

Tuberculosis and the strategy for the New Millennium: not simply “more of same”

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Since the beginning of human history, tuberculosis (TB) has threatened the wellbeing of mankind. The last Global Tuberculosis Report, published by the World Health Organization (WHO) in 2013, highlighted the significant burden in morbidity and mortality that *Mycobacterium tuberculosis* still bears in the world today [1]. The strong association between the TB burden and poverty has been well quantified in recent decades and this link remains ever more relevant today [2,3]. While it is true that wealth shields no individual from TB, it is equally true that the disease exacts its heaviest toll on the poorer communities in the world. The geographical areas most affected by the disease are in sub-Saharan Africa and South-East Asia, where unfavourable political, social and economic factors conspire together against the health of people and in favour of TB and other infectious conditions linked with poverty, such as HIV/AIDS and malaria.

With the wide introduction in the late 1940s of the first antibiotics active against TB, the fate of the disease appeared to be sealed and eradication seemed to be within reach as TB rates and deaths plummeted in many countries. Alas, the optimism soon faded. Few anticipated that *Mycobacterium tuberculosis* would continue to smoulder among the disadvantaged groups and lay latent within a large reservoir of otherwise healthy infected persons, rearing up its head from time to time to declare its ominous presence. New drugs against TB were released in the 1950s and 1960s but public health programmes were not able to deliver them equitably and effectively to all the populations across the world. As the disease seemed to wane in the rich world, its prominence on the global public health agenda also diminished. Control programmes were dismantled in the 1970s. Another adaptive property of TB bacilli is their propensity to develop resistance to the drugs used in their treatment, particularly when these are not given in combination. The sum product of all this is that about one third of the world's population (i.e., over 2 billion persons today) is thought to be infected with TB; some of these individuals are at risk of contracting active disease at some time in their life. The HIV epidemic fuelled the reactivation of TB and led to resurgence of the disease, particularly in Africa but also elsewhere starting in the late 1980s.

As numbers of TB cases rose in both poor settings and some large cities of rich countries WHO declared TB a global emergency in 1993. Advocacy efforts and the effective implementation in many countries of the essential elements of TB control based on political commitment for control, bacteriological diagnosis, standardized anti-TB treatment with

supervision, uninterrupted supply of quality-assured medicines, and a standardized recording and reporting system - a strategy branded as DOTS (originally an acronym for Directly observed treatment short course) - characterized the early global response to TB. In 2006 DOTS was enhanced to the more comprehensive Stop TB Strategy which renewed the drive against TB in the world and expanded it to other important domains, such as the management of drug-resistant TB and TB/HIV and the engagement of the non-state sector and communities, and research [4]. These efforts led to important results. It is currently estimated that 56 million people were cured of TB and 22 million lives saved between 1995 and 2012 [1]. Target 6c of the United Nations' Millennium Development Goal 6 relevant to TB - to halt and begin to reverse TB incidence - has been achieved globally before the target year of 2015 [5]. By current forecasts the other international target of a 50% reduction in TB mortality by 2015 compared with a baseline of 1990 may also be attained. With 5.7 million new and relapse TB cases reported in 2012 global case detection reached 66% (range: 64-69%) of estimated incidence; treatment success in new sputum-smear positive patients was 87% for the 2011 cohort, thus surpassing the global target threshold of 85%.

Despite these successes, in 2012 TB was still responsible for an estimated 1.3 million deaths and 8.6 million new cases of disease. About 450,000 TB cases with resistance to the two most effective drugs, isoniazid and rifampicin (multidrug resistance or MDR-TB), more difficult and expensive to treat, are estimated to have emerged in 2012 [1]. The TB elimination threshold (<1 active TB case per million population per year) will not be reached by 2050 if the current pace of decline in TB incidence, 2% per year, is not increased substantially [6]. A new strategy is clearly needed, which ropes in innovations and new technologies and which gives a better handle on the broader determinants of TB. In brief, a rethink of the approach with eyes fixed firmly upon tomorrow's world.

The new WHO post-2015 strategy, which was endorsed by a resolution of the World Health Assembly on 21 May 2014 in Geneva, was the product of such new thinking [7]. Consultations and discussions between stakeholders took different forms and over 2 years. The strategy sets its vision high and wants to see TB deaths and suffering come down to such a low level that every country in 2035 should have an incidence similar to that of the richest countries today.

More specifically, the TB community will measure its success towards that goal through three key targets to be met by 2035, namely:

1. a 95% reduction of TB mortality (in comparison with 2015 figures);
2. a 90% reduction of TB incidence (down to <10 cases per 100,000 population from 122/100,000 in 2012);
3. no families affected by TB who face catastrophic costs.

The framework for achieving this is built upon three main "pillars":

- a. **integrated and patient-centred care and prevention:** building upon the core components of the previous WHO strategies which served their purpose well and which remain the cornerstones of the approach to TB care but employing new technologies more effectively and innovatively;
- b. **bold policies and supportive systems:** political support needs to be more clearly expressed through appropriate funding available for TB care and prevention, and with broader-based engagement of communities, civil society organizations, and private care providers. An emphasis on universal access to health care and social protection will be essential;
- c. **intensified research and innovation:** more focus on new research in diagnostics, therapeutics, and prevention and the rapid translation of research findings into action for patients.

Clearly we have come a long way from the DOTS mind set of the mid-1990s. But so has TB and the people who live within its long shadow. The new post-2015 strategy holds a mirror to the reinvigorated will of the public health community and the fresh political mandate that a World Health Assembly resolution affords. Only time will tell if this drive will succeed. But if it does then we will close a historical chapter of human suffering, neglect and disease.

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