

resistant strains.²² These results do not guarantee that clinical trials will be successful, but they are encouraging.

The optimal approach to prevent TB is primary prevention through vaccination. For reasons that are not entirely clear, the BCG vaccine has shown inconsistent efficacy in clinical trials, especially in adults. Numerous vaccine candidates are under study and at least 2 are currently in early human trials.²³

With uncharacteristic optimism, the Centers for Disease Control and Prevention still has a Division of Tuberculosis Elimination. Using current tools, resistant TB is unlikely to be eradicated. However, history has shown that resistance can be reduced through more appropriate treatment programs and the spread of resistant strains can be reduced through public health measures. Some of the articles in this issue of *JAMA* clearly show that multidrug resistance in the United States is inextricably linked to resistance in the rest of the world. Therefore, to control resistance in the United States, areas where resistance is epidemic must receive assistance and exquisite care must be taken not to create new problems on continents like Africa. In the future, with new drugs, tests, and vaccines, the elimination of multidrug resistance may be achievable but difficult.

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Tuberculosis, Vulnerability, and Access to Quality Care

Philip C. Hopewell, MD

Madhukar Pai, MD, PhD

AS WITH MOST INFECTIOUS DISEASES, TUBERCULOSIS (TB) is not randomly distributed; it thrives in specific groups and under specific conditions in association with identified and unidentified factors that confer vulnerability to the disease. Available information on the association between TB and the many known conditions and circumstances that influence vulnerability to the disease has been reviewed recently and is summa-

rized in the BOX.^{1,2} These conditions and circumstances mainly include 3 broad categories of factors: individual biological factors (eg, immunodeficiency states), social and economic circumstances (eg, crowding, poverty, poor nutrition), and environmental and institutional factors (eg, silica dust, poor ventilation).

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See also pp 2719, 2726, 2762 and 2767.

Among the biological factors, human immunodeficiency virus (HIV) infection is perhaps the most potent. In the report by Grant and colleagues³ in this issue of *JAMA*, 2 biological factors, HIV infection and exposure to silica dust, have been superimposed in South African gold miners to set the stage for an extraordinarily high incidence of tuberculosis: 11.9 cases per 100 person-years of observation before implementing a program of treatment with isoniazid and 9.0 cases per 100 person-years after the intervention. Two social factors, incarceration and homelessness, are also discussed in this issue of *JAMA*. The study by Drobniowski and coworkers⁴ illustrates the importance of social and institutional factors, such as incarceration, in creating conditions favorable for the transmission of drug-resistant TB. In addition, the report by Haddad and associates⁵ describing TB among homeless persons in the United States reinforces the point that social circumstances play an important role in determining vulnerability to TB. All 3 studies also illustrate the high degree to which social and biological factors interact in individuals.

The traditional framework for conceptualizing vulnerability to tuberculosis involves partitioning the factors into those that influence the likelihood of acquisition of infection with *Mycobacterium tuberculosis* and those that influence the host-immune response to the infection. Not included in this 2-component conceptual model, however, is the vulnerability of individuals to severe consequences of TB, including prolonged disability and death, and the vulnerability of communities to ongoing spread of infection, sometimes with drug-resistant organisms, because of a lack of access to appropriate and effective care for diagnosis, treatment, and prevention of TB. Any person anywhere in the world who is unable to access quality health care should be considered vulnerable to TB. Likewise, any community with no or inadequate access to appropriate diagnostic and treatment services for TB is a vulnerable community.

Appropriate and effective care for TB is not complicated in most instances. Current TB care and control strategies are relatively simple and generally quite effective. The DOTS (directly observed therapy, short course) strategy, described in the article by Dye and colleagues⁶ in this issue of *JAMA*, when appropriately implemented, has been shown in many countries (most recently and effectively in Peru and China) to reduce the incidence and prevalence of tuberculosis.^{7,8} Dye and associates⁶ clearly describe the achievements of the DOTS strategy but also indicate the shortcomings and present some of the reasons why current goals of reducing TB incidence, prevalence, and mortality are not being met. As public health TB control programs implement the DOTS strategy more widely, it is becoming apparent that the lack of access to effective care is one of the main factors limiting global TB control.

