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Editorial

Commemorating World TB Day 2020: "IT'S TIME" — It's time to End the Global TB Epidemic

World TB Day falls on March 24th each year, and it commemorates the day in 1882 when Dr Robert Koch announced that he had discovered the microbial cause of tuberculosis, *Mycobacterium tuberculosis* (WHO, 2020a,b,c). At the time of Professor Koch's announcement in Berlin, TB was an endemic in Europe and the Americas, and caused the death of one in every seven people (Wallstedt and Maeurer, 2015). Koch's discovery opened the way towards diagnosing, treating and curing patients with TB. One hundred and twenty eight years later, according to the WHO Annual TB Report, an estimated 10 million people fell ill with TB and 1.5 million died of it. Tuberculosis remains the top infectious disease killer worldwide (WHO, 2019).

The theme of World TB Day 2020 is the same as last year - 'IT'S TIME'. This places emphasis on the urgency to act on the commitments made by global leaders at the September 2018 UNGA-HLM (WHO, 2020a,b,c) to: scale up access to prevention and treatment; build a multisectorial accountability; ensure sufficient and sustainable financing including research; promote an end to stigma and discrimination, and promote an equitable, rights-based and people-centered TB response. World TB day gives all TB stakeholders time to reflect and raise political, public and donor awareness about the devastating health, social and economic consequences of TB, and to step up efforts to end the global TB epidemic. The End TB Strategy (WHO, 2015) has set ambitious targets to reduce TB incidence and mortality by 90% and 95% respectively by 2035 compared with 2015.

Each day, over 4000 people lose their lives to TB and close to 30,000 people fall ill with this preventable and curable disease. This is nearly 3 decades after tuberculosis was declared a global emergency by the WHO. For a disease where effective treatment has been available for over 60 years, this status quo is unacceptable. Observance of World TB Day 2020 provides yet another opportunity to raise awareness about commitments made by the United Nations and to take forward solutions needed to find, treat, and prevent this devastating disease.

In support of World TB Day 2020, The IJID is publishing this TB theme volume of 17 focused articles, which cover a range of topics:

The review by Alffenaar et al. (2020) highlights the importance of therapeutic drug monitoring (TDM), an important tool in the era of precision medicine recently recommended by the ATS/CDC/ERS/IDSA multidrug-resistant guidelines (Nahid et al., 2020). TDM is only useful for dose optimization if a patient is on an appropriate regimen guided by drug susceptibility testing. Expanding PK/PD research followed by clinical trials including both clinical outcome as well as cost-effectiveness will increase the level of evidence supporting TDM. TDM will also help preventing the development of resistance by ensuring adequate drug levels while reducing adverse events. The challenge is the availability of the techniques to monitors drugs concentrations. Simpler methods like saliva or urine testing are urgently needed. Akkerman et al. (2020) highlight that there is still no guidance for assessing lung function in patients completing their treatment to assess quality of life and need for pulmonary rehabilitation. These patients are often also malnourished which lead to further deterioration of the lung function.

Migliori et al. (2020) discuss the current management of multi-drug resistant (MDR) TB. The core published documents and guidelines have been reviewed including the recently published MDR-TB WHO rapid advice and ATS/CDC/ERS/IDSA guidelines (Sterling et al. 2020). The document, resulting from a Consensus among GTN (Global Tuberculosis Network) experts, represents a comprehensive and complete clinical guidance on this important issue.

Two papers discuss important clinical and public health priorities in core settings around the globe, with special focus on LTBI detection and treatment. The Russian Federation has implemented an annual screening program for LTBI in children. As a result, the annual incidence in Russian children decreased from 19.1 per 100,000 in 2001 to 8.3 per 100,000 population in 2018 (Aksenova et al., 2020). In China, the development of active TB from LTBI in the general rural population was 0.87 per 100 person-years in the first 2 years among individuals who newly converted IGRA positive. The large trials conducted more than 50 years ago were reviewed to describe the historical background for current guidelines on LTBI and to demonstrate similarities with current high-burden populations where there is limited use of Tuberculosis Preventive Therapy (TPT). The trials demonstrated a 27–95% reduction in incidence of active TB among the treated compared with placebo (Mølhave and Wejse, 2020). A 3-month regimen with twice-weekly rifapentine plus isoniazid (3H2P2, both with a maximum dose of 600 mg) has been practiced for LTBI treatment in China for years (Cui et al., 2020). Respiratory clinic follow-up after TB treatment may be useful in the monitoring and management of post-TB infections especially in patients with residual cavitation

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and/or bronchiectasis as further infectious insults can be prevented or mitigated (Hsu et al., 2020).

