ergeben, dass es möglich sein müsste, das Enzym der Bakterien spezifisch zu hemmen“, erklärt die Professorin. Ein Hemmstoff sollte also nur den Bakterien schaden, nicht aber den Enzymen des Menschen.

„Das Steroid bietet uns eine solide Ausgangsbasis für die Entwicklung neuer Hemmstoffe“, sagt Kisker. In Zusammenarbeit mit anderen Arbeitsgruppen, unter anderem mit der von Professor Christoph Sotriffer in der Würzburger Pharmazie, soll dieses Ziel nun weiter verfolgt werden. Angestrebt wird ein Wirkstoff, der das FadA5-Enzym der Tuberkulose-Erreger möglichst spezifisch hemmt.

**Source:** Universität Würzburg, <http://www.uni-wuerzburg.de/sonstiges/meldungen/single/artikel/neuer-schw/> (09.12.2014)

### **2. Diagnostic Delays and Clinical Decision Making With Centralized Xpert MTB/RIF Testing in Durban, South Africa**

Tuberculosis (TB) is the leading cause of death among HIV-infected South Africans; however, diagnosing TB in HIV-infected adults remains a challenge. Sputum smear microscopy for acid-fast bacilli (AFB), the most widely available diagnostic test, achieves poor sensitivity (9%–28%) in studies of HIV-infected South Africans. This has prompted calls for improved TB diagnostics, particularly among HIV-infected individuals. The Xpert MTB/RIF assay (Xpert) is a novel nucleic acid amplification test that has been shown to be more sensitive than AFB for diagnosing pulmonary TB. Following the World Health Organization (WHO) endorsement of Xpert, the South African Department of Health and National Health Laboratory Service (NHLS) initiated a nationwide roll-out of Xpert as the first-line diagnostic test for pulmonary TB.

Because Xpert does not rely on laboratory-trained personnel and provides results in as little as 120 minutes, it could potentially be used at the clinical point-of-care to accelerate the time to diagnosis



and treatment initiation. Instead, because of the operational and financial concerns, the NHLS has placed 203 Xpert machines in centralized laboratories throughout South Africa. Consequently, sputum samples and test results are couriered between a health care facility and off-site laboratories. Thus, centralized use of Xpert may cause unexpected diagnostic delays, which might have clinical consequences for initiation of TB treatment. We sought to determine whether sputum Xpert testing performed at a centralized laboratory accelerated time to pulmonary TB diagnosis for a hospital and outpatient clinic in Durban, South Africa. (...)

In conclusion, this study demonstrates that implementation of Xpert testing at a centralized laboratory causes operational delays that limit the test's clinical utility for diagnosing pulmonary TB. A clinician's assessment and a faster sputum AFB result remained central to a timely diagnosis of pulmonary TB in our setting. Although placing Xpert at the clinical point-of-care may reduce diagnostic delays and improve clinical outcomes, benefits must be weighed against increased technical and operational costs. In the meantime, centralized processing and reporting of Xpert testing should be streamlined to provide faster results to clinicians, and there continues to be a role for sputum AFB testing. There is also a need for the development of new point-of-care tests that are rapid and inexpensive. Like Xpert, the lateral flow test for urinary lipoarabinomannan has shown promise as a point-of-care test for TB screening. Its utility, however, is restricted to a subset of HIV-positive patients with low CD4 counts. To overcome the limitations of tests such as Xpert and urinary lipoarabinomannan, new diagnostics, such as the loop-mediated isothermal amplification sputum assay, will need to be broadly applicable and easy to implement. With these technological advances, it will be possible to identify TB early, start treatment promptly, and reduce TB-associated morbidity and mortality.

**Source:** Journal of Aids Studies, [http://journals.lww.com/jaids/Fulltext/2014/11010/Diagnostic\\_Delays\\_and\\_Clinical\\_Decision\\_Making.12.aspx](http://journals.lww.com/jaids/Fulltext/2014/11010/Diagnostic_Delays_and_Clinical_Decision_Making.12.aspx) (09.12.2014)

### 3. Five cutting-edge TB-HIV research studies you may not have heard about

December 1 is World AIDS Day, a day to solemnly reflect on the more than 35 million lives lost to HIV/AIDS, to stand in solidarity with communities affected and to mobilise action against the epidemic. TB is the leading cause of death among people living with HIV, making addressing TB-HIV co-infection a vital part of the global response against HIV/AIDS.

