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Is the eradication of tuberculosis 'yesterday's ambition' or 'tomorrow's triumph'?

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ABSTRACT – Tuberculosis (TB) remains a serious infectious disease continuing to cause around 1.8 million deaths annually. The great paradox is that despite the availability of effective treatment for the past 60 years, it continues to spread relentlessly, particularly in sub-Saharan Africa due to the fuelling effect of the HIV/AIDS epidemic. It is no longer a medical epidemic, but an epidemic of injustice. Increased political and financial investment by the industrially developed nations, as well as sustained political will in the affected countries, is required to bring TB under control. It is imperative that the control should be linked to that of HIV which is also closely associated with poverty, poor housing and malnutrition. The historical, social, philosophical and political perspectives that may have influenced the failure of TB control are discussed. Once again, therefore, the question is raised – can TB be brought under control?

KEY WORDS: complacency, control, developing countries, eradication, funding, HIV, mortality, tuberculosis

Tuberculosis (TB) remains a serious infectious disease responsible for 1.8 million deaths annually.[1] In sub-Saharan Africa the epidemic is spreading rampantly, being fuelled by the HIV/AIDS pandemic. Tuberculosis is the classical example of a disease which, despite the availability of an evidence-based highly effective and cost-effective intervention, continues to rob millions of people worldwide of their lives. The great tragedy of this disease is failure of the international community to translate numerous advances in medical science over the past half century into workable strategies that demonstrably improve the health, and save the lives, of millions of people living in poor developing nations. Through inadequate use of existing diagnostic, treatment and prevention tools, a golden opportunity to take a significant step towards controlling TB is being missed.

> *The tubercle bacillus is an index by inversion of the real progress of the human race. By it the claim of civilization to dominate human life may fairly be judged. Tuberculosis will decrease with the substantial advance of civilization, and the disease will as surely increase as civilization retrogrades.*

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These words were written in a paper entitled 'Tuberculosis and civilization', by the US physician John B Huber in 1907, long before there was any effective therapy for this disease.[2] Huber's comments emphasise that TB gives a clear measure of the impact of poverty, inequity and injustice on human health and that, despite the contributions of a few dedicated workers, the overall response to this disease, which mainly afflicts the most vulnerable in society, has mostly been one of sustained incompetence and neglect. This is no new phenomenon.

Sir John Crofton, a British pioneer of anti-TB chemotherapy, remarked that, 'It is a sad reflection on society's incompetence that, more than thirty years after the methods for cure and prevention were evolved and before the advent of the HIV epidemic, there were already more patients with active tuberculosis in the world than there had been in the 1950s'.[3] Tragically, over the 16 years since these words were written, the situation remains largely unchanged with gains in some regions being offset by increasing incidences in others. There were, in 2008, an estimated 8.9–9.9 million new cases of TB and, because of the chronic nature of the disease, 9.6–13.3 million active cases in the world.[1] There were an estimated 1.55–2.32 million deaths from the disease in 2008, 1.1–1.7 among HIV-negative, and 0.45–0.62 million among HIV-positive, people.

The ethical and moral imperatives of TB control have been met with ignorance and apathy. In a powerful and hard-hitting article Lee Reichman lays the blame for apathy at the door of physicians, health and community workers, governments, the press and international agencies. He added that '… if any of these parties did what they should do, things might be different, especially if they were to show the wholly justified but shockingly absent outrage for which the situation cries out'.[4]

The World Health Organization (WHO) declared TB a global emergency in 1993,[5] and established the Stop TB Partnership initiative, ensuring the widespread adoption of DOTS, originally an acronym for directly observed therapy, short course, but now the 'brand name' for WHO's five-point control strategy.[6] The WHO DOTS strategy has had a positive impact and the number of cases of TB is falling in all WHO regions with the tragic exception of sub-Saharan Africa. Between 1995 and 2008, 36 million TB patients were successfully treated in DOTS programmes, and an estimated eight million deaths were prevented. Sadly, these encouraging gains have been largely offset by the marked rise in prevalence in sub-Saharan Africa in the wake of the HIV epidemic. Accordingly it is, at the present time, considered unlikely that the WHO goal of halving the 1990 overall prevalence of, and mortality due to TB by 2015 will be achieved.

