

Delays in the Suspicion and Treatment of Tuberculosis among Hospitalized Patients

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Background: Despite increased awareness of tuberculosis, delays in management are common.

Objective: To investigate management delays among hospitalized patients with tuberculosis.

Design: Retrospective cohort study.

Setting: The Barnes-Jewish-Christian Health System, a network of eight community and tertiary-care facilities serving the St. Louis, Missouri, metropolitan area.

Patients: All 203 patients with tuberculosis hospitalized in the Barnes-Jewish-Christian Health System from 1988 to 1996.

Measurements: Time from admission to first consideration of the diagnosis (*suspicion interval*), first consideration and treatment initiation (*treatment interval*), and admission and treatment initiation (*overall management interval*) were determined. Delays were defined as intervals longer than 24 hours.

Results: The overall management interval (median, 6 days [5th and 95th percentiles, 1 and 52 days]) exceeded 24 hours in 152 patients (74.9% [95% CI, 68.9% to 80.9%]). The suspicion interval (median, 1 day [5th and 95th percentiles, 0 and 16 days]) exceeded 24 hours in 54 patients (26.6% [CI, 20.5% to 32.7%]), and the treatment interval (median, 3 days [5th and 95th percentiles, 0 and 51 days]) was prolonged in 130 patients (64.0% [CI, 57.4% to 70.6%]). Overall management delays of more than 10 and 25 days occurred in 33.5% (CI, 27.0% to 40.0%) and 18.7% (CI, 13.3% to 24.1%) of patients, respectively. The 55 patients with smears that were positive for acid-fast bacilli had a median treatment interval of 3 days (5th and 95th percentiles, 0 and 33 days); in 58.2% of patients (CI, 45.2% to 71.2%), this interval exceeded 24 hours.

Conclusions: Delays in initiation of treatment were more common than delays in the initial suspicion of tuberculosis. Both types of delays were common even in patients with disease that was confirmed by a positive smear. These data illustrate a need for improved education of physicians about the benefits of early initiation of therapy for tuberculosis.

One of the factors cited as contributing to the recent resurgence of tuberculosis is a decline in expertise in the treatment of tuberculosis among physicians trained in the postsanitarium era. At least three studies have shown that management errors are common and may contribute to the emergence of drug resistance (1–3). Nosocomial transmission from unsuspected cases of tuberculosis has resulted in rapid propagation of highly resistant strains of *Mycobacterium tuberculosis* (4–6). Improvement of the general competence of physicians in the care of patients with known or suspected tuberculosis has been an important strategy for re-establishing control of tuberculosis in the United States (7–9). Along with diagnostic and treatment guidelines, specific recommendations have been outlined for prevention of nosocomial transmission in hospitals and other health care institutions (10).

Maintenance of a high index of suspicion by clinicians, rapid institution of respiratory isolation, and early initiation of effective therapy are among the key principles of tuberculosis control (7, 9). Several studies have nevertheless suggested that delays in suspicion and treatment of tuberculosis are common among both hospitalized patients and those who visit outpatient clinics (11–13). These delays have been attributed to subtle or unusual disease presentations (12, 14, 15). Subsequent investigations have attempted to identify predictors of tuberculous disease as a means of shortening the interval between patient presentation and diagnosis (16, 17). However, few studies have systematically examined other delays, such as the time from initial suspicion of disease to initiation of therapy, that occur in the management of patients with tuberculosis. We describe the occurrence and patterns of various delays in the management of tuberculosis in our health system between 1988 and 1996.

Methods

Study Setting and Patients

The study was conducted at the Barnes-Jewish-Christian (BJC) Health System, a university-affiliated network that provides medical care to patients from St. Louis and the surrounding regions of central and southern Missouri and southern Illinois.

Ann Intern Med. 1999;130:404-411.

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Table 1. Demographic Characteristics, Risk Factors for Tuberculosis, and Disease Presentation