Clinicians should also be aware of the possibility, and associated higher mortality, of NTM-Aspergillus co-infection (Jhun et al., 2017; Naito et al., 2018). The incidence of NTM infections is rising owing to a growing population of immuno-compromised and vulnerable individuals, complex medical and surgical procedures as well as increased awareness and diagnostic capabilities. Improved and rapid detection of TB cases in high burden countries has however also brought NTM infections into limelight and identified a need for research efforts towards rapid diagnostic tests, and identification of biomarkers to monitor treatment response in patients with NTM infections (Ahmed et al., 2020).

The development and deployment of new tools will certainly accelerate progress towards ending TB, however, the end of TB is only realizable if sustained efforts to actively find TB cases, that cover a large proportion of the population, are adopted even with currently available tools (Chakaya et al., 2020). Contact investigation is the search for secondary cases of tuberculosis (TB) or tuberculosis infection (LTBI) among contacts of patients with a transmissible form of TB. The implementation of preventive therapy for persons with the highest risk of developing TB, that is the reduction of the pool of future cases of TB, is now considered as one of the activities able to support the decline in the prevalence of TB. This implies that the search for *Mtb*- infected contacts and the prevention of TB should be performed in parallel to the diagnostic and curative activities (Zellweger, 2020). In countries with a high proportion of migrants from high endemic countries, screening for LTBI has a high priority. Molecular typing and development of public private partnerships are needed (Al Abri et al., 2020a).

Accurate data on the prevalence of LTBI due to MDR *Mtb* strains are unavailable, since the strains cannot be isolated for resistance testing. The interferon-gamma release assays (IGRA) assays are not ideal due to issues of sensitivity, specificity, inability to distinguish infection with MDR-*Mtb* strains and the high costs. The development of new diagnostic tests which are better than currently available LTBI tests at predicting who is at risk of progression to active TB disease are urgently needed. Mwaba et al. (2020) reflect on the challenges of developing new diagnostic tests for Latent TB infection due multi-drug resistant strains of *Mycobacterium tuberculosis*.

A Markov model was used to estimate cost of screening using an Interferon-gamma release assay (IGRA) or tuberculin skin test (TST), applied to all migrants from high TB endemic countries, followed by preventive TB treatment. The model compared seven different scenarios comparing the direct cost and the quality of life years, QALYs, saved. IGRA testing followed by three months preventive treatment with rifapentine/isoniazid, 3HP was the most cost-effective intervention (Al Abri et al., 2020b).

The TB prevalence among newly enrolled HIV-infected patients during the study period was 13.4% (22/164) in Guinea Bissau (Aunsborg et al., 2020). Using the TBscore and a diagnostic algorithm it was possible to bring the proportion of patients started on TB treatment from 2.7% (10/367) the year before the study to 10.4% (17/164) during the study period (Aunsborg et al., 2020).

FDG PET/CT imaging has high sensitivity in active TB, complementing conventional radiologic imaging (X-ray, CT, MRI) in the diagnosis of primary pulmonary, extrapulmonary and post-primary or miliary TB. FDG PET/CT has low specificity when it is used for solitary pulmonary nodule characterization and its ability to differentiate TB from malignancy is limited in this setting (Priftakis et al., 2020).

The main recommendations and contraindications of sanatorium therapies (i.e., bed rest, fresh air, sunlight) and pulmonary collapse techniques are reviewed, evaluating their physiological basis and their impact on patients' outcomes. Studies describing new interventional pulmonology and surgical techniques, as well as we assess new perspectives based on old medical and surgical treatments, whose potential implementation could help complicated patients were reviewed (Mondoni et al., 2020).

Keeping up to date on the latest developments of TB epidemiology, diagnostics, treatment regimens is vital for continuing medical education (CME) and continuing professional development (CPD). For achieve this, update courses with the latest developments are important, especially. The Queen Mary University of London (QMUL) Certificate in Tuberculosis (TBCert) course provides a unique opportunity for CME/CPD for a global healthcare worker fraternity to receive the latest information from various international experts. It can be accessed remotely from any corner of the globe since it is a distance-based learning course, which was launched in 2019. The course is open to doctors, nurses and public health workers who wish to sub-specialize in tuberculosis (Tiberi et al., 2020).

The papers in this World TB Day 2020 IJID theme series volume not only highlights the many challenges and gaps in meeting the WHO goals to end TB by 2035, but they also show several innovations in the diagnosis and management of this continuing global scourge of TB. More investments and commitments from national governments and donors is needed to bridge the widening implementation gap and to achieve the goals of the UN General Assembly resolution for the UN High-Level Meeting on TB, for ending the TB epidemic by 2035.

Conflict of interest

All authors have a specialist interest in TB. Authors declare no other conflicts of interest.

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