Increased financial investment by the industrially developed nations, which have a mere 5% of the global burden of TB and 2% of the deaths,[7] as well as sustained political will in the affected countries, is required to support this highly effective strategy. It is imperative that the control of TB should be linked to that of HIV which, like the former disease, is closely associated with poverty and especially with the disempowerment of women.

The year 2010 marks the 30th anniversary of the completion of the smallpox eradication campaign. At that time, it was believed that similar strategies would lead to the eradication of other widespread diseases including TB, malaria and polio. Unlike TB, smallpox was an acute disease with very prominent diagnostic characteristics and against which there was a highly effective vaccine. Nevertheless, a further 30 years of research has provided sophisticated molecular technology with the strong potential to provide sensitive diagnostic tools, novel vaccines and immune modulating agents as well as 'designer drugs', based on the detailed sequencing and analysis of the genome of the causative organism.[8]

Cynics might well argue that eradication of a disease such as TB is beyond the capability of the human race at the present time, when so many other major issues clamour for attention and even threaten our survival. With some justification they will point to the financial crisis brought about by a few that will ultimately hurt the most vulnerable and powerless in society, and to the diversion of resources into unwinnable conflicts which are alienating rather than uniting those of different cultures and faiths. They will certainly cite the weak and indecisive outcome of the recent Copenhagen summit on climate change as a clear sign that self-interest at the individual and national level will stand in the way of global cooperation in the face of very real menaces. To refuse to address the pressing needs of the poor and vulnerable would be to abandon our humanity. As already mentioned, the control of TB is just one of many global issues clamouring for urgent attention, yet there are compelling reasons for according it very high priority, perhaps even the highest priority, among the infectious diseases.

Firstly, TB is more than just a disease that is prevalent among the poor – it is a major cause of poverty. As it predominantly affects the economically active age group, three quarters of all cases occur among those aged 14 to 54 years, the indirect economic impact of this disease is severe. On average, a single case of TB reduces the income of a household by 25% and the death of an adult from this disease causes 15 years of lost income.[7] Although most cases occur in the poorer nations of the world, there is a distinct relationship between the disease and poverty and social deprivation in the more wealthy nations including the UK.[9]

Secondly, it has a particular relation to HIV disease; indeed, the two have been termed 'the cursed duet'. The risk of an HIV-positive person developing TB after infection by the tubercle bacillus is very much higher than in an HIV-negative person and the progression from infection to active disease is rapid.[10] Infection by HIV is by far the greatest risk factor for TB – in sub-Saharan Africa, over a half of cases of TB are HIV-related.[1]

Thirdly, it is not restricted to geographical regions – it has the potential to cause disease anywhere and in anyone in the world. No one is safe until all are and TB demonstrates that global health is a local issue.[11] The tubercle bacillus knows no barriers of class and wealth – 'Nor are the rich, in fancied security, any freer from the danger than were the gallants and gentle ladies in Poe's dreadful tale, who thought by isolating themselves to escape the Black Death'.[2]

Finally, while drug susceptible TB readily responds to a six-month course of therapy, treatment of patients with multidrug resistance; namely, resistance to the two most powerful drugs, isoniazid and rifampicin, is far more costly and requires extended treatment under supervision. In the words of Médecins Sans Frontiers, 'It is only a matter of time before multi-drug resistant tuberculosis…becomes a daily reality world-wide. The cost of the epidemic to the world will be counted in billions of pounds and may become unmanageable'. The situation is now far more serious as extreme drug resistance, that is, multidrug resistance with additional resistance to at least the quinolones and an injectable second-line agent, has been detected in several countries.[12] Although, after decades of inactivity, novel anti-TB drugs are now being actively sought.

Access to healthcare, in its broadest sense, is acknowledged as a human right, as enshrined in Article 25 of the United Nations Universal Declaration of Human Rights.[13] Everyone has the right to a standard of living adequate for the health and well-being of themselves and of their family, including food, clothing, housing, medical care and necessary social services, and the right to security in the event of unemployment, sickness, disability, widowhood, old age, or other lack of livelihood in circumstances beyond their control. Article 25 was reaffirmed in 1978 by the WHO and other international agencies in the so-called Alma-Ata Declaration of 'Health for all by the year 2000' and it was stated that the gross inequality in the health of people, particularly between the developed and developing countries, is politically, socially and economically unacceptable, calling for a new international economic order to address this inequality.