Characteristic	Entire Cohort (n = 203)	Patients with Overall Delay of More Than 24 Hours (n = 152)	Patients with No Overall Delay (n = 51)	P Value*
	←————— n (%) —————→			
Demographic				
Ethnic minority	116 (57.1)	80 (52.6)	36 (70.6)	0.03
Contact with an active case of tuberculosis	45 (22.2)	28 (18.4)	17 (33.3)	0.03
Age ≥ 60 years	93 (45.8)	63 (41.4)	30 (58.8)	0.03
Chronic renal failure	15 (7.4)	14 (9.2)	1 (2.0)	0.09
Intravenous drug use	10 (4.9)	5 (3.3)	5 (9.8)	0.13
Alcoholism	44 (21.7)	30 (19.7)	14 (27.4)	>0.2
Diabetes	29 (14.3)	20 (13.2)	9 (17.6)	>0.2
Immunosuppression	27 (13.3)	22 (14.5)	5 (9.8)	>0.2
Male sex	112 (55.2)	86 (56.6)	26 (51.0)	>0.2
Foreign born	23 (11.3)	16 (10.5)	7 (13.7)	>0.2
Presence of ≥ 1 risk factor for tuberculosis	162 (79.8)	121 (79.6)	41 (80.4)	>0.2
10% below ideal body weight	40 (19.7)	30 (19.7)	10 (19.6)	>0.2
HIV infection	16 (7.9)	12 (7.9)	4 (7.8)	>0.2
Homeless	8 (3.9)	6 (4.0)	2 (3.9)	>0.2
Resident of an extended-care facility	5 (2.5)	4 (2.6)	1 (2.0)	>0.2
Incarcerated (past or present)	7 (3.4)	5 (3.3)	2 (3.9)	>0.2
Clinical and radiographic				
Hemoptysis	20 (9.9)	9 (5.9)	11 (21.6)	<0.01
Smear-positive disease	55 (27.1)	32 (21.0)	23 (45.1)	<0.01
Cavitary disease	27 (13.3)	10 (6.6)	17 (33.3)	<0.01
Weight loss	82 (40.4)	54 (35.5)	28 (54.9)	0.02
Night sweats	44 (21.7)	27 (17.8)	17 (33.3)	0.02
Disease type				
Pulmonary	100 (49.3)	67 (44.0)	33 (64.7)	0.02
Extrapulmonary	47 (23.2)	41 (27.0)	6 (11.8)	
Both	56 (27.6)	44 (29.0)	12 (23.5)	
Meningeal disease	11 (5.4)	5 (3.3)	6 (11.8)	0.03
Abnormal chest radiograph	135 (66.5)	95 (62.5)	40 (78.4)	0.04
Presence of ≥ 1 symptom	184 (90.6)	135 (88.8)	49 (96.1)	0.17
Fever	97 (47.8)	70 (46.0)	27 (52.9)	>0.2
Mechanically ventilated for more than 1 day	26 (12.8)	18 (11.8)	8 (15.7)	>0.2
Recent cough	45 (22.2)	32 (21.0)	13 (25.5)	>0.2
Lymphadenopathy	29 (14.3)	23 (15.1)	6 (11.8)	>0.2
Chronic cough	77 (37.9)	56 (36.8)	21 (41.2)	>0.2
Miliary disease	28 (13.8)	20 (13.2)	8 (15.7)	>0.2
Admission to the intensive care unit	53 (26.1)	39 (25.7)	14 (27.4)	>0.2

*Comparison of patients with and without an overall delay.

The specific hospitals enrolling patients in this investigation were Barnes-Jewish (a 1500-bed urban teaching hospital affiliated with Washington University School of Medicine), Christian Northeast (475 beds), Christian Northwest (229 beds), Missouri Baptist (500 beds), Boone (344 beds), Alton Memorial (222 beds), Parkland (133 beds), and Barnes-Jewish-St. Peters (111 beds). All patients admitted to the BJC Health System from January 1988 to December 1996 were eligible for inclusion in this investigation. All patients older than 15 years of age with a positive culture for *Mycobacterium tuberculosis* were entered into the study database. The study was approved by the Washington University School of Medicine Human Studies Committee.

Study Design and Data Collection

We used a retrospective cohort design that segregated hospitalized patients with tuberculosis according to whether or not the initial suspicion or treatment of tuberculosis had been delayed. An infection control nurse reviewed the inpatient and outpatient medical and health department records

of each patient by using a standardized data collection tool. In addition, telephone follow-up was performed for all patients with working telephones. Outcome variables were mortality, duration of hospitalization, administration of antituberculous therapy, and delays in the diagnosis and treatment of tuberculous disease.

Standard risk factors, as defined by the American Thoracic Society and the Centers for Disease Control and Prevention (8), for tuberculous infection and for development of tuberculous disease after infection were sought from the medical record. The following presenting signs and symptoms at the time of hospitalization were recorded: cough present for at least 4 weeks, fever, night sweats, weight loss, hemoptysis, dyspnea, chest pain, fatigue, weakness, and anorexia. The presence of peripheral lymphadenopathy that was palpable on the physical examination was noted along with the findings from chest radiography done at hospital admission. The type of tuberculous disease was recorded by using the following descriptors: pulmonary, extrapulmonary, smear-positive sputum, cavitary, miliary, and menin-