Despite the availability of highly effective therapy for many years and a concerted worldwide effort to improve access to the diagnostic and treatment interventions embodied in

Box. Factors That Increase Vulnerability to Tuberculosis*

Individual Level: Biological and Disease-Related Factors

Age
Sex ratio
Pregnancy
Genetic influences on infection or disease vulnerability
Interaction with other conditions (eg, human immunodeficiency virus infection)

Household and Community Level: Social and Economic Factors

Gender
Poverty
Poor nutrition
Crowding
Livelihoods and occupation
Illness conceptualization and lack of knowledge

Macro Level: Environmental and Institutional Factors

Physical environment (eg, climate, silica dust, indoor air pollution, smoking)
Migration
Increased drug resistance
Inappropriate, delay of, or lack of screening and case detection
Treatment delays
Poor-quality care
Health care system and status of any reform

*Adapted from Bates et al.^{1,2}

the DOTS strategy, a large number of individuals in developing countries with TB, or who have symptoms that might be caused by the disease, fail to get adequate services. In 2003, only about 45% of the estimated total number of individuals with sputum smear-positive TB were detected and reported.⁹ This is especially concerning given that the estimated number of individuals with positive sputum smears probably represents no more than half of all prevalent individuals with TB (ie, all forms, including individuals with sputum smear-positive and sputum smear-negative pulmonary TB and extrapulmonary TB).⁹ More than 80% of individuals diagnosed as having TB were treated successfully in DOTS programs.^{6,9} Thus, effective treatment for TB, while an important concern, is less of a challenge than appropriate case detection and access to effective treatment.

Not much is known about the large number of cases of TB that are not managed under DOTS programs. Some are probably well managed but the available evidence suggests that, at least in the private sector, this is not the case. Evi-

dence from studies from around the world show that delays in diagnosis, delays in treatment, deviations from standard TB management practices, irrational and harmful practices, variability in the quality of TB care, and inadequate efforts to support patients and improve treatment adherence continue to plague global TB control efforts.

A recent global situation assessment conducted by the World Health Organization (WHO) suggests that delays in diagnosis are common,¹⁰ and perhaps more common than delays in seeking care, although both are important.¹¹ The WHO assessment and other studies indicate that physicians, in particular those who work in the private health care sector, often deviate from standard, internationally recommended TB management practices.^{10,12} These include underuse of sputum microscopy and overreliance on radiography for diagnosis, use of inappropriate drug regimens, incorrect combinations of drugs, and inaccurate dosages for the wrong duration.^{10,12-19} These findings highlight flaws in the system of care that lead to lack of access to appropriate services or substandard care to populations that are most vulnerable to TB and are least able to bear the consequences of such systemic failures.

An effort to address the issue of quality of care for individuals with TB, mainly in the private sector, is the development of international standards for TB care. This effort is being led by a consortium of organizations concerned with global TB care and control (American Thoracic Society, US Centers for Disease Control and Prevention, Dutch Tuberculosis Foundation, International Union Against Tuberculosis and Lung Disease, and WHO). A fundamental premise that underlies plans for these standards is that all clinicians who undertake treatment of patients with TB must recognize that they are assuming an important public health function that entails responsibility to the community as well as to the individual patients in their care.

Despite many differences among countries in economic conditions, health care systems, and epidemiological circumstances and among health care professionals, the basic principles of care for persons with or suspected of having TB are the same worldwide. Consequently, the fundamental approaches to TB care can be described in a set of essential standards that can be used in all areas and by all health care sectors—national TB control programs, other public sector agencies, and private health care clinics. Engagement of all clinicians to deliver a high standard of TB care for all patients is essential to protect the health of communities and to restore the health of individuals with the disease, while preventing TB in their families and others with whom they come into contact.

