Errors in the Treatment of Tuberculosis in Baltimore*

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**Background:** Incomplete or incorrect antibiotic therapy, especially in the initial phase of antituberculosis (anti-TB) treatment, is a major cause of acquired drug resistance and treatment failure. We determined the extent of errors in anti-TB treatment regimens by way of nonadherence to recommended treatment protocols among patients with TB in Baltimore, MD, a city with declining rates of disease. An error was defined as using too few drugs or the wrong drugs, giving inadequate doses of drugs, or prescribing an inadequate duration of treatment.

**Methods:** We reviewed the records of all patients with culture-positive, pulmonary TB reported in the city of Baltimore from January 1, 1994, to December 31, 1995. We determined demographic information, initial anti-TB regimen, doses and duration of therapy, history or presence of resistance to anti-TB drugs, injecting-drug or alcohol abuse, HIV status, and whether treatment was given by a private physician or by the Tuberculosis Clinic of the Baltimore City Health Department (BCHD).

**Results:** Of the 110 cases of active pulmonary TB, 17 cases (15.4%) had errors in treatment for control of their current disease. Thirteen of 34 privately treated patients (38%) had some error in their initial anti-TB regimen, compared with 4 of 76 patients (5.2%) treated by the Tuberculosis Clinic of the BCHD (p < 0.0001). Patients were otherwise similar as determined by age, sex, HIV status, drug-resistance characteristics, and injecting-drug use, regardless of whether they had erroneous anti-TB regimens.

**Conclusion:** In a low-prevalence area, private physicians make frequent errors in prescribing anti-TB therapy. Additional educational resources for physicians and increased use of expert consultation may contribute to improved TB control.

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Inappropriate or inadequate anti-TB therapy serves as a major cause of acquired drug resistance, which may result in treatment failure and the spread of drug-resistant organisms to other persons. Among patients with multidrug-resistant TB (MDR-TB) who have been treated in a referral center, physician mismanagement or “error” was the most common cause of acquired drug resistance. The most common errors noted in this study of 35 patients with MDR-TB were the initiation of an inadequate primary regimen and the addition of a single drug to a failing regimen. The multidrug resistance acquired through these errors resulted in...
prolonged hospitalizations, treatment with more toxic drugs, and high-risk resectional surgery. The costs for this “salvage” therapy were extraordinary, averaging $180,000 per patient.

The current TB treatment goals of the Centers for Disease Control and Prevention, the Advisory Council for the Elimination of Tuberculosis, and the American Thoracic Society call for treatment of all TB patients with an initial regimen of isoniazid, rifampin, pyrazinamide, and, depending on local drug-resistance patterns, ethambutol, with a minimum duration of therapy of 6 months. To determine the level of observed therapy (DOT) for the past 20 years, with virtually no MDR-TB. To determine the level of adherence to recommended treatment guidelines in the setting of effective TB control, we analyzed the initial regimen given to patients over a 2-year period. Herein, we report on a citywide, population-based cohort of patients with TB and on the prevalence of errors in their initial anti-TB regimen.

**Baltimore TB Control Program Description**

The Division of Communicable Diseases and Epidemiology of the BCHD administers the TB Control Program. Medical care services are provided by physicians and a nurse-practitioner from the Johns Hopkins University. In 1978, the BCHD implemented a limited program of supervised therapy for high-risk patients. This program of DOT was expanded in 1981 to all patients who were seeking treatment or who had been referred for treatment. Patients with newly diagnosed TB are referred to or are recruited into the program through contact with physicians and hospitals. Cases are identified by physician report, laboratory report, or through a city ordinance that requires the reporting of dispensed anti-TB drugs by pharmacists. All new patients with suspected or confirmed TB are evaluated by a physician and a nurse, and are assigned to a case-management team. Each team includes a nurse supervisor and an outreach nurse to provide DOT for specific sections of the city. Teams maintain caseloads of 25 to 35 patients receiving DOT. The number of teams is adjusted in response to the city’s TB caseload.