#### 1) Uptake of ART among TB-HIV co-infected clients in Nairobi, Kenya

Research conducted in an area of Kenya shows that it's feasible to rapidly increase the numbers of people with TB and HIV who have access to antiretroviral therapy (ART). In Kenya, half of people with TB are also living with HIV, and national guidelines say that they should receive immediate access to lifelong ART. In a targeted TB control zone in Nairobi, however, only 29% of these eligible people were receiving ART in 2010. By improving how TB clinics followed up with patients to ensure they received ART, and by hiring community health workers to escort TB patients to the clinic where they were enrolled on ART, uptake of ART increased from 29% in 2010 to 80% by 2013.

*This research was presented at the 45th Union World Conference on Lung Health (28 October-1 November 2014). See abstract #OPP-407-01 on page S547 here ([http://barcelona.worldlunghealth.org/programme/body/Abstract\\_Book\\_2014-Web.pdf](http://barcelona.worldlunghealth.org/programme/body/Abstract_Book_2014-Web.pdf)).*

#### 2) The cost of TB screening in Gauteng, South Africa

On an individual basis, providing routine TB screening to a person living with HIV is inexpensive. But what happens in a country like South Africa, where the numbers of people living with TB-HIV co-infection are extraordinarily high? Perhaps surprisingly, there aren't many data on the total cost. In this study, researchers found that the average cost of screening a person living with HIV for TB was \$3.39 when the test was conducted by a professional nurse, compared to \$1.38 when it was conducted by a lay health worker. With more than 5 million people living with HIV in South Africa, this is a major savings, and the researchers recommend that the government of South Africa explores using lay health workers more often to provide TB screening as a way to reduce costs and improve TB



screening rates.

*This research was presented last month at the 45th Union World Conference on Lung Health (28 October-1 November 2014). See abstract #PD-1069-01 on page S448 here ([http://barcelona.worldlunghealth.org/programme/body/Abstract\\_Book\\_2014-Web.pdf](http://barcelona.worldlunghealth.org/programme/body/Abstract_Book_2014-Web.pdf)).*

*3) Why do presumptive TB cases refrain from HIV testing in Karnataka, India?*

People in India who are suspected of having TB are supposed to receive provider-initiated HIV testing, but not all of them do. This study by researchers at the State TB Centre in Bangalore shows some of the main reasons why. They collected HIV testing data for 41,325 people suspected of having TB, all of whom were also supposed to receive an HIV test at the same health facility where they were being tested for TB. However, only 62% of them did. The most common reasons were: HIV testing was not available at the health facility (this happened 78% of the time); individuals either refused to receive an HIV test or were not given one because of their advanced age (12%); and/or there were no testing kits or personnel available (8%). This demonstrates that when HIV testing for TB patients fails to happen in India, the cause may more often be due to a lack of testing capacity than to a lack of willingness among those are supposed to receive the tests.

*This research was presented at the 45th Union World Conference on Lung Health (28 October-1 November 2014). See abstract #PD-1070-01 on page S448 here ([http://barcelona.worldlunghealth.org/programme/body/Abstract\\_Book\\_2014-Web.pdf](http://barcelona.worldlunghealth.org/programme/body/Abstract_Book_2014-Web.pdf)).*

*4) Tuberculosis is associated with non-tuberculosis-related deaths among HIV/AIDS patients in Rio de Janeiro*

In a study published in the December 2014 issue of the *International Journal of Tuberculosis and Lung Disease*, researchers divided a large study sample of people living with HIV into two groups: those who had developed active TB disease at some point, and those who had not. They found that those who had had TB, even when it was successfully treated, had double the risk of dying from a non-TB related cause than other people living with HIV. The researchers concluded this increased risk is probably due to long-term immune deficiency or an incomplete recovery of the immune system after having TB. They found that antiretroviral therapy and TB prophylactic treatment each protected people living with HIV from dying from non-TB-related causes.

