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Editorial

It is health that is real wealth & not pieces of gold & silver

Despite the recent progress towards meeting the Millennium Development Goal target to halt and reverse the tuberculosis (TB) epidemic by 2015, the global burden of TB remains significant. In 2011, there were an estimated 8.7 million new cases of TB (13% co-infected with HIV) and 1.4 million people died from TB. Almost one million of these deaths were among HIV-negative individuals and 430,000 among people who were HIV-positive. TB is one of the top killers of women, with 300,000 deaths among HIV-negative and 200,000 deaths in HIV-positive women. In addition, progress in responding to multidrug-resistant TB (MDR-TB) remains slow. While the number of cases of MDR-TB notified in the 27 high MDR-TB burden countries is increasing and reached almost 60,000 worldwide in 2011, this number only reflects one in five (19%) of the notified TB patients estimated to have MDR-TB. In the two countries with the largest number of cases, India and China, the figure is less than one in ten[1]. Clearly, much work needs to be done and it was Einstein who once said 'The problems that exist in the world cannot be solved by the level of thinking that created them.' Not busy work, but smart work, is needed to create a solution. In public health, one solution could be a systems approach and integrated and decentralized laboratory services.

Today, laboratory testing in the mycobacteriology field is experiencing more changes than ever before. Determining what assays will be most useful to the health care provider is a challenge, and rapid acceptance of the new technology by the medical community an even greater one. Health care provider and TB Control officials must use the best available resources to determine the most appropriate care for their patients, and work together with the laboratory community to ensure that the communication channels are open.

The line of open communication and information flow becomes imperative when there is a suspicion of MDR-TB, and especially extensively-resistant TB (XDR-TB). Because the resistance to second-line TB medication severely compromises the treatment regimen options for TB patients, the rapid identification of patients at risk and prevention of further resistance is important. Patients in these subgroups should be prioritized for fast-track drug susceptibility testing, rapid molecular drug resistance tests, and strictly follow supervised treatment based on the drug susceptibility test results. Earlier identification of patients at risk for developing XDR-TB enables more diligent infection control measures, which are critical for preventing transmission of the disease[2].

In many health care settings, programmes for emerging infectious or chronic diseases are still organized vertically, including the establishment of similar testing capacities for different diseases. One effective answer to provide cost-effective, rapid and quality laboratory services with optimal impact on patient care is to move away from disease-specific silos and establish integrated laboratory services. An integrated laboratory network should be able to provide all basic primary diagnostic services for patients at each level of service without requiring patients to go to different facilities for specific tests. Such laboratory services might be delivered either directly by cross-cutting disease programmes at defined levels of the network: *(i)* by provision of integrated services for patients presenting with a particular clinical symptom (*e.g.* fever), *(ii)* by establishing integrated diagnostic platforms targeting several diseases, *(iii)* indirectly, by using an integrated specimen collection, referral, and reporting system eliminating the need for the patient to commute, often too far distances [3].