The BCHD program monitors patients treated by private physicians through periodic contact with physicians and through pharmacy surveillance. The BCHD program staff determine whether therapy is appropriate, whether dosages are adequate, and whether the patients are obtaining drug refills at scheduled intervals. When a problem is identified, a clinic nurse contacts the patient, the physician, or both and attempts to rectify the problem. As a result, many privately treated patients are ultimately referred to the clinic for a more intensive follow-up. Clinic nurses also monitor the results of sputum cultures of privately treated patients during therapy and provide targeted screening, treatment, and case management for case contacts.

**Materials and Methods**

In this study, we included all cases of sputum culture-positive pulmonary TB reported in the Baltimore from January 1, 1994, to December 31, 1995. Patients with diagnoses of TB who were not microbiologically confirmed and patients who died without therapy were excluded. TB is a reportable condition in the state of Maryland. By law, all health-care providers who diagnose patients with active TB and all laboratories that identify *Mycobacterium tuberculosis* in human specimens are required to notify the state or a local health department.

**Data Sources and Analysis**

Data were gathered from medical records and chart reviews. The data were transcribed into a standardized format. The data collected included demographic information, the initial anti-TB regimen, drug doses, treatment duration, HIV status, whether initial treatment was by the BCHD TB Clinic or by a private physician, and the presence of injecting-drug use or alcohol abuse.

Based on the recommendations of the American Thoracic Society and the Centers for Disease Control and Prevention, we defined errors as the following: (1) inappropriate initial regimens for TB (too few drugs or wrong combinations of drugs); (2) inadequate dosage of drugs prescribed; and (3) inadequate length of therapy prescribed.

We compared the characteristics of patients who had errors in their TB treatment with those who did not. The differences in proportions were assessed by the χ² test, and odds ratios (ORs) with 95% confidence intervals were calculated. Student’s t-test was used for continuous variables. Two-tailed p values are reported.

**Results**

There were 128 cases of culture-confirmed pulmonary TB reported during the study period. Twelve patients were diagnosed postmortem and were not considered for the purpose of this study. Of the remaining 116 cases, complete information could be gathered on 110 cases. The medical records of the remaining six patients were incomplete because they had either moved away soon after diagnosis or were untraceable.

For the remaining 110 patients, the mean age was 54.1 years (range, 4 to 91 years), 75 patients (68%)
were men, 32 (29%) had histories of alcohol abuse, 20 (18%) were HIV-seropositive, and 22 (20%) were injection drug users. Thirty-four patients (32%) were treated by private physician and 6 (5%) had *M tuberculosis* isolates that were resistant to isoniazid or rifampin.

Of the 110 patients, 17 (15%) were given erroneous treatment for TB. Eight of those patients were given inadequate dosages of anti-TB drugs, four were put on inappropriate combinations, three were treated for inadequate lengths of time, and two were put on inadequate dosages and treated for inadequate lengths of time.

As shown in Table 1, there was no difference by sex, HIV status, drug resistance, or drug use in patients with or without erroneous anti-TB treatment. However, patients who had been cared for by a private physician were more likely than patients treated at the TB clinic to have had erroneous treatment for TB. Thirteen of the 34 privately treated patients (38%) had some error in their anti-TB regimen as compared with 4 of the 76 patients (5%) treated by the BCHD (OR, 11.4; *p* < 0.0001). Although the mean age of the patients treated by private providers (60.2 years) was higher than that of patients treated by the BCHD (51.6 years), further stratification by treatment errors failed to reveal any statistical significance. Patients abusing alcohol were significantly less likely to have errors in their treatments than nonalcoholic patients. Alcoholic patients were more likely to be treated at the BCHD, however.