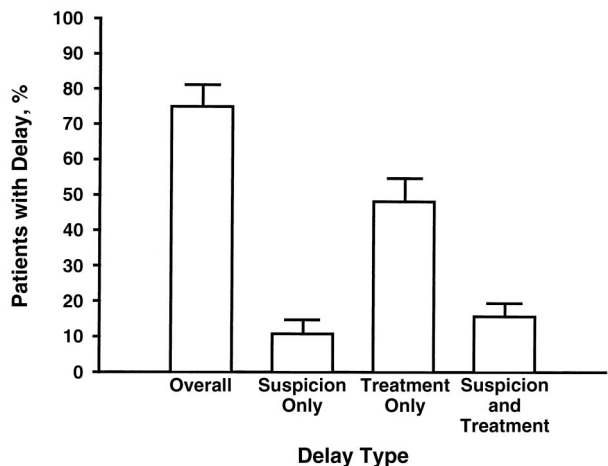


Figure 1. Percentage of patients with delays in diagnosis and treatment of culture-proven tuberculosis. Upper 95% CIs are shown.

geal. Extrapulmonary tuberculosis was defined as disease in organs other than the lungs (including pleurisy but not mediastinal lymphadenopathy) (18). Miliary disease was defined by using standard criteria (19). Mortality was defined as death from any cause within 12 months (360 days) from the date of initial hospital admission. Samples for mycobacterial smears and cultures were processed, stained, and cultured according to standard procedures (20).

Three time intervals were calculated by using dates obtained from review of medical and public health records. The *overall management interval* was defined as the time from admission to initiation of antituberculous chemotherapy. The *suspicion interval* was defined as the time from admission to the first suspicion of tuberculosis, and the *treatment interval* was the time from the first suspicion of disease to initiation of treatment. Intervals that exceeded 24 hours were considered indicative of a delay. Suspicion of tuberculosis required either an order for respiratory isolation or submission of specimens for acid-fast smear or culture. Mortality during the follow-up period was determined by using a combined review of the medical and health department records and telephone follow-up and was confirmed by using the death certificate registry of Missouri and records of the U.S. Social Security Administration.

For the past 3 years, the infection control department of Barnes-Jewish Hospital, the largest institution in the BJC Health System, has maintained a database describing employees who sustained a workplace exposure to patients with tuberculosis. From this database, we extracted the numbers of employees with documented exposures for each patient with tuberculosis who was not efficiently isolated and treated.

Statistical Analysis

All comparisons were unpaired, and all tests of significance were two-tailed. Continuous variables were compared by using the Student *t*-test for normally distributed variables and the Wilcoxon rank-sum test for non-normally distributed variables. The chi-square test and the Fisher exact test were used to compare categorical variables. The primary data analysis compared patients who experienced an overall management delay with those who had not experienced such delays. Relative risks, odds ratios, and their 95% CIs were calculated by using standard methods (21). All values are expressed as the median \pm SD (continuous variables) or as a percentage of the group from which they were derived (categorical variables), along with fifth and ninety-fifth percentiles. A *P* value of 0.05 or less was considered statistically significant.

Kaplan–Meier curves were used to analyze patient survival. Multiple logistic regression analysis, done by using a commercial statistical package (22), was used to identify predictor variables that were significantly related to the likelihood of having an overall management delay during the period of observation (that is, overall management delay was the dependent outcome variable). Baseline covariates were included in models that were judged a priori to be clinically sound. This was prospectively determined to be necessary to avoid producing spuriously significant results with multiple comparisons (23). Potential predictor variables for model entry were identified by using univariate analysis, in which a *P* value of 0.15 was used to determine entry into the logistic regression model. Results of the logistic regression analysis are reported as adjusted odds ratios with 95% CIs.

Results

Culture-positive tuberculosis was diagnosed in 203 patients hospitalized in the BJC Health System. Patients ranged in age from 16 to 95 years (mean, 58.0 ± 21.4 years); 55.2% were men and 44.8% were women. Demographic characteristics, risk factors for tuberculous infection, and characteristics of disease presentation are shown in **Table 1**.

Overall Management Delay

The median interval from hospital admission to initiation of antituberculous chemotherapy (overall management interval) was 6 days (5th and 95th percentiles, 1 and 52 days). An overall delay in management (overall management interval longer than 24 hours) occurred in 152 patients (74.9% [95% CI, 68.9% to 80.9%]) (**Figure 1**). An overall

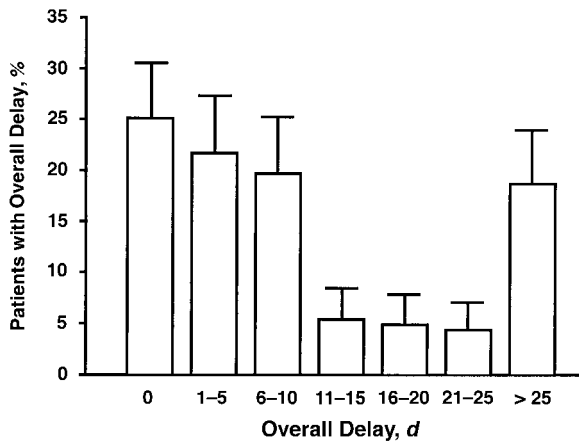


Figure 2. Distribution of overall delays for the study cohort. Upper 95% CIs are shown.

