



MORBIDITY AND MORTALITY WEEKLY REPORT

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Outbreak of Multidrug-Resistant Tuberculosis — Texas, California, and Pennsylvania

On January 9, 1986, a 30-year-old black man (patient 8 in Tables 1–3) presented to a hospital emergency room with an illness of 2 months' duration. The illness was characterized by cough, weakness, malaise, fever, night sweats, shortness of breath, and hemoptysis. The patient's chest radiograph showed extensive cavitary disease that was highly suggestive of pulmonary tuberculosis (TB). Sputum cultures were positive for *Mycobacterium tuberculosis*, and the organisms demonstrated resistance to isoniazid (INH), rifampin (RIF), and streptomycin (Table 2). The patient was treated with pyrazinamide (PZA), ethambutol, capreomycin (CAP), ethionamide (ETH), and an experimental drug (ofloxacin). Although totally compliant with this treatment regimen, the patient, after initial improvement, experienced relapse on therapy, and surgery was recommended. In March 1987, he died of postoperative complications of a right pneumonectomy. The patient had been hospitalized from the time of diagnosis to death (nearly 14 months). Autopsy revealed active disease in his left lung.

Subsequent epidemiologic investigation revealed that patient 8 had been a close contact of four persons (patients 1–4) who were being treated for infectious drug-resistant TB. All four persons were members of an extended family whose members interacted extensively and lived intermittently in three states. From July 1971 through May 1990, eight persons in and two close contacts of this extended family have been diagnosed with clinically active pulmonary TB. The most recent case was diagnosed in January 1989.

TABLE 1. Characteristics of patients with multidrug-resistant tuberculosis — Texas, California, and Pennsylvania

Patient no.	Relationship to index patient	Date first diagnosed	Age at diagnosis	State of diagnosis	Status
1	Index patient	Jul. 1971	41 yrs.	Texas	Died (Aug. 1987)
2	Relative	Apr. 1976	26 yrs.	Texas	Recovered
3	Relative	Jan. 1981	48 yrs.	Texas	Recovered
4	Relative	Oct. 1981	27 yrs.	Texas	Ill
5	Relative	Feb. 1982	4 mos.	California	Recovered
6	Relative	Oct. 1984	31 yrs.	Texas	Recovered
7	Relative	Apr. 1985	37 yrs.	Texas	Ill
8	Friend	Jan. 1986	30 yrs.	Texas	Died (Mar. 1987)
9	Friend	Apr. 1986	29 yrs.	Texas	Recovered
10	Relative	Jan. 1989	10 yrs.	Pennsylvania	Recovered

Tuberculosis — Continued

The index patient (patient 1) was a 41-year-old man whose TB was diagnosed in Texas in 1971. He was hospitalized and treated with an unknown regimen from July 1971 to April 1972 and discharged on INH and para-amino salicylic acid. From 1971 to 1982, patient 1 was admitted to the hospital on six occasions because of recurrences of pulmonary TB; recurrence was attributed to his noncompliance with outpatient therapy. In January 1983, he was admitted to the hospital for 3 months because of persistently positive cultures and was treated with INH, PZA, RIF, ETH, CAP, and cycloserine. After discharge, he was placed on daily supervised therapy and was more compliant with this regimen. In November 1984, he was readmitted for nearly 4 months to optimize therapy before surgery. He declined surgery and died in August 1987 from hemoptysis caused by TB.

TABLE 2. Drug-resistance patterns of sputum cultures from patients with multidrug-resistant tuberculosis — Texas, California, and Pennsylvania

Patient no.	Initial resistance pattern*	Final resistance pattern*†
1	Sensitive to all drugs tested	INH, RIF, SM, PAS, CS
2	INH	INH, RIF, SM
3	RIF	RIF
4	INH, RIF, PAS	INH, RIF, SM, EMB, CS
5	§	§
6	INH	INH
7	INH, RIF, SM	INH, RIF, SM, EMB
8	INH, RIF, SM	INH, RIF, SM, EMB
9	INH, RIF, PZA	INH, RIF, PZA
10	¶	¶

*INH = isoniazid; RIF = rifampin; SM = streptomycin; PAS = para-amino salicylic acid; CS = cycloserine; EMB = ethambutol; PZA = pyrazinamide.

†Before cure or death.

§Diagnosis established on the basis of exposure to patients 1–4, positive skin test, and abnormal chest radiograph with hilar adenopathy.

¶Diagnosis established on the basis of exposure to patient 4, positive skin test, and abnormal chest radiograph with infiltrate.

TABLE 3. Characteristics of hospitalization of patients with multidrug-resistant tuberculosis — Texas, California, and Pennsylvania

Patient no.	Quarantine	No. hospitalizations	No. hospital days	Cost of hospitalization*
1	Yes	9	971	\$251,320
2	Yes	7	617	217,445
3	No	3	81	20,250
4	No	5	509	263,500
5	No	1	14	11,200
6	No	0	0	0
7	Yes	4	128	57,158
8	No	2	427	119,560
9	No	2	40	10,000
10	No	0	0	0
Total cost				\$950,433

*Based on average cost per day from respective institutions or actual cost when available.