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However, integration of laboratory services requires the development of new, innovative, more accurate and often more complex analytical tests or pre- and post-analytical services, including specimen collection and transportation, commodity management and reporting of results. In remote high burden settings, mobile phone and SMS-based technologies are starting to prove to be an effective tool to increase the efficacy of specimen collection and reporting results of acid-fast bacilli (AFB) microscopy, and to organize reporting and commodity management for rapid diagnostic testing of HIV and malaria. Patients have better access to these services at the community level without the need to travel[4]. New cost-effective quality microscopes with dual light and fluorescent capacity are able to perform screening for more than one disease. A wider access to quality consumables such as bacterium filters enabled the recent development of a simple and cost-effective filter concentration method that is improving the sensitivity of AFB smear microscopy, and consequently, the case detection rate[5]. In the future, the AFB microscopy-positive filters may be submitted to a molecular laboratory for confirmation of *Mycobacterium tuberculosis* complex and molecular drug resistance, along with dried blood spot samples for HIV PCR. Molecular techniques are one of the best tools to develop either multi-disease platforms or to decentralize highly sensitive diagnostic systems, since no costly Biosafety Level III laboratory facilities are needed. Earlier molecular technologies were restricted to highly sophisticated reference laboratories partly due to their costs and complexity. Therefore, for example, rapid diagnosis of TB and MDR-TB patients could not benefit from the advantages of these techniques since most patients did not have access to these reference laboratory services. A quantum leap was realized when molecular line probe assays (LPA) began to be used directly on clinical specimens of TB and MDR-TB suspects, resulting in a paradigm shift of setting up cultures only when resistance-associated mutations are detected[3]. This allowed for a much faster turnaround time for initial diagnosis and decentralization of services to district and regional levels and use of LPAs as a more near-patient diagnostic tool. Further advances of molecular assays such as the GeneXpert MTB/RIF® system included additional milestones such as a less complex, better standardized, uniform platform-based testing; significantly lower biosafety and contamination control requirements; higher sensitivity on AFB smear-negative patients; and potentially lead to improved paediatric and extrapulmonary TB diagnosis including TB meningitis[6,7]. The roll-out of Xpert MTB/RIF, a rapid molecular test that can diagnose TB and rifampicin resistance within 100 minutes, has been impressive. Since its endorsement by WHO in December 2010 and the end of June 2012, 1.1 million tests had been purchased by 67 low- and middle-income countries; South Africa (37% of purchased tests) is the leading early adopter. A 41 per cent price reduction (from US$ 16.86 to 9.98) in August 2012 should accelerate uptake[1]. The most important improvement of Xpert MTB/RIF is that it can be used directly on unprocessed clinical samples; other molecular tests use the leftover from specimens processed for growth detection using early 20th century methods. The recently developed PrimeStore Molecular Transport Medium (Longhorn, USA) makes a further major step towards integrated and simplified specimen collection and transport for molecular testing, allowing the preservation and stabilization of RNA and DNA in a wide range of clinical specimens at ambient temperature. Specimens are chemically shielded from degradation and an internal control provides a built in measure of integrity and serves as a carrier for increasing extraction yield from low level specimens[8]. These features enable TB molecular testing to be performed also by a non-mycobacterium laboratory trained personnel in an integrated setting or after regular service hours for urgent or fast-track testing in a general routine diagnostic setting. The novel platform based approach will soon allow not only the integrated testing of other organisms but also reflex testing for additional drug resistance such as fluoroquinolones (screening for XDR-TB) based on initial testing results. Laboratory-based accuracy data are not sufficient to judge the contribution of new diagnostic tools for case finding, treatment, cure, and ultimately TB control. Despite numerous microbiological studies of improved TB diagnostic technologies, we remain remarkably ignorant of how best to implement better tests to improve patient care; who should receive the limited capacity for better tests to maximize health impact; how these tests may impact patient-relevant outcomes; and how these issues vary between settings. The impact of better diagnostic tests applied in the routine and non-trial controlled circumstances on the equity of care is largely unexamined. We do not know yet how this novel technology will affect the delays and costs faced by patients in their journey towards a cure for this disease of poverty. In some countries for example, the rapid roll-out of Xpert MTB/RIF has exacerbated the already sharp need for improved access to second-line drugs to treat M/XDR-TB and highlighted the

insufficient financial and organizational capacities of national TB programmes to introduce and scale-up the WHO recommended Programmatic Management of Drug Resistant TB. To ensure universal access to MDR-TB care, as contemplated by World Health Assembly[9] international as well as domestic resource will need to be mobilized and spent more cost-effectively to reduce the economic burden on patients and health systems[10]. Fortunately, the pipeline of newer molecular platforms is not empty and these new assays will most likely be the first point-of-care (POC) systems, allowing further decentralization of testing to health care centre level or to mobile diagnostic units, similar to advanced POC flow cytometry testing for HIV viral load.

In order to accommodate testing of the magnitude needed to diagnose the dreadful diseases such as AIDS, TB and malaria (ATM), more robust public-private partnerships need to be developed, especially with decentralization and integration of testing services for ATM.

We all aspire to a world free of TB, and health in general for all. It was Mahatma Gandhi who poignantly stated 'It is health that is real wealth and not pieces of gold or silver'. It is one mission and we are one team!

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