

Persistence of a Highly Resistant Strain of Tuberculosis in New York City during 1990–1999

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One multidrug-resistant *Mycobacterium tuberculosis* (MDRTB) strain, strain W, caused several nosocomial outbreaks in New York City (NYC) during 1 January 1990–31 July 1993. We reviewed all MDRTB cases verified during 1 August 1993–31 December 1999 that had isolates with either this DNA pattern or a variant of this strain, and we compared them to the outbreak cases. Of 427 DNA-confirmed cases from 1990–1999, 161 (37%) were from 1 August 1993–31 December 1999; these 161 cases, from 56 hospitals and 2 correctional sites, constituted 28% of all MDRTB cases in NYC during this period. Compared with those from 1 January 1990–31 July 1993, patients from 1 August 1993–31 December 1999 were less likely to be infected with human immunodeficiency virus, to have been born in the United States, to be homeless, to have been incarcerated, and to have epidemiological links; 16% of patients had nosocomial- and 9% had community-exposure links. This strain was disseminated widely in the community during the outbreaks; postoutbreak cases likely represent reactivated disease among individuals infected during the outbreak periods in the community.

The resurgence of tuberculosis (TB) in New York City (NYC) during the early 1990s was complicated by nosocomial outbreaks of multidrug-resistant TB (MDRTB)—that is, disease with *Mycobacterium tuberculosis* isolates resistant to at least isoniazid and rifampin. Several of these outbreaks involved 1 strain, referred to as “strain W,” which is usually resistant to ≥ 6 anti-TB medications—isoniazid, rifampin, rifabutin, ethambutol, streptomycin, kanamycin—and often ethionamide, with variable resistance to pyrazinamide [1–5]. In these outbreaks, most patients were infected with human immunodeficiency virus (HIV); mortality exceeded 80%, with death occurring a median of 2 months after disease

onset. More recently, strain W isolates have been identified that have also acquired fluoroquinolone resistance [6]. During the 10 years since the institutional outbreaks, strain W has disseminated across the country [7] and has been identified in Europe as well [8].

Strain W accounted for nearly one-third of NYC cases with MDRTB during the initial outbreak, 1 January 1990–31 July 1993 (hereafter denoted “1990–1993”), as well as for one-fourth of US patients with MDRTB during the same time. Two hundred sixty-seven cases were DNA confirmed, and there were 90 cases that were highly suspected but that could not be confirmed by DNA analysis [1]. The purpose of this investigation is to describe the epidemiology of strain W during 1 August 1993–31 December 1999 (hereafter denoted “1993–1999”) and to compare it with that during the preceding period.

PATIENTS, MATERIALS, AND METHODS

Study population. *M. tuberculosis* isolates diagnosed during 1 August 1993–31 December 1994 were genotyped if they had resistance to isoniazid, rifampin, ethambutol, streptomycin, and kanamycin. From 1995 onward, 1 *M. tuberculosis* isolate from each patient di-

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agnosed with MDRTB was prospectively obtained and was sent to the Public Health Research Institute Tuberculosis Center (PHRITC), where DNA fingerprint analysis based on IS6110 Southern blot-hybridization pattern was performed. A case was defined as any patient with an isolate collected during 1993–1999 that had the 18-band IS6110 pattern identified as strain W or a closely related pattern (i.e., a strain W variant) whose relatedness could be confirmed by a combination of molecular markers, as described below, and resistance to at least isoniazid, rifampin, ethambutol, and streptomycin. Susceptibility results were reviewed for the following first- and second-line TB-treatment drugs: isoniazid, rifampin, pyrazinamide, ethambutol, streptomycin, and rifabutin (first-line drugs) and fluoroquinolone (usually ciprofloxacin or ofloxacin), kanamycin or amikacin, capreomycin, ethionamide, para-aminosalicylic acid, and cycloserine (second-line drugs). The Bactec radiometric method was used to perform susceptibility tests for first-line drugs except rifabutin, for most isolates [9], and the standard-proportion method with Middlebrook 7H10 media was used to perform susceptibility tests for both first- and second-line drugs, for all isolates [10]. The majority of these tests were conducted at 2 reference laboratories—the New York City Department of Health Mycobacteriology Laboratory and the New York State Department of Health, Wadsworth Center.