Today it is abundantly evident that no such new international economic order has emerged. On the contrary, the rich – poor divide is increasing, with devastating effects on the physical and mental health of the world's population of whom a quarter, some 1.3 billion people, live in extreme poverty, with a daily income of less than one US dollar, and are 10 times more likely to die under the age of 15 years than those in the richest quarter, with infection as a major cause.[14] Women are likely to die at an earlier age than men due to a multitude of causes and are between 10 and 100 times more likely to die in childbirth than their counterparts in affluent countries such as the USA and UK. Infectious disease, especially TB, malaria and HIV, are more frequent causes of death during pregnancy and childbirth than obstetric complications.[15] An estimated 190 million children under five years of age suffer from chronic malnutrition, and one million become homeless orphans each year while millions die of diseases that are preventable by immunisation programmes, clean water supplies and adequate sanitation.

One error that has led to much complacency is the concept, known as the McKeown thesis, that the decline in the incidence of, and mortality due to, TB and other infectious diseases is the result of general socio-economic improvement.[16] There is a danger that this attitude will divert attention and effort from specific disease control measures towards a more general alleviation of poverty and injustice, even though at present there are no strategies in place to achieve this goal. This attitude also leads the historical role of the medical profession as a champion for healthcare through advocacy as well as evolving medical practice being overlooked. Public health advocacy has been defined as 'the process of overcoming major structural (as opposed to individual or behavioural) barriers to public health goals', with the comment that these barriers 'include some of the most formidable political, economic and cultural forces imaginable'.[17]

Another erroneous assumption that has had very serious adverse consequences is that if an infectious disease has been in more or less steady decline for several decades in a given region or country, it will continue to decline to elimination. Inevitably, the dismantling of TB control services leads to a resurgence of the disease, as graphically portrayed by Reichman in a paper appropriately entitled 'The U-shaped curve of concern'.[18]

One of the great challenges facing health service reform is the need to ensure a just and fair distribution of medical care capable of responding to local needs. It is now evident that the so-called health sector reforms of the 1990s formulated by the World Bank and other international donor agencies,[19] aimed at generally strengthening local healthcare provision, destabilised or disrupted specific control programmes for TB and other major threats to health. It is indeed only too evident that Tudor Hart's Inverse Care Law – 'the availability of good medical care tends to vary inversely with the need for it in the population served' – still applies in many situations. With prophetic foresight Hart noted that the law applies most especially when medical care was most exposed to market forces and affirmed that market-based medical care is 'a primitive and historically outdated social form, and any return to it would further exaggerate the maldistribution of medical care'.[20] This, alas, is just what has so often happened, due in no small part to the dogmatic adherence to concepts linked to the vaguely defined ideology of the 'free market', driven by competitive private initiatives rather than altruistic concern for the under-privileged.

In the case of TB, the declaration of this disease as a global emergency 17 years ago and, more recently, the threat of a pandemic of untreatable strain has led to a number of commendable and inspired European Union, Gates Foundation, WHO and Global Fund led initiatives including the recently established Foundation for Innovative New Diagnostics, European Developing Countries Clinical Trials Partnership, Global Alliance for TB Drug Development and the WHO Stop TB 'Research Movement', but far more is needed in respect to international funding and cooperation. New TB diagnostics, TB drugs or shorter treatment regimens, and vaccines are currently being developed and evaluated. Despite this investment, few new interventions or tools have emerged. An editorial in *The Guardian* (14 December 2009) concluded with the assertion that the eradication of TB, as well as HIV disease, malaria and polio, is 'yesterday's ambition'.

Once again, the question is raised – can tuberculosis be brought under control? Will the WHO goal of a 15% annual reduction in incidence in regions where DOTS is proving effective and there is a low incidence of HIV infection be met? Can the serious problems of HIV-related TB in sub-Saharan Africa and those posed by extensively drug resistant TB be overcome? Or is the eradication of TB, as well as the pandemics of malaria and HIV disease, indeed 'yesterday's ambition'? On the answer to this question rests another question – has the human race, despite phenomenal advances in scientific endeavour, lost control of its destiny? In recent decades, the word 'apocalypse' has often been used in predictions of an impending disaster of unprecedented magnitude, yet the true meaning of the word is 'revelation'. Certainly the Apocalypse of John in the Bible speaks of struggle and catastrophe, but this is the prelude of a new age of peace and harmony. Perhaps the conquest of TB, 'the captain of the apocalyptic men of death', will determine whether we can indeed usher in this new age. Only time will tell.

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