

Partners in Crime: The Deadly Synergy of Tuberculosis and Tobacco Smoke?

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The tuberculosis epidemic is under control in most of the developed world. Incidence rates for new cases in Eastern Europe and North America are less than 10 per hundred thousand of the population [1]. In developing countries the situation is far from controlled: South Africa has an incidence rate of 1170 (per hundred thousand of the population) closely followed by Zimbabwe (799) Mozambique (746) and Cambodia (506). India and China however share the biggest burden of cases accounting for over one third of the global caseload [1]. With the advent of MDR and XDR TB [2,3] and increasing global migration, rates of TB are increasing in low incidence countries like the UK.

The control of tuberculosis in Europe in the early part of the 20th century was largely due to improved living conditions and nutrition – the first effective TB drugs only become available in the early 1960s. The risk factors associated with active tuberculosis are well described with poverty, malnutrition and overcrowding remaining major challenges to global health. HIV is undoubtedly driving the epidemic in sub Saharan Africa where enormous effort and resources are being directed to anti-retroviral therapy and HIV control. However, an often-overlooked risk factor driving TB is tobacco smoking. The attributable fraction of TB due to various risk factors has been estimated for high burden countries; these include malnutrition (26.9%), air pollution (22.2%), tobacco smoking (15.8%), HIV (11%), alcohol misuse (9.8%) and diabetes (7.5%) [4]. This implies that ~16% of all TB cases globally are attributable to tobacco smoking. It is noteworthy that this risk factor, although less than air pollution and malnutrition, exceeds the fraction attributable to HIV infection, and is a more easily modifiable factor. Epidemiological data indicate that tobacco smoking increases the risk of becoming infected (i.e. developing latent TB infection), developing active TB, and dying from TB by roughly 2 fold [5-7].

It could be argued that enough is known about the deleterious effects of tobacco smoke and therefore studying this in the context of TB is unnecessary. This is both short sighted and premature. Though the epidemiological evidence suggests a deleterious effect of smoking on TB there are a number of factors (poverty, poor nutrition, alcohol etc) that confounds the relationship. Further study of this interaction may yield novel insights as very little is known about the direct effects of tobacco smoke on TB-specific immune responses. Recently, Shang and colleagues demonstrated that tobacco smoke altered T cell responses, and modulated mycobacterial containment in a murine model of TB [8]. Preliminary human data (published in abstract form) have shown that BCG-driven monocyte-derived macrophage cytokine responses (TNF- α , IL-10, INF- γ) are significantly impaired by tobacco smoke [9]. Nicotine alone may have similar effect [9] and has been shown to be immunomodulatory [10]. Several questions however remain unanswered – is the increased risk of active TB due to the direct immunological effects of tobacco smoke resulting in increased progression from latent to active disease or due to the

tobacco-associated structural lung disease attenuating mycobacterial pulmonary defences?

The benefits of quitting smoking are wide ranging: not only does one reduce the risk of COPD, cancer and cardiovascular disease, but one may potentially eliminate 16% TB cases globally. There are further positive cost-related 'knock-on' implications as money spent on tobacco (more than half a days wage in some countries) [11] may assist in reducing poverty and malnutrition. However, will quitting smoking whilst on TB treatment alter clinical outcomes? Will stopping smoking affect the progression from latent to active disease? Answering these questions will require well-designed clinical trials. The potential that nicotine alone may increase TB susceptibility raises concerns and adds support to the FDA efforts to control nicotine-containing products such as electronic cigarettes and hookah/ water pipes [12]. It furthermore questions the role of nicotine replacement as an aid to quitting smoking in those with TB.

Tobacco cessation is likely to be one of the most cost effective strategies in reducing the global burden of TB whilst also potentially impacting poverty and malnutrition. Although many unanswered questions remain about the immunological effects of tobacco and nicotine, and the best approach to promoting cessation alongside TB control, the time to act is now so that global TB control can more rapidly be achieved. It is crucial for policy makers and national TB programmes to take note of the deleterious impact of smoking on TB control. High quality research on how best to quit smoking in those with TB is urgently required.

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