### Table 1—Characteristics of TB Patients With Treatment Errors in Baltimore, MD, January 1, 1994, to December 31, 1995

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<thead>
<tr>
<th>Characteristics</th>
<th>No. of Patients (%)</th>
<th>Sex</th>
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<th>HIV status*</th>
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<th>IV drug use</th>
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<th>Treatment facility</th>
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<th>Alcohol abuse</th>
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<th>Isoniazid/rifampin resistance</th>
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<th>Total cases</th>
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<td>Total</td>
<td>With Treatment Errors</td>
<td>OR</td>
<td>p Value</td>
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<td>Total cases</td>
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*HIV status was unknown in 47 cases.

**Discussion**

We have found that 15% of a cohort of TB patients from Baltimore had inappropriate treatment for active pulmonary TB. Private physicians had treated most of those patients who had treatment errors (77%). Almost half of these patients were treated with inadequate dosages of anti-TB drugs. Because of the aggressive TB control program of the BCHD, however, most of these errors were recognized before serious harm had occurred to the patient or the community.

Although TB traditionally has been the responsibility of public health departments, TB care is frequently provided by private physicians, either independently or in collaboration with public clinics. Our study illustrates that those private physicians who diagnose TB often treat their patients inappropriately. Suboptimal treatment (too few drugs, inadequate doses, and inadequate durations of regimens) contribute to the emergence of drug resistance and a higher risk of treatment failure.11,12 Previously, we have found that patients treated by private physicians are less likely to have documentation of sputum culture conversion to negative than patients treated by the public TB program,9 a finding recently confirmed among TB patients in New Jersey.13

A major reason for inappropriate management of complex illnesses is physician inexperience. Experienced physicians and institutions produce better treatment outcomes than their less experienced
counterparts for diverse conditions, such as HIV infection. The physicians in this study whose management of patients was inappropriate generally treated only one or two TB patients per year. Because of falling case rates of TB in Baltimore, physicians, group practices, and hospital staff also have less experience with TB patients than in past years. It is possible that with higher TB case loads, physicians may make fewer errors in management. However, it is important to recall that high case loads by no means guarantee good care or outcomes. As demonstrated in New York and other American cities recently, physicians can contribute to poor outcomes of TB therapy even in a setting of high incidence. Indeed, a study done in India, the country with the largest number of TB cases in the world, found that private physicians caring for TB patients in a high-incidence setting frequently made treatment errors: among the 105 physicians who were treating TB who were surveyed, 79 different treatment regimens were prescribed. Thus, it is likely that both experience and instruction in state-of-the-art management practices for TB are necessary to ensure optimal care for patients who are treated by private physicians.

This study has several limitations. This was a pilot study involving cases from the years 1994 and 1995 only. Hence, the sample size obtained was predictably small. In addition, although we could calculate the proportion of patients who had errors in their TB treatment, we could not be certain that appropriate control measures and treatment protocols, if adhered to, would have led to better outcomes, as case management by the program also identified most serious errors. However, based on the known effectiveness of chemotherapy in treating active TB (≥ 90% effective) and in preventing relapse (≥ 95% effective), we found that, in Baltimore, substantial improvement in TB control practices could be made by fully implementing the existing recommendations, especially among the private providers.

To prevent serious errors in the care of TB patients, we recommend aggressive professional education and support for physicians and institutions treating patients with TB. The rapid availability of expert clinicians and the monitoring of treatment should be available through public health departments. As the treatment of TB becomes more complex with drug resistance and HIV, consultation with specialists experienced in the treatment of such cases should be routine. In many settings, such as in Baltimore, the most efficient way to avoid treatment errors and poor outcomes is to have all patients with TB treated by the health department or by a center of excellence in TB treatment, a strategy that we are actively encouraging. In other areas with larger caseloads and/or fewer public resources, a public-private partnership in TB control is essential. Active monitoring of all patients, both public and private, by a quality-assurance team is essential for optimizing the care of patients with TB.

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REFERENCES