Tuberculosis — Continued

In 1976 and 1981, TB was diagnosed in two different relatives (patients 2 and 3) of the index patient. Contact investigation and follow-up over time of these patients, and later of patient 8, by health agencies in the three states subsequently identified patients 4, 5, 6, 7, 9, and 10. In addition, investigations revealed that 60 (47%) of 127 contacts of the extended family were tuberculin positive (skin test reaction: ≥ 5 mm induration), including 27 (43%) of 63 contacts in Texas, 25 (56%) of 45 contacts in California, and eight (42%) of 19 contacts in Pennsylvania. Thirty (50%) of those infected were children or adolescents. Infected contacts were monitored by sputum smears and cultures and chest radiographs at 3, 6, and 12 months for the first year, and every 6 months for 2 years. No prophylaxis was given to infected contacts because the contacts were presumed infected with multidrug-resistant organisms.

At least five family members and numerous contacts suffered from alcohol and drug addiction; however, none of the patients reported using intravenous drugs. Seven of the 10 patients were tested for human immunodeficiency virus antibody and were seronegative. Because members of the family had been incarcerated at various times, the family was suspicious of outsiders and secretive about their contacts, which complicated and impeded contact investigation. In addition, some family members believed that TB was incurable and that medications were ineffective.

Several of the patients were hospitalized for extended periods until they became culture negative, only to experience relapse once they were released and again were noncompliant with their medications. Patients 1 and 2 were legally quarantined on three occasions each. Patients 2 and 3 recovered only after supervised therapy. Patient 4, although now undergoing therapy, was frequently lost to follow-up. Patient 7 experienced relapse because of noncompliance, twice left the hospital against medical advice, and ultimately was quarantined. Because of health department experiences with this outbreak, patient 9 was placed on supervised therapy from onset. As of June 1, 1990, patients 2, 3, 5, 6, 9, and 10 are culture negative; patient 4 remains culture positive; and patient 7, although culture negative, remains in treatment.

As a result of this outbreak, supervised therapy with an initial regimen of four drugs is now used for all patients with active TB treated by the Fort Worth/Tarrant County Health Department.

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Editorial Note: Community outbreaks of drug-resistant TB have been reported in Mississippi (1); California, Montana, Nevada, and Utah (2); and North Carolina (3). Although the epidemiologic investigation in this report did not conclusively establish that all the patients were infected with the same strain of tubercle bacilli (because phage typing was not performed), epidemiologic evidence and drug-resistance patterns suggest a link.

Two prominent features of this outbreak are 1) its extended length and 2) its public health and economic burden. The cost of hospitalization of these 10 patients is estimated at \$950,433 (Table 3). This is more than five times the yearly budget of the Fort Worth/Tarrant County Tuberculosis Control Program, which treats approximately 100 cases of TB and 1000 persons with TB infection per year.

Tuberculosis - Continued

Containment of a TB outbreak involves treatment of patients and preventive therapy for infected contacts. The preventive therapy regimen for infected persons is 6-12 months of INH or, for suspected infection with INH-resistant organisms, 12 months of RIF (4). However, in this outbreak, preventive therapy was not viable because the 60 infected contacts were presumably infected with organisms resistant to INH and RIF. Bacillus of Calmette and Guérin (BCG) vaccine should be considered for uninfected children exposed to persons with multidrug-resistant TB (5).

Regimens for treatment of TB must contain multiple drugs to which the organisms are susceptible. Administration of a single drug or the addition of a single drug to a failing regimen can lead to development of a bacterial population resistant to that drug. Although patients 2-10 were initially infected with drug-resistant tubercle bacilli, patient 1 acquired drug resistance because of noncompliance and/or inappropriate therapy. Drug-resistant TB is difficult to manage, and consultation with experts in treating mycobacterial diseases is warranted for such patients.

The duration of therapy for TB is usually 6-9 months, and noncompliance is a major problem. For patients at high risk for noncompliance, supervised therapy should be administered by a health department worker at a clinic or other location convenient for the patient (6-8). As evidenced by this outbreak, it is critical to initiate supervised therapy early, before patients develop drug-resistant disease or are lost to follow-up. Interstate and intrastate communication may be essential in managing TB in persons who frequently change their state of residence.

If supervised therapy is not successful in managing TB patients, other approaches must be considered. Long-term hospitalization (9) and TB treatment in special residential facilities for the homeless (10) have been used in some areas. Quarantine measures, including temporary institutionalization, should be used in those rare cases when an infectious TB patient refuses to comply with self-administered or supervised therapy (11). Documentation of the cost of treating patients with drug-resistant disease, as was done in this investigation, may help support the need for strengthening outpatient treatment of TB, especially the use of supervised therapy.

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