Prompt and accurate diagnosis and effective treatment are not only essential for good patient care, they are the key elements in the public health response to TB and are the cornerstone of TB control. Good care for individuals with TB is unquestionably in the best interest of the wider community. Community contributions to TB care and control are

increasingly important in raising public awareness of the disease, providing treatment support, reducing the stigma associated with TB infection, and demanding adherence to a high standard of TB care.²⁰ The community should expect that standards of care will be provided and will be met. Substandard care will likely result in poor patient outcomes, continued infectiousness with transmission of the infection to other community members, and, perhaps, generation and propagation of drug resistance.

In accordance with the DOTS strategy, the standards should address the basic elements of diagnosis and treatment of TB with a series of straightforward statements that are backed by evidence. The intent is to secure a broad base of endorsements—national governments, national TB programs, professional medical and nursing societies, academic institutions, nongovernmental organizations that provide medical care, and HIV-focused organizations—to use the standards to create peer pressure for clinicians to conform to the principles, as well as to serve as the basis for preservice and inservice training.

The areas to be addressed by the standards include identification of persons who should be evaluated for TB, bacteriological confirmation of the diagnosis in all persons with suspected TB, use of drug regimens of proven effectiveness, provision of treatment support and supervision, appropriate HIV counseling and testing under defined epidemiological circumstances, consideration of antiretroviral treatment for patients with HIV infection who have TB, evaluation of all patients with TB infection for the possibility of drug resistance, and required reporting of all cases to the relevant public health authority. A set of standards is only a tool, and having a tool does not guarantee that the job will be done correctly. However, with proper use and broad-based support, the standards could be a useful means of improving the quality of care for TB.

To reduce the vulnerability of individuals to TB, a multipronged approach is essential. Efforts to improve living circumstances, alleviate poverty, minimize crowding, prevent malnutrition, and prevent and treat HIV infection, as well as research and development for new tools, are all critical undertakings. Among these activities should be vigorous efforts to address shortcomings in the quality of care for individuals with TB, an often overlooked reason for increased vulnerability to the disease.

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EDITORIAL

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Tuberculosis—A Global Problem Requiring a Global Solution

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TUBERCULOSIS (TB) CONTINUES ITS 3000-YEAR HISTORY of decimation,¹ currently infecting one third of the world's population and killing approximately 2 million individuals annually.^{2,3}

Some developed countries, such as the United States, have had declining numbers of individuals infected with TB over the past decade, but 23 countries account for 80% of all new TB cases, with more than half concentrated in 5 countries (Bangladesh, China, India, Indonesia, and Nigeria).⁴ Most new cases in the United States, and probably a substantial proportion of new cases in other developed countries, occur among individuals born in other countries. Clearly, TB is a global health problem.

The articles in this theme issue of *JAMA* devoted to TB address a number of important concerns including screening; treatment for active and latent infections; multidrug-resistant strains; and improving screening, treatment, and quality of care for all vulnerable populations. These are se-

rious problems that must be solved before TB can be controlled. Each of these concerns is addressed in a series of commentaries in this issue by Hopewell and Pai,⁵ Nettleman,⁶ and Whalen.⁷

Individuals with human immunodeficiency virus (HIV) infection are especially vulnerable to TB, and TB may be the first infection that causes a patient with HIV to seek health care. Grant and associates⁸ report on a clinic offering primary isoniazid preventive therapy to HIV-infected men who work in a South African mine. Unfortunately, while the therapy reduced TB by 38% overall and 46% in miners with no history of TB, the incidence of TB remained high. Haddad et al⁹ provide evidence that homelessness in the United States continues to be strongly associated with TB, but with good case management, excellent treatment outcomes can be achieved.

Geng and associates¹⁰ studied the clinical and radiographic correlates of primary TB and reactivation of TB. They found that HIV status is the only independent predictor of what appears on radiographic images. The radiographic ap-

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