delay of more than 10 days occurred in 68 patients (33.5% [CI, 27.0% to 40.0%]), and an overall delay of more than 25 days was seen in 38 patients (18.7% [CI, 13.3% to 24.1%]) (Figure 2). No significant differences in the likelihood of an overall management delay ($P > 0.2$), suspicion delay ($P > 0.2$), or treatment delay ($P > 0.2$) were found among patients admitted to a tertiary-level, university-affiliated medical center compared with patients who received care in community hospitals.

Univariate analysis identified demographic factors and disease characteristics that were significantly associated with an overall management delay (Table 1). Multiple logistic regression analysis that controlled for sex, age, ethnicity, and other potential risk factors for overall management delay as identified by the univariate analysis showed that absence of cavitary infiltrates, absence of meningeal disease, absence of hemoptysis, and smear-negative sputum were independently associated with overall management delay (Table 2). No significant relation was found between the presence or absence of an overall management delay and 1-year mortality ($P > 0.2$) (Figure 3).

Suspicion and Treatment Intervals

The median duration of the suspicion interval, the period between hospital admission and the first consideration of the diagnosis of tuberculosis, was 1 day (5th and 95th percentiles, 0 and 16 days). The median interval between first suspicion of disease and initiation of treatment (treatment interval) was 3 days (5th and 95th percentiles, 0 and 51 days). The suspicion interval was prolonged beyond 24 hours in 54 patients (26.6% [CI, 20.5% to 32.7%]). The treatment interval was prolonged beyond 24 hours in 130 patients (64.0% [CI, 57.4% to 70.6%]). Thirty-two patients (15.8%) had delays in both suspicion and initiation of treatment. Among the 55

patients with sputum smears that were positive for acid-fast bacilli, treatment initiation was delayed for 32 (58.2% [CI, 45.2% to 71.2%]). The duration of the treatment interval for patients with smear-positive sputum (median, 3 days [5th and 95th percentiles, 0 and 33 days]) was significantly shorter than that of patients with smear-negative sputum (median, 4 days [5th and 95th percentiles, 0 and 66 days]) ($P < 0.001$) (Figure 4).

Effect of Delays in Management of Tuberculosis

Of patients with tuberculosis who were hospitalized at Barnes-Jewish Hospital over 3 years, 25 were identified by the infection control department as the source of health care worker exposures. In these patients, a diagnosis of tuberculosis was not considered at admission and initiation of isolation and treatment was delayed. The number of employees exposed over this period was 598 and ranged from 1 to 76 employees (mean, 23.9; median, 19) per hospitalized patient with tuberculosis.

Changes in the Prevalence of Various Delays over Time

During the 9-year study period (1988–1996), the prevalence of an overall delay ranged from 59.1% (CI, 38.5% to 79.7%) to 84.0% (CI, 69.6% to 98.4%). Similarly, the prevalence of a delay in suspicion ranged from 9.1% (CI, 0.0% to 21.1%) to 41.2% (CI, 17.8% to 64.4%), and the prevalence of a delay in initiation of treatment ranged from 54.6% (CI, 33.8% to 75.4%) to 77.3% (CI, 58.9% to 95.7%). In 6 of the 9 years, suspicion was delayed less than half as frequently as was treatment. No statistically significant changes in the pattern of delay types were observed during the study period.

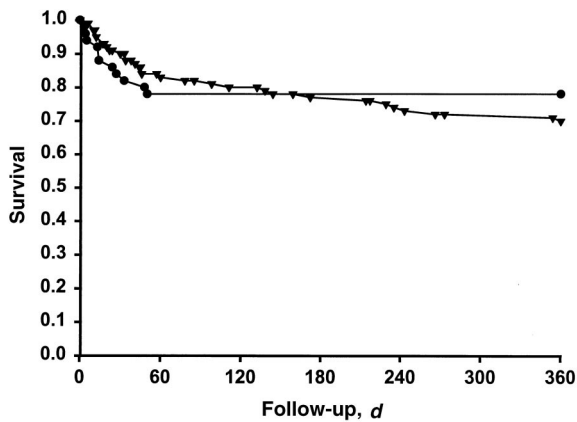
Discussion

Despite recent advances in culturing techniques, several weeks often pass between the initial suspi-

Table 2. Logistic Regression Analysis Identifying Variables Associated with the Presence of a Delay in the Diagnosis of Tuberculosis*

Variable	Adjusted Odds Ratio (95% CI)	P Value
Absence of cavitary lung disease	5.9 (3.6–9.5)	<0.01
Absence of meningeal disease	8.8 (4.6–17.1)	<0.01
Absence of hemoptysis	3.8 (2.2–6.6)	0.01
Smear-negative sputum	2.4 (1.6–3.5)	0.03
Baseline odds	0.1 (0.1–0.2)	–

* Other variables that were considered but discarded from the model because they were not statistically significant included sex, age, ethnicity, contact with an active case of tuberculosis, presence of chronic renal failure, intravenous drug use, abnormal chest radiograph, weight loss, night sweats, and disease type (pulmonary or extrapulmonary).