IS6110 DNA analysis and other molecular studies. DNA analysis of isolates was performed by a standard method, as described elsewhere [11]. The IS6110 Southern blot-hybridization patterns were compared on a Sun Sparc5 workstation using Bio Image Whole Band Analyzer software, version 3.4 (Bio Image). The IS6110 pattern of the *M. tuberculosis* strain under investigation is defined by an 18-band Southern blot-hybridization pattern that was first assigned the name “strain W” at the PHRITC [8]; previously, the W strain had been noted to have 17 IS6110 bands, because of an unresolved doublet band [1]. IS6110 banding patterns similar to those of strain W but differing by 1 or 2 hybridization bands were denoted by the addition of a number to the cluster letter W (e.g., W1–W7). All W cases considered in the present study, including W variants, had to meet strict molecular criteria, as described elsewhere and summarized below.

Strain W and the closely related and epidemiologically significant W variants are distinguished from all other phylogenetically related W variants by a specific nested-PCR technique based on 2 IS6110 insertions in the *NTF* locus as well as by a combination of mutations in the drug-target genes conferring resistance to antibacterial agents [12]. The mutations associated with drug resistance in strain W and its variants are invariably as follows: *rpoB* (codon 526 His→Tyr), causing rifampin resistance; *rpsL* (codon 43 Lys→Arg), causing streptomycin resistance; *embB* (codon 306 Met→Val), causing resistance to ethambutol, and a rare dinucleotide change in *katG* (codon 315

Ser→Thr), causing isoniazid resistance [8]. Isolates that did not meet all of these molecular criteria were considered to be epidemiologically unrelated and were not included in the present study.

Epidemiological and statistical methods. Demographic, clinical, and outcome data for each of the patients studied were obtained from direct patient interviews and medical-record review, by trained Bureau of Tuberculosis Control staff, on standardized data-collection instruments. Patients were considered to be HIV seropositive if there was documentation of a positive HIV-antibody test result in the medical record or if AIDS was diagnosed before TB. Date of diagnosis of TB was defined as the collection date of the first specimen from which a strain W or a strain W-variant *M. tuberculosis* isolate was cultured. Appropriate treatment was considered to be the start of ≥ 2 anti-TB medications to which the patient's isolate was not known to be resistant. Patients were considered adherent if $\geq 80\%$ of the expected doses were ingested under direct observation of a health-care worker (HCW) or if, as verified by pharmacy medication-pickup logs, the self-administered regimen had no treatment gaps > 2 weeks. Homelessness was defined as either being in a public or private shelter or having no address at the time of the MDRTB diagnosis. Alcohol- and drug-abuse history during the 12 months before diagnosis was obtained. Information on duration of hospitalization at the time of diagnosis of TB and the minimum number and duration of hospitalizations while the patient was still receiving TB treatment was reviewed.

At the treatment or residential facilities, trained case managers obtained information about suspected and confirmed nosocomial and community exposure, on the basis of patient interviews, contact investigations, and medical-record reviews. Probable nosocomial transmission was considered if the newly infected patient was in the same section of an institution as another patient who had the identical *M. tuberculosis* strain and who had been infectious (i.e., the patient had a positive culture from a respiratory site) ≥ 30 days before disease onset in the newly infected patient.

Community transmission was considered probable if either of the following occurred:

1. A patient was exposed to another patient who had the identical *M. tuberculosis* strain and who had been infectious (i.e., had a positive culture from a respiratory site) ≥ 30 days before disease onset in the subsequently exposed patient; the exposure would have occurred in a home, single-room-occupancy hotel, homeless shelter, or some other noninstitutional setting.
2. The patient named, as a contact, another patient, who had either the same *M. tuberculosis*-isolate DNA pattern or MDRTB for which DNA-genotyping results were not available.

