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**Proﬁling Drug Resistance in Immigrants With Tuberculosis**

The burden of tuberculosis (TB) is a major impediment to improved health for the world’s population. Increasing global TB rates led the World Health Organization (WHO) to declare TB a global emergency in 1993. Global TB control efforts, however, are seriously threatened by increasing rates of drug-resistant TB. The treatment of TB patients who have drug-resistant strains is exceedingly costly, difficult, and less effective.

Although drug-resistant strains of TB have been detected in all parts of the world, the identiﬁcation of speciﬁc drug resistance patterns at the local level is dependent on resources for mycobacterial culture and drug sensitivity testing. Unfortunately, ongoing drug resistance surveillance is not affordable in many countries of the world, especially in those with the greatest burden of TB. In wealthier countries with a strong laboratory infrastructure, the detection of drug resistance has resulted in strengthening of TB control efforts. For example, in New York City, the emergence of drug resistance led to public health action and the subsequent decline in drug resistance.

As wealthy countries with a strong TB infrastructure chip away at their domestic TB cases, an increasing percentage of their TB cases occur among immigrants from countries with a higher incidence of both drug-susceptible and drug-resistant TB. In the United States, 40% of TB cases occur among persons born outside the country. The percentage of foreign-born persons among TB cases in other developed countries is even higher: for example, 80% of TB cases in Australia and > 50% of TB cases in several countries of Europe occur among the foreign-born populations. Furthermore, a substantial proportion of drug-resistant TB diagnosed in afﬂuent countries occurs among foreign-born persons. In an era of disparate global TB rates, TB highlights an age-old epidemiologic fact: migration is an effective conduit for infectious disease. Indeed, although legal immigration into the United States requires the immigrant to be smear-negative on entry to the United States, the risk for reactivation of TB, possibly drug-resistant TB, persists for many years after arrival.

In the current issue of *CHEST* (see page 738), Gilad et al assess the impact of immigration on TB disease, including drug-resistant strains, in southern Israel. Overall TB rates are low; however, 45% of all persons with TB were from the former Soviet Union. Israeli immigrants from the former Soviet Union disproportionately contribute to the prevalence of drug resistance in this community; 50% of TB cases in this immigrant population had isolates that were resistant to at least one of the standard ﬁve drugs, and almost 17% were resistant to at least isoniazid and rifampin (multidrug-resistant tuberculosis [MDR-TB]). These rates compare to 8% and 22%, respectively, in a comparison population, including those born in Israel and those who immigrated prior to 1980. Although this study identiﬁes an association between drug-resistant strains of TB and an immigrant ethnic group, it is clear from previous literature that a high level of drug resistance is a surrogate marker for TB control program quality and social factors of vulnerability in the country of origin.

Given the recent reports of TB and drug resistance in the former Soviet Union, these results may not seem surprising. However, public health action should be based on local data. A comparison of data from Israel and the United States illustrates this point. In contrast to the data presented by Gilad et al, the percentage of MDR-TB in TB cases occurring among immigrants from the Russian Federation in the United States is much lower, 3.5% (from 1994 to 1997; unpublished data; Centers for Disease Control and Prevention, Division of Tuberculosis Elimination). This difference may be attributable to differences in immigrating populations, including socioeconomic status, geographic origin, or differences in prearrival TB screening practices. Thus, because the epidemiology of drug-resistant TB is local, drug resistance surveillance of foreign-born populations in each community is crucial. Although caution is needed to avoid possible misuse of ethnic information on patients with TB, this information can help guide treatment and prevention interventions. The evaluation of local data on drug resistance should lead to TB treatment policy development and planning for each community.

Under the leadership of the WHO, the TB healthcare community has increasingly promulgated a standardized programmatic response for TB control: directly observed therapy, short course (DOTS). The components of DOTS include government commitment to TB control, passive detection of active TB disease with laboratory conﬁrmation, standardized short course chemotherapy with directly observed
therapy, continuous and reliable drug supply, and an efficient recording and reporting system. Global DOTS coverage is expanding and in 1997 included 35% of the world’s population. The Russian Federation is still in the pilot phase of its DOTS efforts, with current coverage of < 10% of the total population. Although the adequacy of DOTS to reduce TB incidence rates is debated (especially in countries with high HIV rates), there are data that DOTS effectively thwarts the emergence of drug resistance.

What does the medical community do in a locality once significant drug resistance has been observed? This is an important issue for both public health officials and practicing clinicians. In countries that have successfully implemented DOTS but where drug resistance is contributing to poor treatment outcomes, experts have suggested expansion and modification of DOTS, including more-complicated treatment regimens for patients with MDR-TB.