	0	60	120	180	240	300	360
Patients with delay	51	40	40	40	40	40	40
Patients without delay	152	126	122	117	112	109	108

Figure 3. Kaplan-Meier survival curves for patients with an overall delay in the management of tuberculosis (circles) and patients without an overall delay (triangles).

cision of tuberculosis and the final microbiological confirmation. During this time, an untreated patient's condition will worsen and he or she will remain a source of secondary spread throughout the community. Therefore, antituberculous chemotherapy should ideally be started as soon as tuberculosis is suspected and should certainly be instituted if smears are positive for acid-fast bacilli (7, 8, 10, 24). Surprisingly, of the 203 hospitalized patients in whom tuberculosis was diagnosed, the management of only 51 patients (25.2%) attained this ideal. Although delays in suspicion of tuberculosis occurred, delayed initiation of antituberculous chemotherapy after the diagnosis of tuberculosis had already been considered was more common. Initiation of treatment was delayed in 64% of patients in our cohort. Even smear positivity did not prevent such delays; 58.2% of this subgroup experienced treatment delays (median time to treatment, 3 days) (Figure 4). Management delays resulted in an average of 23.9 employees exposed per case of tuberculosis. Finally, the proportion of patients in our cohort who experienced these delays seems to have been relatively constant over the 9 years of the study.

The two groups of patients, those for whom management had been delayed and those for whom management was timely, differed little with respect to demographic characteristics, risk factors for tuberculosis, or clinical characteristics (Table 1). Only the absence of four characteristics associated with the most severe forms of tuberculosis were independent predictors of such delays. The absence of the most common characteristics of tuberculous disease, including weight loss, night sweats, and radiographic abnormalities, was not independently associated with the presence of overall management delays.

Two previous studies determined that tuberculosis is not suspected at hospital admission in roughly 40% of cases (11, 12). In both studies, delays in suspicion were attributed primarily to subtle disease presentations such as those that might be expected in elderly patients. In contrast, our study suggests that tuberculosis is managed more efficiently in elderly patients, possibly because of an increased awareness of the prevalence of the disease in this population. Of interest, delay and ethnicity seemed to be associated; white patients were more likely than members of ethnic minority groups to experience delays in management, suggesting that the occurrence of tuberculosis among white patients may be underestimated by clinicians. In contrast to previous studies, which have asserted that a causal relation exists between diagnostic delay and mortality, we were unable to demonstrate such an association over 12 months of follow-up (Figure 3) (11, 12, 14, 15). Delayed treatment is considered particularly detrimental to patients who are co-infected with HIV (25, 26). Thus, the absence of an association between delayed management and mortality may reflect the low incidence of HIV co-infection in our population.

The high prevalence and greater mean duration of treatment delays compared with suspicion delays suggests the presence of an artificial threshold for the initiation of antituberculous chemotherapy. Clinicians seem to prefer to receive culture results before committing the patient to treatment. The current standard of care dictates that all positive acid-fast smears be regarded as diagnostic of *M. tuberculosis* disease until proven otherwise (8). It was surprising that smear positivity was not independently associated with prompt initiation of treatment. Indeed, most patients (58.2%) with positive smears had delayed initiation of treatment.

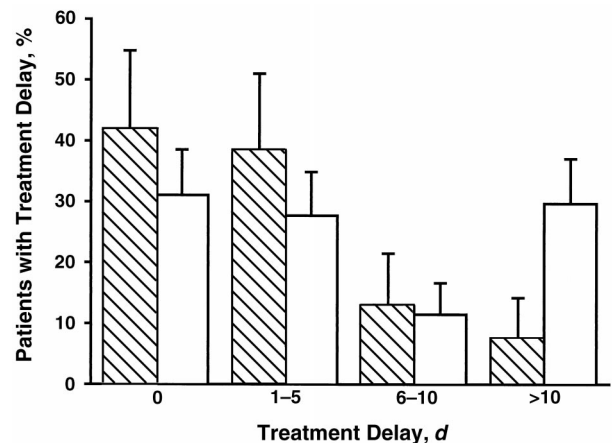


Figure 4. Percentage of patients with treatment delay according to specified delay intervals. Striped bars represent patients with positive sputum smears; white bars represent patients with negative sputum smears. Upper 95% CIs are shown.