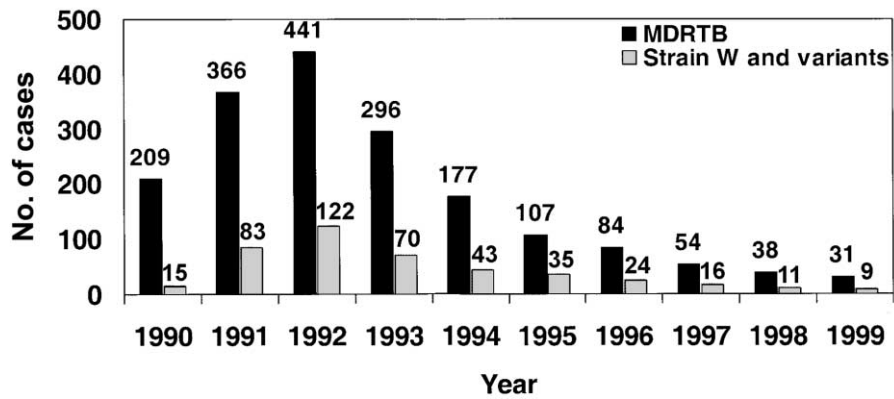


Figure 1. Incidence of strain W and its variants and of multidrug-resistant *Mycobacterium tuberculosis* (MDRTB), in New York City during 1990–1999. Susceptibility data for 1990–1992 are incomplete, and the total number of MDRTB cases in these years is likely underestimated.

Transmission could have been from a patient whose condition had been diagnosed before the study period. If evidence of nosocomial or community transmission was found, patients had an epidemiologic link. The source patient was not considered to have an epidemiologic link.

Data management and analyses were performed by use of Epi-Info, version 6.04d [13], and categorical variables were compared by the Mantel-Haenszel χ^2 test and Fisher's exact test. Continuous variables, which were limited to age and the time when appropriate treatment was started, were compared by the Wilcoxon rank-sum test. $P < .05$ was regarded as significant.

RESULTS

During 1993–1999, 567 patients were diagnosed with MDRTB. Of these, 161 (28%) were found to have an isolate that was identified as either strain W or one of its variants (W1, W12, W25, W31, W34, and W40) and that was resistant to at least isoniazid, rifampin, streptomycin, and ethambutol. The epidemiologic curve for cases during 1990–1999 that had either strain W or one of its variants is shown in figure 1. The incidence of cases peaked in 1992, with 122 cases, and reached its low in 1999, with 9 cases. However, among all patients with MDRTB who reside in NYC, the proportion of strain W and its variants has remained relatively constant, at 23%–33% (χ^2 for linear trend; $P = .56$).

Molecular analysis of the isolates of the 161 patients studied identified 7 closely related IS6110 patterns: of these 161 patients, 119 (74%) had strain W, and 32 (20%) had a pattern W1, which differed from the predominant pattern by the addition of a single IS6110 insertion; of the remaining 10 (6%) patients, 3 cases each had patterns W12 and W40, 2 cases had pattern W25, and 1 case each had patterns W31 and W34 (figure 2).

All 161 patients' isolates expressed resistance to streptomycin,

isoniazid, rifampin, and ethambutol. Resistance to other antimycobacterial agents is as shown in table 1. Compared with isolates from 1990–1993, isolates from 1993–1999 were less likely to be resistant to ethionamide and pyrazinamide, whereas those which were resistant to capreomycin and fluoroquinolone were more

