

for bullying in medicine will ultimately be “evolutionary as opposed to revolutionary.”

“The new incoming cohort of students and residents over the last few years are more willing to identify these issues, and are more willing to exercise the options available to them,” he says. “That also bears out in faculty over time: as people have experienced different ways of learning, the old environment is gradually going to disappear.”

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Top-down measures, such as stronger accreditation standards requiring medical schools and residency programs to have effective mechanisms for addressing abuse, are part of that evolution, says Bandiera, who chairs the committee on accreditation for the Royal College of Physicians and Surgeons of

Canada. “We’ve taken a very aggressive stance on reviewing programs ... and we’re currently rewriting the standards of accreditation in Canada to increase their rigor,” he explains. “There’s going to be a new standard, called the learners, teachers and administrators’ standard, and it has a lot to do with the positivity of the learning experience.”

The degree to which residency programs can “demonstrate concrete positive outcomes to residents, that’s proba-

bly the most important thing,” Bandiera adds. This is often complicated by the need to preserve confidentiality of investigations, even after they’ve been resolved, he says. “Sometimes the perception may be nothing is happening, when in fact a lot of work may be happening in the background.”

Medical schools and residency programs are also making it easier and safer for trainees to log complaints through web-based reporting tools and options to flag abuse anonymously, among other strategies. At the University of Toronto, for example, residents have “multiple routes to access the system, whether through a direct supervisor, a rotation coordinator, a program director or a third party,” says Bandiera.

Dr. Armand Aalamian, associate dean of postgraduate medical education at McGill University in Montréal, says preventing abuse will also require putting more resources into supports for trainees and faculty. “We’re all dealing with a system, in Quebec and across Canada, that is under quite a bit of stress in terms of budget cuts, in terms of working hours, in terms of resources, so when people are stressed that’s when you have issues of behaviour conflicts.”
— Lauren Vogel, *CMAJ*

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Drug-resistant tuberculosis plagues India

Part one of a series

“India is unlucky to be lucky.” This non sequitur, repeated by health care providers in both Delhi and Mumbai, India, was invariably followed by a pause for effect, then the explanation. India’s 1.3 billion people have easy access to inexpensive drugs — often extraordinarily easy at neighbourhood pharmacy counters, where prescriptions are unnecessary. But this access is exacting a high price: drug resistance. Tuberculosis (TB) is a case in point.

Of the nine million reported cases of TB worldwide, 2.3 million are in India, according to the World Health Organization’s (WHO) *Global Tuberculosis Report 2015*. That number is relatively stable (though it has decreased everywhere else, according to the report), but the number with multi-drug resistant TB (MDR-TB) is on the rise. In 2008, about 99 000 people were newly diag-

nosed or in retreatment for MDR-TB; by 2014, that number had increased nearly four times, to about 395 600, or 17.2% of all TB patients.

“India is unlucky to be lucky,” said Dr. Sylvie Jonckheere, the medical technical referent at the Médecins sans Frontière (MSF) clinic in Mumbai. In part, this is because drugs are inexpensive. India is the pharmacy to the developing world because its unique patent system allows it to legally manufacture and sell drugs at a fraction of the price charged in other countries. But the availability of inexpensive meds also means they are overused. For example, most of the first-line antitubercular drugs and fluoroquinolones are routinely available over-the-counter and used to treat minor illnesses.

“We have patients who have already been exposed to reconverted drugs so even with the new drugs, it’s difficult to have an effective regime,” said Jonckheere. “Women with urinary tract infections are taking drugs that are scary

because the infections aren’t sensitive to many things any more. Abuse of antibiotics is widespread. In this country you can get anything without a prescription.” Things are improving somewhat these days, she adds: “You kind of have to say you’re a doctor.” Nevertheless, “we’re creating a future nightmare for my future colleagues in the infectious diseases business I think.”

Like other infectious diseases, at least four drugs are needed to treat TB. Jonckheere is seeing some TB that’s resistant to 12 or 14 drugs.

According to WHO definitions, MDR-TB is resistant to isoniazid and rifampin — the two most potent and frequently used TB drugs — and may also be resistant to other first-line drugs. Extremely drug-resistant TB (XDR-TB) is resistant to isoniazid and rifampicin, and to any fluoroquinolone, as well as to any of the three second-line injectables (amikacin, capreomycin and kanamycin). While XXDR-TB is resistant to all first-

and second-line drugs. A 2012 report documented the first four patients with XXDR-TB; by 2012, there were 14 such patients at just one Mumbai hospital.

“We’re seeing patients with patterns of resistance that are terrible,” Jonckheere said. “Whether it’s HIV or TB, we’re ending with a horrific genotype drug-sensitivity test. With HIV we still have some weapons, I’d say, but the TB pipeline is really shallow.”