Although the median interval to treatment among this subgroup (3 days) was significantly lower than that in patients with negative sputum smears (**Figure 4**), it was well beyond the 24-hour period mandated by the Centers for Disease Control and Prevention for reporting of smear results by laboratories to health care practitioners (7, 9). Because of the retrospective nature of our study and the large number of individual clinicians involved, we were unable to determine with certainty the reasons for the delayed treatment of patients with positive smears. However, because our cohort included only inpatients, procedural barriers to treatment initiation should have been minimal. A more likely explanation is a poor understanding among some clinicians of the implications of a positive acid-fast smear, with a tendency to wait for final identification so that the presence of mycobacteria other than tuberculosis can be excluded.

Many investigators have commented on a general lack of familiarity with the protean manifestations of tuberculosis among general physicians trained in the past 20 years (4, 5). Our study coincided with an intensive national educational campaign designed to improve the knowledge base of clinicians likely to encounter patients with tuberculosis (9). This cohort thus offered a unique opportunity to examine changes in practice over 9 years. We were unable to find any measurable improvement in the timeliness with which tuberculosis was suspected or treated during the study period. Our cohort included patients who had been admitted to a tertiary-level, university-affiliated medical center as well as to community hospitals. Although one might expect educational policies to penetrate community hospitals more slowly, we found no significant differences in the likelihood of an overall management delay, suspicion delay, or treatment delay between these two types of institutions.

Our study had several limitations. Because we studied physician practices within a single health system, our findings may not be widely generalizable. In addition, by including only hospitalized patients, our data may not accurately reflect the patterns of care in physicians' offices. It would have been useful to examine the delays between hospital admission and initiation of respiratory isolation because such delays would probably affect the risk for nosocomial transmission more directly. Although in most cases, the initial suspicion of tuberculosis and the initiation of respiratory precautions coincided, the retrospective study design precluded us from confirming that this was always the case. In addition, the first clinical suspicion may have occurred earlier than was documented in the medical record. There is, however, less uncertainty about the initiation of treatment, which can be verified by phar-

macy records. It is also possible that our criteria for delay were overly strict. We believe, however, that when dealing with hospitalized patients, clinicians must consider tuberculosis at admission so that patients may be placed in respiratory isolation and the risk for nosocomial spread can be minimized. Finally, although no effect on patient mortality could be demonstrated, other consequences of delays in the management of tuberculosis are apparent. We show that each unrecognized case of tuberculosis resulted in an average of 23.9 health care worker exposures. The subsequent evaluation of each of these workers would add substantially to the overall costs of hospitalization (27–30).

To assist in clinical decision making, we offer the following recommendations for management of inpatients with suspected tuberculosis, based on guidelines established by the American Thoracic Society and the Centers for Disease Control and Prevention (8, 10). All patients admitted to the hospital should undergo prompt assessment of their risk for active tuberculosis. The stringency of this assessment must be based on the prevalence of tuberculosis among hospital admissions. Patients in whom the diagnosis is suspected must be placed in respiratory isolation immediately and diagnostic studies, including chest radiography, collection of sputum for acid-fast smear and culture, and tuberculin skin testing must be done in the first 24 hours of hospitalization. The timing of initiation of treatment is less straightforward and must rely on the clinical judgment of the treating clinician. However, certain guiding principles are applicable. Treatment for tuberculosis should be started immediately in all cases in which acid-fast organisms are present on smears unless infection with a nontuberculous mycobacterial species has been confirmed and the diagnosis of tuberculosis has otherwise been excluded. In addition, patients whose chest radiographs or symptoms (or both) are highly suggestive of tuberculosis should also begin antituberculous therapy while results of smears are awaited. In high-risk patients with negative smears, treatment should be continued until final culture results are available or further diagnostic studies are undertaken. The threshold for initiation of antituberculous therapy in the absence of confirmatory evidence for the diagnosis (positive smears or cultures) must be low in patients with demographic or clinical characteristics that increase their risk for tuberculosis. Once treatment is initiated, it should be administered under direct observation and continued until hospital discharge or until an alternative diagnosis is confirmed and tuberculosis definitively excluded. Local health authorities should be notified so that arrangements for continuation of treatment after discharge can be made.

We acknowledge that application of these guidelines will result in the unnecessary initiation of treatment in some instances. Indeed, our study is limited by not including data on noninfected persons in whom tuberculosis was suspected. Therefore, we could not assess the cost-benefit of early treatment for suspected tuberculosis. We believe, however, that the hospital setting necessitates a more conservative treatment approach to minimize the risk for nosocomial spread posed by unisolated, untreated inpatients with active tuberculosis. This risk has been demonstrated in a series of hospital outbreaks over the past several years (2, 31–33). Moreover, the benefits of early treatment for prevention of nosocomial spread have been well described (7, 8, 24, 34). Therefore, until more accurate means of risk assessment become available, we believe that this type of standard would be most prudent.