See (<http://www.ingentaconnect.com/content/iatld/ijtld/2014/00000018/00000012/art00011>)

*5) Detection and management of drug-resistant tuberculosis in HIV-infected patients in lower-income countries*

Drug-resistance threatens the ability of public health programmes to control TB among people living with HIV. In a study published in the November 2014 of the *International Journal of Tuberculosis and Lung Disease*, researchers assessed 47 ART programmes across sub-Saharan Africa, Latin America and the Asia-Pacific with regard to their capacity to diagnose and treat drug-resistant TB (DR-TB). They found that ART programmes had limited capacity to carry out this function, and that a lack of directly observed treatment (DOT) for TB – where health workers ensure that people with TB take their medicine as prescribed – and regular interruptions in TB drug supplies may be contributing to the global emergence of TB drug resistance. Less than half of the ART programmes assessed were able to provide any kind of testing for drug-resistance; 30% had no access to medicines needed to treat DR-TB; and of those programmes that had access to medicines, 38% reported facing regular interruptions in drug supplies.

See (<http://www.ingentaconnect.com/content/iatld/ijtld/2014/00000018/00000011>)

**Source:** The Union, <http://www.theunion.org/news-centre/news/five-cutting-edge-tb-hiv-research-studies-you-may-not-have-heard-about> (09.12.2014)

#### **4. Diagnostic TB tests performed accurately among adults, poorly in children**

Despite accuracy among adults, two diagnostic tests performed poorly when diagnosing tuberculosis in Tanzanian children, according to data published in *Pediatrics*.

Line Lindebo Holm, MD, of Copenhagen University Hospital Hvidovre in Denmark, and colleagues compared diagnostic accuracy of IP-10 and QuantiFERON-TB Gold In-tube (QFT-IT)



among 203 children suspected to have tuberculosis with 102 adults confirmed to have tuberculosis. Children had at least one of the following tuberculosis symptoms: a cough lasting at least 14 days, fever lasting at least 7 days, or a weight-for-age z score of  $-2$  or less. The median age of the children in the study was 3 years. This was a substudy of a prospective study conducted at Muheza District Hospital in Tanzania from 2008 to 2010.

Thirty-eight percent of children had HIV; 36% were aged younger than 2 years; and 58% had low weight-for-age. Data indicated 72% of adults were positive responders to IP-10, and 75% were positive responders to QFT-IT. Positive responder rates were significantly lower among children. When excluding indeterminate test results, the proportion of positive test responders was 33% among children with confirmed tuberculosis and 29% among children with probable tuberculosis for IP-10 and QFT-IT. Overall agreement between IP-10 and QFT-IT results was 69% among children ( $P < .0001$ ). Twenty-nine percent of children had indeterminate IP-10 results, and 26% had indeterminate QFT-IT results.

Exposure to pulmonary tuberculosis was associated with positive IP-10 results (adjusted OR=3.6; 95% CI, 1.3-9.9). Previous exposure to pulmonary tuberculosis, however, was not associated with positive QFT-IT results. Age younger than 2 years was associated with indeterminate results for both IP-10 (aOR=2.2; 95% CI, 1.12-4.34) and QFT-IT (aOR=2.4; 95% CI, 1.21-4.92). IP-10 and QFT-IT performed poorly when diagnosing active tuberculosis in severely ill Tanzanian children, according to the researchers.

“IP-10 and QFT-IT offer little diagnostic value in tuberculosis-suspect children from high-burden hospital settings,” the researchers wrote. “We emphasize the need for studies investigating other test modalities.”

**Source:** Healio, <http://www.healio.com/pediatrics/respiratory-infections/news/online/%7B079ba3c2-6501-4c46-b147-081dff97f11c%7D/diagnostic-tb-tests-performed-accurately-among-adults-poorly-in-children> (09.12.2014)

## Reportage

### 1. ‘Superbugs’ Kill India’s Babies and Pose an Overseas Threat

A deadly epidemic that could have global implications is quietly sweeping India, and among its many victims are tens of thousands of newborns dying because once-miraculous cures no longer work.

These infants are born with bacterial infections that are resistant to most known antibiotics, and more than 58,000 died last year as a result, a recent study found. While that is still a fraction of the nearly 800,000 newborns who die annually in India, Indian pediatricians say that the rising toll of resistant infections could soon swamp efforts to improve India’s abysmal infant death rate. Nearly a third of the world’s newborn deaths occur in India. (...)“Five years ago, we almost never saw these kinds of infections,” said Dr. Neelam Kler, chairwoman of the department of neonatology at New Delhi’s Sir Ganga Ram Hospital, one of India’s most prestigious private hospitals. “Now, close to 100 percent of the babies referred to us have multidrug resistant infections. It’s scary.” These babies are part of a disquieting outbreak. A growing chorus of researchers say the evidence is now overwhelming that a significant share of the bacteria present in India — in its water, sewage, animals, soil and even its mothers — are immune to nearly all antibiotics. Newborns are particularly vulnerable because their immune systems are fragile, leaving little time for doctors to find a drug that works. But everyone is at risk. Uppalpu Shrinivas, one of India’s most famous musicians, died Sept. 19 at age 45 because of an infection that doctors could not cure.

