Multidrug-resistant tuberculosis in children can be treated

Multidrug-resistant (MDR) tuberculosis is a global public health concern, as its management is complicated and expensive.1–3 First, it is difficult to diagnose. Several weeks are needed to identify mycobacterial strains and to do drug susceptibility testing with traditional bacteriological methods; with new rapid methods, diagnosis is faster and easier, but these methods have not been scaled up for use at programme level and have not been extensively validated.4 Second, MDR tuberculosis is difficult to treat. Second-line tuberculosis drugs are much more expensive and toxic than first-line drugs, meaning that only specialised centres can treat patients with MDR tuberculosis and that universal access of these drugs is still far from being achieved.1–3,5,6

These issues are further exacerbated in children. In particular, the diagnostic challenge—spanning from difficulty in the obtaining of specimens to the paucibacillary nature of childhood disease, which in turn hampers the yield of smear microscopy and culture—makes children particularly vulnerable to misdiagnosis and ineffective treatment of resistant forms of tuberculosis.7–10

Children have for too long been neglected by tuberculosis programmes, meaning that little evidence is available on different aspects of their management. This situation has hampered the building of evidence-based guidelines and the development of empirical approaches. Most worryingly, these challenges have led to the acceptance of the idea that the treatment of childhood tuberculosis is a nearly impossible task.

In The Lancet Infectious Diseases, Dena Ettehad and colleagues11 present the results of a systematic review and meta-analysis assessing treatment outcomes for children with MDR tuberculosis. They searched for studies that reported outcomes, with treatment success as the primary outcome, and mortality, treatment defaults, and treatment-related adverse events as secondary outcomes. Only eight studies met the inclusion criteria, with a total of 315 children with MDR tuberculosis. They recorded substantial variations in the characteristics of patients and programmes. Treatment delay (up to 46 months) and long treatment duration (ranging from 6 months to 34 months) were also recorded. The pooled estimate for treatment success was high (81·67%, 95% CI 72·54–90·80), with the proportion of deaths (5·9%, 95% CI 1·3–10·5) and treatment defaults (6·2%, 2·3–10·2) being what can be thought to be low in view of the in-built complexity of management of these patients. A substantial proportion of children (39·1%, 28·7–49·4) had adverse events, suggesting the need for specific expertise when managing children with MDR tuberculosis.

Compared with studies of paediatric MDR tuberculosis, which are characterised by small sample sizes, the systematic review and meta-analysis done by Ettehad and colleagues11 improved the robustness of treatment outcome estimates (success vs death, failures, and default): the pooling of previously published data increased the low statistical power of individual studies. Furthermore, the random-effects model allowed the investigators to overcome the high heterogeneity of the selected studies, whereas the sensitivity analyses effectively assessed the role of confounding variables related to the inclusion of observational studies.

Well beyond its methodological strength, Ettehad and colleagues’ study does much to show that the treatment for MDR tuberculosis in children and the achievement of high treatment success rates are feasible. The study draws attention to the need for improvement in diagnostic practices and the importance of the recording and reporting of all cases and treatment outcomes in cohorts of children younger than 15 years if programmes to treat childhood tuberculosis and MDR tuberculosis are to be successful.

The diagnostic challenge in children is the crucial stumbling block, discouraging physicians from tackling childhood tuberculosis head on. Even in high-resource settings such as the European Union, bacteriological confirmation of childhood tuberculosis is well below an acceptable level, with merely 16% of children diagnosed in the past decade having a culture-confirmed diagnosis.8

Evidence exists, albeit from a high-resource setting (Norway),10 that a meticulous and systematic approach to specimen collection can result in bacteriological confirmation of disease in as much as 70–80% of cases. Although this coverage target might not be achievable worldwide, the attitude and approach to the diagnosis of childhood tuberculosis needs to be addressed urgently.

Finally, as Ettehad and colleagues11 allude to in their concluding remarks, the responsibility for correct
diagnosis and treatment is not solely that of physicians. Changes and improvements are needed at the core of tuberculosis programmes, with surveillance, recording and reporting, and policy making tailored to the needs of children and childhood tuberculosis.

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5 Dheda K, Migliori GB. The global rise of extensively drug-resistant tuberculosis: is the time to bring back sanatoria now overdue? Lancet 2011; published online Oct 26. DOI:10.1016/S0140-6736(11)61062-3.