Abstracts

A public health disaster

A comment in a recent edition of the *Lancet* suggests that the emergence of extensively drug-resistant tuberculosis (XDR TB) in rural South Africa is an indication of public health negligence. Certainly, the death rate associated with the strain is nothing short of a public health disaster. And yet, there still appears to be very little attention being paid to this potentially devastating situation by our Minister of Health.

Writing in the *Lancet*, Neel Gandhi and colleagues report what we all know – that the epidemics of HIV-1 and TB in South Africa are closely linked. Although the high mortality associated with co-infection has been reduced by antiretroviral drugs, drug-resistant TB has emerged as a major cause of death. From January 2005 to March 2006 the team obtained sputum from 1 539 patients. Multidrug-resistant TB (MDR TB) was detected in 221 patients, of whom 53 had XDR TB. The prevalence of MDR TB among 475 patients with culture-confirmed TB was 39% (185 patients) and 6% (30 patients) for XDR TB. Only 55% of patients (26 of 47) with XDR TB had never previously been treated for TB; 67% (28 of 42) had a recent hospital admission. All 44 patients with XDR TB who were tested for HIV were co-infected. Fifty-two of 53 patients with XDR TB died, with a median survival of 16 days from time of diagnosis among the 42 patients with confirmed dates of death. Genotyping of isolates showed that 39 of 46 patients (85%; 95% CI 74 – 95) with XDR TB had similar strains.

What does this mean? About 80% of patients in KwaZulu-Natal who present with active TB are HIV-infected. Mortality rates of up to 40% per year have been reported in patients co-infected with TB who are receiving treatment for TB but not for HIV. This could be expected to be reduced as antiretroviral therapy becomes more widely available, but the effect is likely to be reduced if TB programmes are not simultaneously improved. The current DOTS system is only achieving treatment success rates of 67% overall, far below the WHO recommended 85% – and most of this reduction is because of HIV co-infection. Low treatment success will place patients at risk for relapse and the development of drug resistance.

Resistance to second-line TB treatment has been emerging for some time. Investigators have found emerging resistance not only to isoniazid and rifampicin (MDR TB), but also to at least 3 classes of second-line drugs, which is called XDR TB. Worldwide, only 347 patients had been described with XDR TB, but data from Africa were sparse. The current authors, in a study of HIV-TB integration in KwaZulu-Natal, found that 6 of 119 patients (5%) co-infected with both diseases met the revised criteria for XDR TB, 17 defined as resistance to at least isoniazid, rifampicin, fluoroquinolones, and either aminoglycosides (amikacin, kanamycin) or capreomycin, or both. This finding raised the concern that not only MDR TB, but also XDR TB, was emerging in this region with high HIV prevalence.

This prompted the current study, looking at the prevalence of XDR TB. Their findings are summarised above. What is particularly alarming is the death rate among those with XDR TB. Roughly 70% of patients died within 30 days of the time that their sputum was collected for culture. The duration of survival did not vary significantly on the basis of age, sex, data collection group, previous treatment for TB, previous hospital admission, HIV status, CD4 count, or use of antiretroviral drugs.

These findings cause concern for several reasons, beyond the lethal nature of the disease. More than half the patients with XDR TB had never previously been treated for TB; an additional third had either been cured or had completed treatment for previous TB illness. With only 15% of patients having treatment failure or default, most patients were unlikely to have developed resistant TB as a consequence of unsuccessful treatment. Instead, transmission of XDR strains between individuals has probably occurred; this assumption is supported by the genotyping results. About 85% of the XDR isolates were from the KZN family of TB strains, which was first described in 1996. At that time, the KZN strains were either fully susceptible or had resistance to only first-line TB drugs. Resistance to second-line drugs was not seen until the past 2 – 3 years, further supporting the notion of recent transmission of XDR TB to our patients.

The authors also found evidence of nosocomial transmission of the strain. Two health care workers – and possibly 4 others – also died of XDR TB. This is particularly worrying in a situation of poor resources, where about 40% of patients admitted to the local hospital are HIV-infected and where infection control facilities and practices are limited at best.

The authors have three main recommendations arising from this study:

1. A rapid and comprehensive approach that determines the full extent of MDR and XDR TB in areas of high HIV prevalence is essential.
2. TB treatment programmes must be strengthened to improve treatment completion rates and provide treatment for drug-resistant disease. Infection control facilities also urgently need to be improved.
3. Simpler diagnostic tools for detecting active TB and drug resistance must be developed for use in resource-limited settings.

Gandhi N, *et al. Lancet* 2006; 368: 1575-1580.

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