Drug-Resistant Tuberculosis in 2017: At a Crossroads

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In this issue of *The Lancet Respiratory Medicine*, Dheda and colleagues present one of the most comprehensive pictures to date of the global epidemic of drug-resistant tuberculosis (DR TB).¹ This comes at a time of increasing awareness of antimicrobial resistance as a global threat² – and TB has had a 50-year head start in developing resistance to current first-line therapy. In reading about such phenomena as compensatory mutations, increasing prevalence of incurable TB, and widespread transmission of DR TB, it is easy to become disheartened. If – as suggested in modeling studies³ and recently demonstrated in KwaZulu-Natal, South Africa⁴ – the majority of new multidrug-resistant (MDR) and extensively drug-resistant TB cases now reflect transmission in communities rather than acquisition during treatment – is there any hope for preventing the eventual replacement of all TB by drug-resistant strains?

While the picture painted by Dheda and colleagues is indeed a sobering one, there are strong reasons not to adopt a fatalistic approach to DR TB. The year 2016 heralded the first time in history that a treatment regimen for MDR TB of less than a year's duration was recommended on a global scale.⁵ If this regimen's effectiveness is borne out in larger trials

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and facilitates the global scale-up of appropriate MDR TB treatment, the global incidence of MDR TB could fall by 20% or more.⁶ Indeed, preliminary evidence suggests that a six-month, all-oral regimen for DR TB may achieve very high levels of treatment success.⁷ Diagnostic capacity for DR TB – in the form of Xpert MTB/RIF scale-up⁸ and improving susceptibility testing for second-line drugs⁹ – is more accurate, more rapid, and more widespread than ever before, and will likely soon be available at the peripheral level. Target regimen profiles for improved treatment of DR TB have been developed and disseminated¹⁰, providing a roadmap to DR TB treatment regimens that could rival the tolerability and efficacy of current first-line therapy. In short, while DR TB continues to evolve, the response to this growing threat has not been an idle one.

Important parallels exist between the DR TB situation in many areas of the world today and that of the United States (US) in the late 1980s. Three decades ago, the DR TB epidemic in the US was widely underappreciated, rapidly growing, and with a sorely underfunded response.¹¹ Similarly today, the extent of the DR TB problem in many countries (e.g., in West and Central Africa) is not fully recognized, and global investment in TB is at its lowest level since 2008.¹² In the case of the US in the early 1990s, deeper understanding of the DR TB epidemic was met with a renewed financial commitment and multifaceted response that generated a 67% nationwide drop in DR TB incidence in just five years (see Figure). Such success has not been confined to low-burden settings, either – similar reversals of MDR TB rates have been documented in Estonia¹³ and KwaZulu-Natal, South Africa,¹⁴ and equivalent MDR TB treatment success (as high as 89%) has been achieved in countries as resource-constrained as Niger.¹⁵ Now, just as the US became aware of its DR TB epidemic in the early 1990s, Dheda and colleagues have sounded an even greater alarm regarding the DR TB pandemic on a global scale. It is up to us, as a global public health community, to respond.

When we have achieved success against DR TB at the population level, we have done so by prioritizing a comprehensive approach to DR TB management and prevention, including control of transmission in congregate settings, rapid diagnosis and initiation of treatment, appropriate financial investment, and patient-centered care. As our tools for DR TB diagnosis and treatment continue to improve, there is no reason to believe that we cannot produce similar results in a wide number of other high-burden settings – but it will take a level of commitment to a DR TB-specific response that currently appears lacking. Given that DR TB is now a transmitted disease, we cannot expect to control it simply by improving our diagnosis and treatment of drug-susceptible strains. But we now have the diagnostic assays to understand the extent of the DR TB problem, the drugs to effectively treat patients afflicted with DR TB, and simple measures (e.g., naturally ventilated rooms) to prevent DR TB spread. And additional tools for combating DR TB (point-of-care tests, shorter and more tolerable regimens, preventive therapy using novel agents) are on the very near horizon. What is needed now is a stronger commitment by the governments of high-burden countries to use those tools as part of a comprehensive DR TB response – and by the broader community to ensure that such country-level commitment is matched by appropriate financial investment at the global scale.

Ultimately, Dheda et al are describing an epidemic that is at a crossroads. Every year, strains of DR TB will emerge that are more transmissible, more difficult to treat, and more widespread in the community. Yet we also have more tools at our disposal than ever before – tools that are making effective diagnosis and treatment of DR TB broadly accessible worldwide. And unlike for most other drug-resistant pathogens, we have evidence that – with a comprehensive response – epidemics of DR TB can be rapidly reversed. Over the next decade, it is quite possible that we will see a DR TB epidemic of unprecedented global scale. But it is also possible that the next decade could witness an unprecedented reversal of the global DR TB burden. The difference between these two outcomes lies less with the pathogen and more with us as a global TB control community – and whether we have the political will to prioritize a DR TB-specific response. DR TB is not standing still; neither can we.

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Figure 1. Surveillance of multidrug-resistant tuberculosis (TB) in New York City and the United States

The global epidemic of drug-resistant TB in 2017 may be compared with that in the United States in 1990. The orange line depicts the percentage of new TB cases in New York City with documented rifampin resistance between 1980 and 1990 (from [11]). Following a reinvigorated, comprehensive national response, the number of notified cases of multidrug-resistant TB in the United States nationwide (shown in blue) fell dramatically after 1993 and has remained at the same low level for two decades. US surveillance data are from the Online Tuberculosis Information System, US Centers for Disease Control and Prevention, <https://wonder.cdc.gov/tb.html>.