Accelerating efforts to end TB

Fittingly for a bacterium whose slow growth rate has frustrated researchers for decades, progress towards ending the TB epidemic has built only at a snail's pace. 2018 should see a much needed stimulus, with increased political awareness of the scale of the problems faced, and the adoption of a coordinated global response.

Despite notable progress in recent years, the figures for tuberculosis (TB) continue to make for grim reading. According to the World Health Organization (WHO) Global Tuberculosis Report 2017 (ref. ¹), an estimated 10.4 million people were infected with *Mycobacterium tuberculosis* in 2016, with deaths estimated at more than 1.6 million (including HIV-associated TB infections). Of these new cases, 600,000 were resistant to the first-line drug rifampicin, including 490,000 cases of multidrug resistance. More than 40% of TB cases still go undiagnosed and although greater than 45% of those infected now complete a treatment course, the majority of which survive with no further recurrence of disease, there remains a 16% mortality rate. While current efforts to counter TB have seen global incidence and mortality rates falling, 2% and 3% each year, respectively, if initial targets laid out in the WHO End TB Strategy are to be reached by 2020, these reduction rates would need to be improved dramatically (and quickly). Underlying these figures is a US\$2.3 billion funding gap that, despite a decade of increased financing, continues to see poor-quality health systems with limited reach to at-risk and affected populations in many of countries. Not surprisingly, TB therefore remains the leading cause of death by an infectious disease, and the ninth leading cause of death in general. The picture painted is sobering indeed, and illustrates why many working to eradicate the disease will find it hard to become excited by the approaching World TB Day 2018 (24 March) and its theme of 'Wanted: Leaders for a TB-Free World'. The very idea of a TB-free world for the moment remains stubbornly out of the frame.

The collective mood need not be dominated only by doom and gloom, however, and 2018 could yet turn out to be a highly significant year for efforts to tackle TB. Scheduled for September (the exact timing not yet formalized) is the United Nations (UN) General Assembly High-Level Meeting on TB, which represents the culmination of a gradual cranking up of political pressure over the past few years by groups such as the Stop TB Partnership. Only the fifth time that a UN high-level meeting has been devoted to

a health issue (prior meetings focusing on HIV/AIDS, non-communicable diseases, Ebola and antimicrobial resistance), the upcoming session will promote TB to the very top of the global health agenda and command the attention of heads of state and governments worldwide. This will be especially welcomed by those still smarting from TB's initial exclusion from the 2017 WHO list of pathogens to be prioritized for development of new therapeutics. Discussions at the high-level meeting are expected to build on the outcomes of the Global Ministerial Conference on TB held in Moscow in November 2017, at which ministers and participants representing 114 countries agreed to increase cooperation and act on four key points. Firstly, to strengthen health systems and improve access to TB-prevention care so that appropriate health coverage is universal. Secondly, to ensure that financing is both sufficient to the task and sustainable in the long term, by increasing national and international investment for healthcare implementation and research. Thirdly, to increase investment in research and development of tools to diagnose, treat and prevent TB. And finally, to create a multisectoral framework to provide accountability through tracking and reviewing progress made.

If the high-level meeting can consolidate sufficient political will among global leaders to increase economic inputs and improve coordination among relevant stakeholders, there is genuine hope that TB health-care systems can be improved and a serious dent made in global infection and mortality rates. Recognition that greater support is needed for researchers developing effective tools should be welcomed; such tools will be absolutely fundamental to achieving ambitious targets to halt the TB epidemic. Yet a blank cheque will not be offered and so decisions on how best to prioritize any additional resources made available must be carefully considered to ensure maximum benefit. Ongoing improvement of sequence-based diagnostics in the last decade have helped to speed up the identification of TB infection, including rifampicin-resistant (and soon multidrug-resistant (MDR))² strains, and yet their introduction has not had a substantial impact on infection rates,

in part owing to high cost, the lack of point-of-care delivery solutions, and resource-limited health systems. Knowing that a patient has drug-resistant TB is only useful if the systems are in place to provide rapid and effective treatment³. Fortunately, on the treatment front, several new drugs are currently undergoing clinical trials, while initial results from the STREAM randomized controlled trial to test the efficacy and safety of shorter regimens treating for TB and MDR-TB look promising⁴. Progress, however slow, is therefore being made in better diagnosing and treating TB, yet in terms of bang-for-the-buck, prioritizing an effective new vaccine could well prove to be the most cost-effective approach, since it would tackle infection by both drug susceptible and MDR-TB strains. There are currently 12 TB vaccines in phase I, II and III trials, but an expansion of the vaccine pipeline alone will not be sufficient in the absence of better understanding the correlates of protection, biomarkers that indicate a TB-exposed host is immune from developing disease. Prioritizing the identification of suitable correlates of protection would facilitate screening of vaccine candidates at early stages and reduce reliance on pre-clinical animal models that have proven limited in predicting human efficacy.

For those affected by and working to tackle TB, the overall picture is not going to change anytime soon and the ideal of a TB-free world will remain distant. Yet the upcoming high-level meeting provides an opportunity for our political leaders to step forward, build on the strategic plans being established and infuse not only additional money, but also some much needed morale into the TB field. □

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