

## Controlling Tuberculosis in India

**TO THE EDITOR:** The report by Khatri and Frieden (Oct. 31 issue)<sup>1</sup> on tuberculosis control in India echoes the official line of the Indian government, health policy bureaucrats, and the World Health Organization. Sadly, data collection in India cannot be taken at face value, and the accuracy of the impressive cure rates has been questioned.<sup>2</sup> The 200,000 new health workers alluded to are but a small fraction of those required to take on the additional burden imposed by direct observation. This shortage constrains the Revised National Tuberculosis Control Program (RNTCP) to recommend direct observation of only 6 of the 18 continuation-phase doses, and this incomplete supervision at a time when the illness is improving and the patient is least compliant has been dismissed as only partially observed therapy.

Marginalized persons (homeless persons, alcoholics, migrants, and drug abusers) are not enrolled lest they spoil neat quarterly calculations. Thus, the most “successful” centers providing directly observed treatment, short course (DOTS) are also those with the highest rates of exclusion of potential patients.<sup>3</sup>

Finally, Khatri and Frieden underestimate the extent and the effect of multidrug-resistant tuberculosis and the human immunodeficiency virus (HIV) on tuberculosis control. Multidrug-resistant tuberculosis, the main saboteur, occurs far more frequently than in 1 to 3 percent of cases. At our referral mycobacterial laboratory in Mumbai, 60 percent of all strains are multidrug-resistant.<sup>4</sup> The RNTCP has abjured itself of the responsibility of treating these patients who are the true “untouchables” of the Indian health care system. HIV-control programs and tuberculosis-control programs continue to be run in isolation, despite the fact that India has the world’s largest dually infected population.<sup>5</sup>

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**TO THE EDITOR:** Khatri and Frieden omit mention of an important population group: children. As many as half of children living in contact with adults who have tuberculosis may be infected with tuberculosis through their caregivers’ coughs and breaths. Bacille Calmette–Guérin vaccination limits the dissemination of tuberculosis but does not prevent primary infection. Childhood tuberculosis often remains unrecognized. Diagnosis on the basis of positive sputum smears is rarely possible, because children produce little sputum. Children with tuberculosis have nonspecific symptoms, including fevers, malaise, and stunting. Only those with overt pulmonary or disseminated disease are easily identified as having tuberculosis. Tracing of contacts has not been routine in much of the world, even though evaluation of and chemoprophylaxis in child contacts until they are proved to be uninfected represent the gold standard. We thus allow tubercle bacilli to survive in a large pool of infected children, which is especially disturbing in the light of the perpetuation of drug-resistant organisms. Furthermore, some 10 to 15 percent of children with unrecognized infection will have full-blown but preventable tuberculosis in adulthood.

Solutions to these problems include incorporation of childhood tuberculosis into national tuberculosis-control programs, development of contact-tracing programs, and exploration of the feasibility of chemoprophylaxis for exposed children. Better diagnostic tools for childhood tuberculosis are also needed.

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**THE AUTHORS REPLY:** The Indian tuberculosis-control program has now treated more than 1.5 million patients and saved more than 250,000 lives, but it is true that, in some areas, not all patients with diagnosed tuberculosis are included in the program. The program recommends that all patients, and certainly no less than 90 percent of them, be treated according to the DOTS strategy. The proportion of patients newly diagnosed who are treated in the

program has increased steadily to 94 percent. Contrary to Udawadia's assertion, areas that fail to enroll a high proportion of patients in the program tend to have lower cure rates — a reflection of weaker implementation of the program. For example, the area with the lowest proportion of patients with diagnosed tuberculosis who were treated in the program in the most recent quarter was also the area with the lowest cure rate.<sup>1</sup> Direct observation is essential in the intensive phase of treatment, when the burden of organisms and the risks of treatment failure and development of drug resistance are highest; in the continuation phase, the program uses direct observation for at least the first of three doses per week.

The proportion of patients at a referral hospital who have multidrug-resistant tuberculosis has no relevance to the actual proportion of people in the community who have multidrug-resistant disease.<sup>2</sup> All valid studies in India have found rates of multidrug resistance of 1 to 3 percent among previously untreated patients.<sup>3-6</sup> Multidrug-resistant tuberculosis is a symptom of poor performance of programs; the highest priority is to prevent multidrug-resistant tuberculosis by effective treatment. As we state in our article, more than 1 million patients each year with newly diagnosed tuberculosis do not yet have access to basic treatment, and the top priority must be to ensure that they have such access. Both HIV-positive and HIV-negative patients are treated in the program; models to improve coordination are being evaluated.

With regard to the issues raised by Schaller and Starke, the new program includes treatment of children with active disease as well as investigation of

contacts and preventive treatment of children who are contacts of those with infectious cases. These efforts have met with varying degrees of success in different parts of the country.

There are several errors in our article. Clinical features are provided in Table 2, not Table 1. On page 1422, the top line of the right column should read "More than 200,000" rather than "Nearly 200,000." The sentence beginning on line 12 of that column should read "By September 2001, about 3.4 million symptomatic patients had been assessed for tuberculosis, and in the case of nearly 800,000, treatment had been started — in more than half of them, within the previous 12 months."

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## Genomic Medicine

**TO THE EDITOR:** The first case vignette in Guttmacher and Collins's primer on genomic medicine (Nov. 7 issue)<sup>1</sup> is not a good example of the value of genomic medicine; rather, it may be an example of excessive laboratory testing. Heparin prophylaxis during pregnancy would be indicated for Kathleen, the woman described in the vignette, on the clinical basis of her prior estrogen-related deep venous thrombosis, even if she were not heterozygous for the factor V Leiden mutation.<sup>2</sup> Conversely, although she is heterozygous for the factor V Leiden mutation, heparin prophylaxis would not be indicated if she had never had an episode of deep venous

thrombosis.<sup>3,4</sup> Therefore, knowing that she is heterozygous for the factor V Leiden mutation is neither necessary nor sufficient for guiding her clinical care. There may come a time when we can generate an adequately sensitive and specific genomic profile of coagulation, but even then, before ordering a test, we should consider whether the result will have any bearing on the patient's clinical care.

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