One important aspect of these proposals is the determination of specific treatment algorithms for patients infected with drug-resistant strains. International consensus currently suggests that treatment for drug-resistant TB, especially MDR-TB, should comprise at least three drugs, preferably four or five, to which the patient’s isolate is susceptible, including the use of an injectable agent for approximately 12 to 18 months after sputum conversion. It is critical that a single drug not be added to a failing regimen, because drug resistance may develop to the new drug, rendering the treatment ineffective and further diminishing the arsenal of TB drugs. Analysis of locally derived drug resistance surveillance data may form the foundation of rational treatment options for the affected communities. These analyses may yield treatment plans that can be used empirically to treat cases infected with suspected resistant strains based on epidemiologic profiling until susceptibility results on individual patients are available. For example, in New York City, an empiric six-drug regimen was temporarily used to check the epidemic in the setting of routine drug susceptibility testing (personal communication; Dr. Paula Fujiwara, New York City Department of Health; August 1999). If resistance patterns in a given community are extremely variable, more resources must be obtained to increase rapid drug susceptibility testing in order to tailor treatment to each individual drug-resistant case. As a first step, more detailed analyses are required that examine the predicted impact of specific proposed regimens given a measured distribution of drug resistance in a given locality. We must also increase the use of DOTS worldwide to prevent further increases in drug-resistant TB.

The global burden of TB is increasing, and the epidemiology of drug resistance should remind practitioners in wealthy nations that TB is a serious threat to everyone. There are reasons to be optimistic. However, global TB control will require more investment. Although more monetary resources are needed, more personal investment is also needed. In some senses, TB has been prematurely forgotten in the community of pulmonary physicians in developed nations, because the burden of TB is felt mainly in poorer countries. A renewed interest and commitment to TB is necessary.

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Noninvasive Positive Pressure Ventilation

Testing the Bridge

Patients with preexisting problems like COPD and neuromuscular problems, or newly developed conditions like overwhelming pneumonia and acute pulmonary edema may decompensate and develop acute respiratory failure. Such patients may need assistance with their ventilation while their underlying acute or exacerbating problems are managed by other medical means. Mechanical ventilation in these cases acts as a bridge to recovery and a return to their baseline status. Traditionally, an endotracheal tube is inserted into the trachea to deliver oxygen under positive pressure to the patient’s lungs. On the other hand, the alveolar ventilation can be augmented noninvasively by external negative pressure, chest wall oscillations, or positive pressure ventilation administered through a tight-fitting facial or nasal mask (noninvasive positive pressure ventilation [NIPPV]).

Numerous studies have shown noninvasive ventilation (NIV) to be useful in chronic respiratory failure secondary to conditions such as muscular dystrophies and multiple sclerosis. It has also been found to be useful in hypoventilation associated with severe chest wall deformity, central disorders, obesity/hypoventilation syndrome, and obstructive sleep apnea syndrome. Although the efficacy of NIV in most cases of severe, stable COPD has not been proven, the subgroup of patients with severe hypercarbia has been shown to benefit from NIV. COPD patients who have severe nocturnal oxygen desaturation may also benefit from NIV.

Interest in the use of NIPPV for cases of acute respiratory failure has increased in the recent past due to the availability of better-tolerated nasal masks, but the main advantages are the convenience and lower cost of NIPPV and the avoidance of the morbidity and complications associated with intubation. The indications of NIPPV are the same as those for invasive ventilation with tracheal intubation, but there are situations in which NIPPV cannot be used.

Respiratory arrest, cardiorespiratory instability, uncooperative patient, high aspiration risk, inability to protect the airways, and fixed anatomic abnormalities of the nasopharynx are considered contraindications. Extreme anxiety, massive obesity, and copious secretions also make a patient unsuitable for the use of NIPPV. Various studies have provided evidence for the efficacy of NIPPV in acute exacerbations of COPD. The benefits have included the following: (1) a significant decrease in the rate of intubation by approximately 66% in NIPPV patients when compared to controls receiving conventional care; (2) a significant decrease in mortality (9% vs 29%); (3) a significant decrease in the ICU length of stay (13 vs 32 days); and (4) a significant decrease in the hospital length of stay (23 vs 35 days). However, the results of these studies cannot be generalized, and NIPPV is useful only in selected cases. In one of the studies, only 31% of COPD patients were ultimately randomized. This means that there are only a small number of patients who fall in that intermediate zone where NIPPV can be tried; patients who are very ill or have other conditions that make them unsuitable for NIPPV get intubated immediately, whereas others who do not need assistance with their ventilation can be managed successfully with conservative methods. But then, not all patients who are placed on NIPPV do well: in one study, 31% of patients who were initially started on NIPPV required intubation for various reasons after an average of 15 ± 7 h. It is important, therefore, to select suitable cases for NIPPV as promptly and as accurately as possible, so that there is no undue delay in the intubation if it is eventually required. Can we predict the cases in which NIPPV will succeed? Committed caregivers and a cooperative patient are the prerequisites for any NIPPV trial. The chances of success are dictated by some factors that can be identified before the trial is begun. For example, it has been shown that patients who did not respond...