While far from alone in creating antibiotic resistance, India’s resistant infections have already begun to migrate elsewhere. “India’s dreadful sanitation, uncontrolled use of antibiotics and overcrowding coupled with a complete lack of monitoring the problem has created a tsunami of antibiotic resistance that is reaching just about every country in the world,” said Dr. Timothy R. Walsh, a professor of microbiology at Cardiff University. Indeed, researchers have already found “superbugs” carrying a genetic code first identified in India — NDM1 (or New Delhi metallo-beta lactamase 1) —



around the world, including in France, Japan, Oman and the United States. (...) Health officials have warned for decades that overuse of antibiotics — miracle drugs that changed the course of human health in the 20th century — would eventually lead bacteria to evolve in a way that made the drugs useless. In September, the Obama administration announced measures to tackle this problem, which officials termed a threat to national security. (...)

Some health experts and officials here say that these killer bugs are largely confined to hospitals, where heavy use of antibiotics leads to localized colonies. But India's top neonatologists suspect the large number of resistant infections in newborns in their first days of life demonstrates that these dangerous bacteria are thriving in communities and even pregnant women's bodies. "Our hypothesis is that resistant infections in newborns may be originating from the maternal genital tract and not just the environment," Dr. Paul said in an interview. In a continuing study in Delhi at several government-run hospitals that has so far included more than 12,000 high-risk newborns, and was made available to The New York Times, about 70 percent of the babies' infections were found to be immune to multiple powerful antibiotics, confirming the results of earlier and smaller studies.

Doctors interviewed in hospitals across India said that a large number of the infections they found in newborns were resistant to many antibiotics. Awareness of the problem has begun to grow, with Indian medical associations calling for efforts to reduce unnecessary antibiotic use. But there is keen sensitivity here to any alert to the dangers. A 2010 discovery of a New Delhi "superbug" caused intense controversy because of fears that publicity would threaten India's profitable medical tourism industry. Government officials have stopped some studies of the problem, Dr. Walsh said.

The effects of antibiotic-resistant bacteria on treating disease in India could be enormous. Tuberculosis is just one example of the challenges doctors face. India has the world's largest number of cases, and recent studies using the latest genetic tests have shown that as many as 10 percent of untreated patients in places as far apart as Mumbai and Sikkim have resistant infections. These patients are catching resistant bugs at home, not hospitals, making the epidemic very difficult to control, Dr. Soumya Swaminathan, director of the National Institute for Research in Tuberculosis, said in an interview. "It's startling and very worrying," Dr. Swaminathan said. Unless the government makes profound and drastic changes, tuberculosis in India may soon become untreatable, she said.

Although resistant bugs are everywhere here, hospitals have become factories for untreatable "superbugs." A government program that pays women to have babies in hospitals has in 10 years more than doubled the share of hospital-born babies to 82 percent, but the government did little to increase hospital capacity to deal with the crush. Maternity wards often have two and three women in each bed, allowing infections to spread rapidly. (...)

India and other developing nations are by no means alone in threatening the future of antibiotics. Overuse of the drugs in chicken, hog and cattle farms in the United States has led to the rise of resistant strains there, and research has shown that as much as half of antibiotic prescriptions in the United States are unnecessary. The Centers for Disease Control and Prevention estimated last year that two million people are sickened by resistant bacteria every year in the United States and 23,000 die as a result. But efforts to crack down on inappropriate antibiotic use in the United States and much of Europe have been successful, with prescriptions dropping from 2000 to 2010. That drop was more than offset, however, by growing use in the developing world.

Global sales of antibiotics for human consumption rose 36 percent from 2000 to 2010, with Brazil, Russia, India, China and South Africa accounting for 76 percent of that increase. In India, much of that growth has been driven by private doctors who deliver about 90 percent of care here and are often poorly trained. Much of these doctors' income comes from drug sales. (...)

**Source:** NYT, <http://www.nytimes.com/2014/12/04/world/asia/superbugs-kill-indias-babies-and-pose-an-overseas-threat.html> (29.11.2014)





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