

More XDR TB among patients with HIV

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Although antibiotics have saved millions of lives, their use and misuse has often led to the development of resistance in the agents that they are intended to fight. SACEMA's Brian Williams recently published a commentary on an article in published in *Science Translational Medicine* in which Sergeev et al. used dynamical models to investigate the relationship between HIV and drug-resistant strains of TB (1,2). With the increasing use of antibiotics to cure TB the incidence of strains of TB resistant to first-line single drugs [drug-resistant (DR) TB] began to spread, followed by resistance to several drugs [multidrug-resistant (MDR) TB], and now to the main first-line drugs as well as three or more classes of second-line drugs [extensively drug-resistant (XDR) TB]. The emergence of XDR TB as potential threat to public health was first seen in an outbreak in Tugela Ferry in KwaZulu-Natal (3,4) in which there was very high mortality and in which almost all of the patients were coinfecting with HIV. Fortunately, it is likely that good first line TB control measures may still be able to control an epidemic of both drug sensitive TB as well as drug-resistant TB. However, the global HIV pandemic has led to dramatic increases in the incidence of TB, and the impact on the incidence of drug-resistant TB, both in absolute numbers and as a proportion of all forms of TB, remains uncertain.

The article in *Science Translational Medicine* used a dynamic model to examine five reasons why antibiotic resistance may be more common among TB patients if they are also infected with HIV (2) which had first been suggested by Chris Dye ten years earlier. Although the relevance of mathematical models in epidemiology is often contested because they do not provide definite answers, these models further our understanding of the dynamics of the processes under investigation, enable us to ask more sensible questions of the data,

and suggest areas in which more data and further research are needed. Perhaps the most important insight from the modelling study by Sergeev et al. is that single, cross-sectional studies of the relationship between HIV and drug-resistant strains of TB may be misleading precisely because they do not allow for the dynamic effects in the processes under investigation. Given time and money, good temporal data - collected over many years, perhaps in sentinel populations - will provide better insights into time trends in the incidence of TB, DR TB, MDR TB, and now XDR TB. The current analysis should help to inform the development of such long-term studies, which in turn will provide better data for further developing and refining dynamic models and ensuring that drug-resistant TB is brought under control.

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