In summary, we identified a series of delays in the management of patients with tuberculosis, including delays in initial suspicion and in initiation of antituberculous chemotherapy. These delays were not dependent on the subtlety of the clinical presentation. Most significant is the finding that despite recent educational efforts, delays most commonly occurred in institution of treatment, not in initial suspicion of tuberculosis (9, 10). Thirty-two (58.2%) of the 55 patients with positive sputum smears experienced delays in treatment. The delays we describe are therefore more likely dependent on the experience and practice styles of individual clinicians, a variable that should be modifiable with education. It is evident that future efforts must be directed toward improving the management of tuberculosis once it is suspected, the most problematic aspect of tuberculosis management in our cohort. The dramatic reductions in the incidence of tuberculosis in such large urban areas as New York City and Baltimore illustrate, in part, the benefits of recent educational programs (35, 36). Our data, however, indicate that continued efforts to educate clinicians on appropriate management of tuberculosis are required, particularly in such areas as St. Louis, where the prevalence of tuberculosis is lower and clinicians may be less experienced.

Acknowledgments: The authors thank Vic Tomlinson, MPA, Chief, State of Missouri Bureau of Tuberculosis Control and the staff of the state and local health departments of Missouri and Illinois for providing follow-up information.

Grant Support: In part by grant U50-CCU-710076-04 from the Centers for Disease Control and Prevention and the National Institute for Occupational Safety and Health.

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References

1. Byrd RB, Horn BR, Solomon DA, Griggs GA, Wilder NJ. Treatment of tuberculosis by the nonpulmonary physician. *Ann Intern Med.* 1977;86:799-802.
2. Mahmoudi A, Iseman MD. Pitfalls in the care of patients with tuberculosis. Common errors and their association with the acquisition of drug resistance. *JAMA.* 1993;270:65-8.
3. Sumartojo EM, Geiter LJ, Miller B, Hale BE. Can physicians treat tuberculosis? Report on a national survey of physician practices. *Am J Public Health.* 1997;87:2008-11.
4. Fischl MA, Uttamchandani RB, Daikos GL, Poblete RB, Moreno JN, Reyes RR, et al. An outbreak of tuberculosis caused by multiple-drug-resistant tubercle bacilli among patients with HIV infection. *Ann Intern Med.* 1992;117:177-83.
5. Pearson ML, Jereb JA, Frieden TR, Crawford JT, Davis BJ, Dooley SW, et al. Nosocomial transmission of multidrug-resistant *Mycobacterium tuberculosis*. A risk to patients and health care workers. *Ann Intern Med.* 1992;117:191-6.
6. Valway SE, Richards SB, Kovacovich J, Greifinger RB, Crawford JT, Dooley SW. Outbreak of multi-drug-resistant tuberculosis in a New York State prison, 1991. *Am J Epidemiol.* 1994;140:113-22.
7. Control of tuberculosis in the United States. American Thoracic Society. *Am Rev Respir Dis.* 1992;146:1623-33.
8. Bass JB Jr, Farer LS, Hopewell PC, O'Brien R, Jacobs RF, Ruben F, et al. Treatment of tuberculosis and tuberculous infection in adults and children. *Am J Respir Crit Care Med.* 1994;149:1359-74.
9. The American Lung Association Conference on re-establishing control of tuberculosis in the United States. *Am J Respir Crit Care Med.* 1996;154:251-62.
10. Guidelines for preventing transmission of *Mycobacterium tuberculosis* in health-care facilities, 1994. Centers for Disease Control and Prevention. *MMWR Morb Mortal Wkly Rep.* 1994;43:1-132.
11. Counsell SR, Tan JS, Dittus RS. Unsuspected pulmonary tuberculosis in a community teaching hospital. *Arch Intern Med.* 1989;149:1274-8.
12. Mathur P, Sacks L, Auten G, Sall R, Levy C, Gordin F. Delayed diagnosis of pulmonary tuberculosis in city hospitals. *Arch Intern Med.* 1994;154:306-10.
13. Liam CK, Tang BG. Delay in the diagnosis and treatment of pulmonary tuberculosis in patients attending a university teaching hospital. *Int J Tuberc Lung Dis.* 1997;1:326-32.
14. Enarson DA, Grzybowski S, Dorken E. Failure of diagnosis as a factor in tuberculosis mortality. *Can Med Assoc J.* 1978;118:1520-2.
15. Heffner JE, Strange C, Sahn SA. The impact of respiratory failure on the diagnosis of tuberculosis. *Arch Intern Med.* 1988;148:1103-8.
16. Moran GJ, McCabe F, Morgan MT, Talan DA. Delayed recognition and infection control for tuberculosis patients in the emergency department. *Ann Emerg Med.* 1995;26:290-5.
17. Bock NN, McGowan JE Jr, Ahn J, Tapia J, Blumberg HM. Clinical predictors of tuberculosis as a guide for a respiratory isolation policy. *Am J Respir Crit Care Med.* 1996;154:1468-72.
18. World Health Organization. Tuberculosis Programme. Framework for Effective Tuberculosis Control. Geneva, Switzerland: World Health Organization; 1994. World Health Organization publication WHO/TB/94.170.
19. American Thoracic Society. Diagnostic standards and classification of tuberculosis. *Am Rev Respir Dis.* 1990;142:725-35.
20. Murray PR, Baron EJ, Pfaller MA, Tenover F, Tenover FC, eds. *Manual of Clinical Microbiology.* 6th ed. Washington, DC: American Society of Microbiology; 1995.
21. Rothman KJ. Analysis of crude data. In: Rothman K, ed. *Modern Epidemiology.* Boston: Little, Brown; 1986:153-74.
22. SAS/STAT User's Guide. Cary, NC: SAS Institute; 1990:1071-126.
23. Concato J, Feinstein AR, Holford TR. The risk of determining risk with multivariable models. *Ann Intern Med.* 1993;118:201-10.
24. Gordin FM, Slutkin G, Schecter G, Goodman PC, Hopewell PC. Presumptive diagnosis and treatment of pulmonary tuberculosis based on radiographic findings. *Am Rev Respir Dis.* 1989;139:1090-3.
25. Pablos-Mendez A, Sterling TR, Frieden TR. The relationship between delayed or incomplete treatment and all-cause mortality in patients with tuberculosis. *JAMA.* 1996;276:1223-8.
26. Tacconelli E, Tumbarello M, Ardito F, Cuda R. Tuberculosis significantly reduces the survival of patients with AIDS. *Int J Tuberc Lung Dis.* 1997;1:582-4.
27. Arno PS, Murray CJ, Bonuck KA, Alcapes P. The economic impact of tuberculosis in hospitals in New York City: a preliminary analysis. *J Law Med Ethics.* 1993;21:317-23.