Depending on who you ask, TB ranks as the number one or number two (after malnutrition) health problem in India. The country has one-quarter of the world’s TB. WHO estimates that 251 000 Indians died with this curable disease in 2014; others put that number today at 300 000.

Inaccurate testing

While the availability of inexpensive drugs facilitates drug-resistant TB, it’s only one factor: how patients get those drugs is also crucial.

It begins with often inaccurate testing. The United Nations–based, Stop TB Partnership reports that India’s public health sector relies almost entirely on smear microscopy to diagnose TB and drug-resistance testing is offered only to a small proportion of all TB patients.

“This has two problems,” said Dr. Suvanand Sahu, deputy executive secretary for Stop TB Partnership. Smear microscopy misses over 40% patients with TB, and in the absence of drug-resistance testing many DR-TB patients are incorrectly given a first-line regimen,



Barbara Sibbald

An estimated 395 000 Indians have drug-resistant tuberculosis, which is challenging to diagnosis and treat.

That would require a massive scale up of capacity; a 2012 article in *Tuberculosis* reports that there is only “around one intermediate reference lab in each state accredited for culture and drug susceptibility.”

Inadequate testing, and other issues, often means substandard treatment. An estimated 60%–80% of people with TB choose private over public care, because of the notoriously long waits in the latter — a half-day isn’t unusual — and the lack of sick leave for most people. But

treatment, including a survey published in 2010 by *PloS One* that indicated only 6 of 106 private practitioners in a Mumbai slum could prescribe correctly for a hypothetical patient with MDR-TB. “The majority of the prescriptions were inappropriate and served to merely amplify resistance.”

Unfortunately, treatment in the public system is also fraught. “All patients with MDR-TB are given a standard one-size-had-better-fit-all regimen called category four,” writes Dr. Zarir F. Udhwadia in an email. According to the renowned TB expert and consultant physician at the PD Hinduja National Hospital and Medical Research Centre in Mumbai, “The problem is many patients are resistant to multiple drugs in that regimen so this set of drugs are unlikely to work. You wouldn’t treat a patient with pneumonia or peritonitis with a drug or drugs to which you know they are resistant, yet that’s precisely what many MDR-TB patients receive.”

India is one of only three countries not offering the WHO-recommended fixed-dose combinations for DR-TB, according to a 24-country survey by MSF and Stop TB Partnership published in November 2015. In addition, India and China alone recommend

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which leads to more drug resistance.

In the private health sector, which ranges from Ayurveda specialists to intensive care units, some practitioners use good-quality molecular tests, such as GeneXpert, or culture, but others diagnose TB without doing a bacteriology test to confirm it, said Sahu. “We must change this and ensure that uniform good quality of TB testing is offered everywhere.”

many private practitioners defy government rules and don’t report the disease, much less follow up with patients to ensure they are following treatment protocol. All this, despite the introduction of the MDR-TB-specific directly observed treatment short-course protocol (DOTS-plus) by the Revised National Tuberculosis Control Program in 2000.

There is extensive evidence of inaccurate diagnostics and inappropriate

intermittent rather than daily treatment for DR-TB, which increases the risk of loss to follow-up and further resistance. (Daily treatment is supposed to be rolled out in 104 districts in India this year.)

Patients stop treatment

Noncompliance is likely another factor contributing to the increase in DR-TB, although concrete figures are elusive. “There’s a lot of anecdotal evidence that patients stop treatment,” said Sahu from Stop TB. Some quit when they begin to feel better after a few weeks, others because the drugs are too expensive for them. Side effects, particularly with DR-TB treatment, can also lead to noncompliance. “The drugs are severely toxic,” said Shau. “One of side effects is a tendency to suicide. You really need social support. You need some system to make you adhere.” An estimated one million TB-affected Indians are lost to follow-up annually.

