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EDITORIAL

Elimination of tuberculosis by 2050 by rapid molecular detection

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Only a small fraction of the estimated 500,000 patients who have multidrug-resistant tuberculosis and 1.37 million patients who have co-infection with tuberculosis and the human immunodeficiency virus (HIV) worldwide each year have access to sufficiently sensitive case detection or drug-susceptibility testing (1). Diagnostic delay, aggravated by the disproportionate frequency of smear-negative disease in HIV-associated tuberculosis, is common (2). The failure to quickly recognize and treat affected patients leads to increased mortality, secondary resistance (including extensively drug-resistant tuberculosis), and ongoing transmission (3). The complexity of mycobacterial culture and current nucleic acid–amplification technologies for the detection of tuberculosis and multidrug-resistant tuberculosis (4) and the need for the associated infrastructure restrict the use of such tests to reference laboratories.

The effective treatment of tuberculosis is a lifesaving intervention. The global scale-up of tuberculosis therapy has averted 6 million deaths over the past 15 years, making it one of the greatest public health interventions of our lifetime. Unfortunately, by the time most patients are treated, they have already infected many others. This failure to interrupt transmission fuels the global epidemic so that every year there are more new cases of tuberculosis than in the previous year.

National tuberculosis programs are particularly challenged by multidrug-resistant tuberculosis. Globally, fewer than 2% of the estimated cases of multidrug-resistant disease are reported to the World Health Organization (WHO) and managed according to international guidelines. The vast majority of the remaining cases are probably never properly diagnosed or treated, further propagating the epidemic of multidrug-resistant tuberculosis. The situation is further worsened by the epidemic of human immunodeficiency virus (HIV), especially in Africa.

For decades there has been little effort to improve techniques for diagnosing tuberculosis. Consequently, tuberculosis tests are antiquated and inadequate. The most widely used test (smear microscopy) is 125 years old and routinely misses half of all cases. These inadequacies are particularly problematic since such tests are generally performed in underfunded and dysfunctional health care systems. The problem is exacerbated by the widespread use of inaccurate and inappropriate diagnostic tools, such as serologic assays, in many countries (5).

Fortunately, in the past few years, several improved tuberculosis tests have received WHO endorsement for widespread use. Boehme and colleagues describe a new automated nucleic acid–amplification test that may allow a relatively unskilled health care worker to diagnose

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tuberculosis and detect resistance to a key antibiotic within 90 minutes. This test and others that are likely to follow have the potential to revolutionize the diagnosis of tuberculosis. Thus, in the coming years, rapid diagnosis and targeted treatment will provide the greatest opportunity for stopping the tuberculosis epidemic.

In a large, well-conducted, multi-country study, an automated tuberculosis assay (Xpert MTB/RIF) was evaluated for the presence of *Mycobacterium tuberculosis* (MTB) and resistance to rifampin (RIF). With a single test, this assay identified 98% of patients with smear-positive and culture-positive tuberculosis (including more than 70% of patients with smear-negative and culture-positive disease) and correctly identified 98% of bacteria that were resistant to rifampin (6).

If an improved rapid nucleic acid–amplification test is adopted globally, it could help avert more than 15 million tuberculosis-related deaths by 2050. However, even the most promising diagnostic test will have only limited impact if it does not reach the patients who need it. As with any diagnostic test or intervention, its actual impact will depend on the system in which it is used. Health systems must be strengthened so that patients do not delay in seeking care and have prompt access to appropriate treatment once they receive a diagnosis. Health-system barriers to the use of improved technologies must be anticipated and addressed. Although the burden on health systems will be reduced by a simple dipstick-like, point-of-care assay, such tests are not likely to be available in the short term (7).

Some developing countries now have the capacity to develop low-cost generic or novel assays adapted to local contexts and incorporate their scale-up in both national tuberculosis-control programs and private laboratories, supported by successful public–private partnerships. Emerging economies have the potential to become global leaders in innovative product development and delivery. If these countries successfully tackle their own tuberculosis problems, the elimination of tuberculosis by 2050 might become a reality.

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