28. Brown RE, Miller B, Taylor WR, Palmer C, Bosco L, Nicola RM, et al. Health-care expenditures for tuberculosis in the United States. *Arch Intern Med.* 1995;155:1595-600.
 29. Mohle-Boetani JC, Miller B, Halpern M, Trivedi A, Lessler J, Solomon SL, et al. School-based screening for tuberculous infection. A cost-benefit analysis. *JAMA.* 1995;274:613-9.
 30. Kellerman S, Tokars JI, Jarvis WR. The cost of selected tuberculosis control measures at hospitals with a history of *Mycobacterium tuberculosis* outbreaks. *Infect Control Hosp Epidemiol.* 1997;18:542-7.
 31. Beck-Sague C, Dooley SW, Hutton MD, Otten J, Breeden A, Crawford JT, et al. Hospital outbreak of multidrug-resistant *Mycobacterium tuberculosis* infections. Factors in transmission to staff and HIV-infected patients. *JAMA.* 1992;268:1280-6.
 32. Daley CL, Small PM, Schecter GF, Schoolnik GK, McAdam RA, Jacobs WR Jr, et al. An outbreak of tuberculosis with accelerated progression among persons infected with the human immunodeficiency virus. An analysis using restriction-fragment-length polymorphisms. *N Engl J Med.* 1992;326:231-5.
 33. Edlin BR, Tokars JI, Grieco MH, Crawford JT, Williams J, Sordillo EM, et al. An outbreak of multidrug-resistant tuberculosis among hospitalized patients with the acquired immunodeficiency syndrome. *N Engl J Med.* 1992;326:1514-21.
 34. Levy H, Feldman C, Sacho H, van der Meulen H, Kallenbach J, Koornhof H. A reevaluation of sputum microscopy and culture in the diagnosis of pulmonary tuberculosis. *Chest.* 1989;95:1193-7.
 35. Chaulk CP, Moore-Rice K, Rizzo R, Chaisson RE. Eleven years of community-based directly observed therapy for tuberculosis. *JAMA.* 1995;274:945-51.
 36. Frieden TR, Fujiwara PI, Washko RM, Hamburg MA. Tuberculosis in New York City—turning the tide. *N Engl J Med.* 1995;333:229-33.
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CIGARETTE, something that should be obscene, not smoked.

Rodman Philbrick
Freak the Mighty
New York: Scholastic; 1993

Submitted by:
John Fornace, DO
Norristown, PA 19401

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