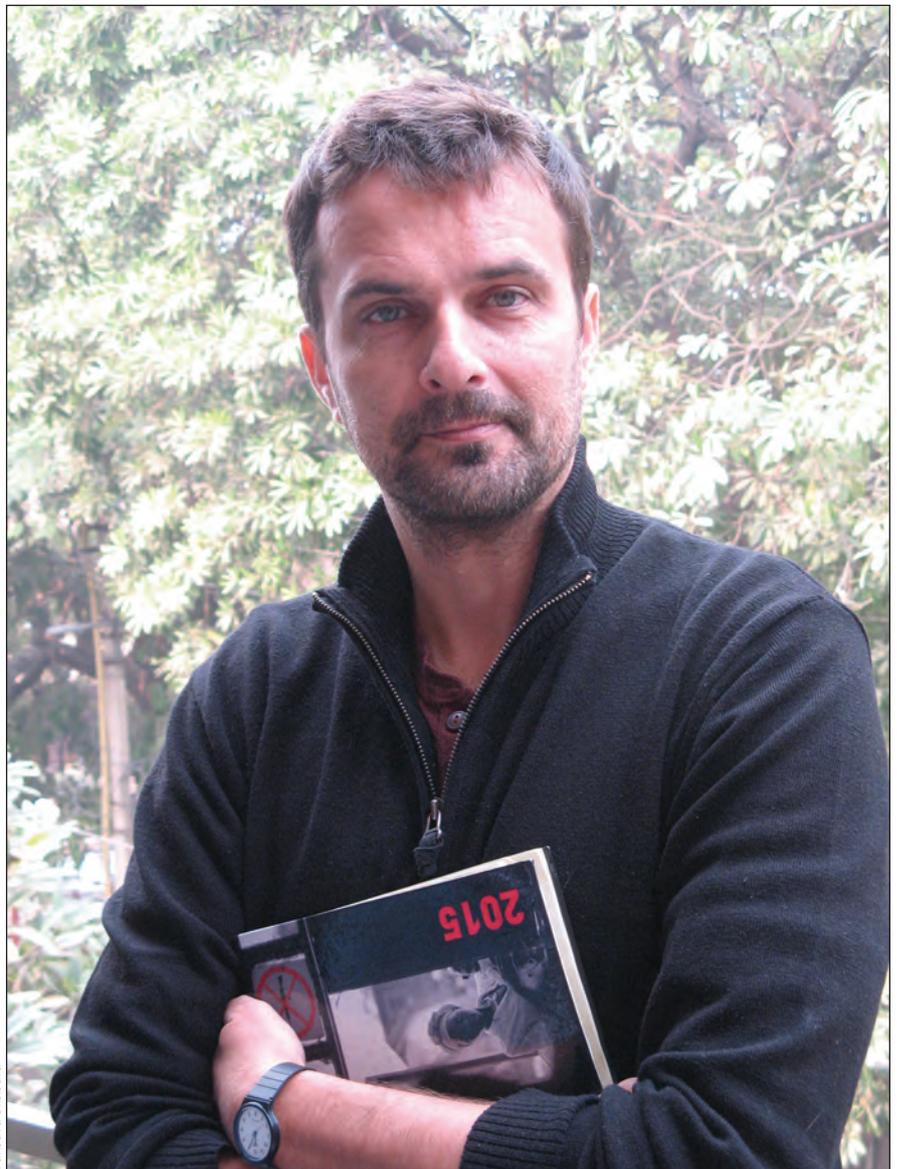
“There is a big challenge in ensuring protocols for diagnostics and treatments are followed,” confirms Dr. Daniel Remartinez Ferrer, MSF Belgium’s medical coordinator in Delhi. “We’re seeing the progression of DR-TB very quickly — to resistance beyond drugs normally used in treatment.”

The one-size-fits-all drug regimen for DR-TB “means they’re not treated,” adds Remartinez Ferrer. “Patients are failing on the government treatment.”

Three government officials did not respond to emailed inquiries from *CMAJ*.

Udwadia isn’t shy to point fingers. “DR-TB has arisen from a combination of factors, chief of them being a short-sighted government [national treatment plan] which ... pretended MDR didn’t exist.” For many years, patients who failed to respond to standard treatment were not even offered drug-sensitivity testing but given 8/12 months of “morally and medically reprehensible category two treatment which served to amplify resistance. What I call PPP (public policy paralysis). Private doctors with dreadful, inappropriate prescriptions worsened the problem.”

The solution, according to Udwadia, includes more and better diagnostic testing, new drugs and laws to ensure only designated specialists prescribe and treat patients with MDR-TB.



Barbara Sibbald

“Patients are failing on the government treatment,” said Dr. Daniel Remartinez Ferrer.

The government has made great strides with regular TB: 1.5–1.6 million are treated each year and treatment success tripled in 1997–2006, from 25% to 85%. The government’s aim is to treat 90% of all cases by 2017.

However, treatment for DR-TB patients remains problematic. Due to inconsistent results and other factors, patients typically move between private and public care, becoming increasingly impoverished and ill while spreading their disease in crowded home and work environments.

Before the advent of antibiotics, the mortality rate for TB was about 50%. The survival rate for MDR-TB is about 50% at five years; that plummets to

20% for XDR or even pre-XDR. “It’s horrendous,” said MSF’s Jonckheere.

In the Ebola epidemic in Guinea, where Jonckheere worked in 2015, mortality dropped in some places from 75% to about 50%. With Ebola, “Within a week, you die or not. With TB it’s three, four, five years. But it’s the same: you infect the children, the husband, the wife. It’s slow, but there’s much more suffering. It is only the speed [of Ebola] that is tremendously different. But seriously, the outcome, the risk for the families — it’s the same.” — Barbara Sibbald, Mumbai, India

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