A new paradigm for multidrug-resistant tuberculosis?

One of the most daunting of global health problems is the multidrug-resistant tuberculosis (MDR-TB) pandemic. An entirely man-made problem that arises when patients are improperly treated or fail to take their properly prescribed medications appropriately, it remains a massive burden for TB care and control globally.

While, according to the World Health Organization (WHO), drug-susceptible TB is effectively treated in most patients, MDR-TB, even when utilizing the principles of the programmatic management of drug-resistant tuberculosis1 endorsed by the WHO and other international experts, still has a dismal overall treatment success rate of less than 50%, with very high mortality,2,3 approaching reported TB cure rates in the 1940s before TB chemotherapy was introduced.4

Together with a drive to improving access to appropriate, improved MDR-TB treatment, it has perhaps become time to introduce a new tool to help control the spread of MDR-TB, which is as transmissible as drug-susceptible TB.

One of the more effective means of TB control that is widely used in industrialised countries is contact investigation and treatment for latent tuberculosis infection.5 The theory here is that those in close contact with infectious pulmonary TB cases have the highest incidence of infection with TB bacilli. This initially paucibacillary infection can be treated and eliminated more easily than when it manifests as clinical TB.

Contact investigation and preventive treatment is widely acknowledged to be effective in contacts of drug-susceptible TB, but it has rarely been studied in contacts of MDR-TB due to operational and ethical issues. In this issue of the Journal, Bamrah et al. from the US Centers for Disease Control and Prevention describe a study in Chuuk, Federated States of Micronesia, where two simultaneous MDR-TB outbreaks occurred.6 Identified contacts of each case were offered a 12-month fluoroquinolone-based preventive regimen by directly observed therapy (DOT). From January 2009 to February 2012, 119 exposed contacts were followed up. Of these, 15 refused preventive treatment, 104 began treatment and 93 completed it as prescribed. Most dramatically, none (0%) of the 104 who undertook preventive treatment of any duration developed clinical MDR-TB (or any type of TB), while three of the 15 (20%; P = 0.001) contacts who refused treatment and 15 previously unidentified contacts developed clinical MDR-TB.

Although this was not a randomized controlled trial, the data provided are extremely compelling, and the fluoroquinolone-based regimens were safe, as has also previously been shown in children.

It may be time to start identifying well-defined, high-risk contacts of MDR-TB patients and to treat them with appropriate fluoroquinolone-containing preventive therapy, the new paradigm being to prevent development of MDR-TB in close contacts rather than to treat them after they develop the disease. During contact investigations many prevalent cases may also be identified earlier with less severe disease and could be started on appropriate MDR-TB therapy with improved outcome.

In addition, longer term data on the treated and untreated Chuuk contacts could improve our knowledge on the efficacy of this intervention.

After all, MDR-TB treatment would be hard pressed to be any less successful!

References

5 Centers for Disease Control and Prevention. Guidelines for the investigation of contacts of persons with infectious tuberculosis; recommendation from the National Tuberculosis Controllers Association and CDC. MMWR Recomm and Reports 2003; 54(RR15): 1–37.