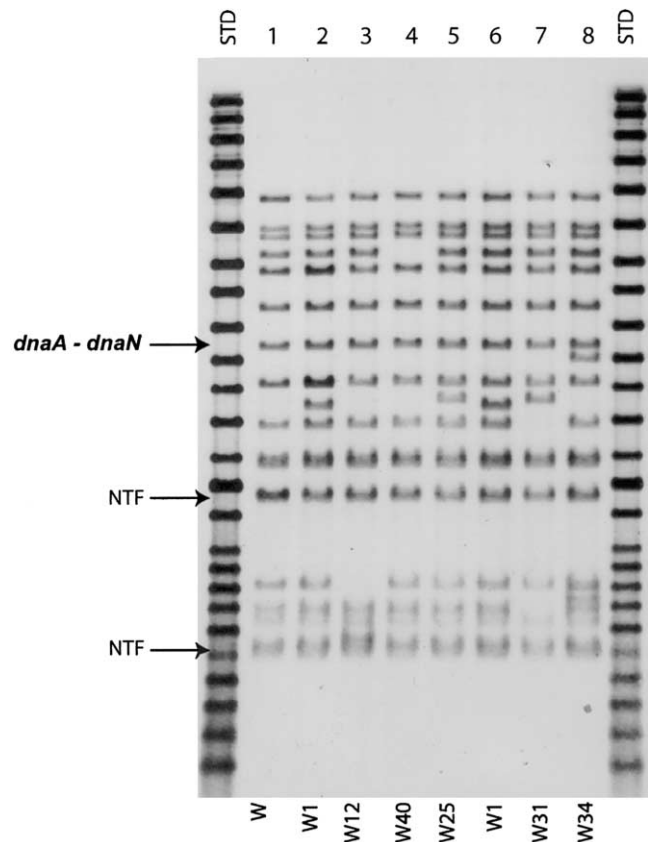


Figure 2. IS6110 Southern blot–hybridization pattern of strain W and its variants, in New York City during 1 August 1993–31 December 1999.

Table 1. Drug-susceptibility results for strain W and its variants, in New York City during 1 January 1990–31 July 1993 (1990–1993) and during 1 August 1993–31 December 1999 (1993–1999).

Drug	No. (%) of cases with either strain W or one of its variants				P
	1990–1993		1993–1999		
	Tested	Resistant	Tested	Resistant	
Capreomycin	204	10 (5)	151	24 (16)	.001
Cycloserine	200	2 (1)	152	2 (1)	NS
Ethionamide	204	110 (54)	153	42 (27)	<.001
Fluoroquinolone	195	0	153	9 (6)	.001
Kanamycin	208	191 (92)	158	150 (96)	NS
Para-aminosalicylic acid	120	1 (1)	147	2 (1)	NS
Pyrazinamide	188	104 (55)	150	68 (46)	.03

NOTE. By definition, all strains were resistant to isoniazid, rifampin, ethambutol, and streptomycin.

common. Notably, there had been no primary fluoroquinolone resistance identified in isolates from 1990–1993.

During this 1993–1999, these 161 patients studied were more likely to be HIV infected and US born, compared with other patients with MDRTB and with patients without MDRTB ($P < .0001$, for both comparisons). Patients resided in all 5 NYC boroughs and were diagnosed at 56 medical and 2 correctional facilities, as well as at the Medical Examiner's Office; of these 59 facilities, 26 reported 1 case each, 10 reported 2 cases each, and 23 reported ≥ 3 cases. One facility reported 20 (13%) of the 161 cases, and 4 other facilities reported 28 (17.5%) of them. Analysis of residences at the time of diagnosis identified 1 zip code with 9 patients, 1 with 6 patients, 3 with 5 patients each, 6 with 4 patients each, 8 with 3 patients each, and 16 with 2 patients each; 44 patients resided in unique NYC zip codes, 2 had unknown zip codes, and 5 lived outside NYC (figure 3). Demographic and clinical information of the 161 patients is presented in table 2. Compared with the cases reported during 1990–1993, the patients in the present study were less likely to be HIV seropositive, to have a history of injection drug use or alcohol abuse, to have been incarcerated, or to be homeless. Patients in the present study were more likely to be foreign born (21% vs. 10%). They originated from 18 different countries, and the median time since arrival in the United States was 20 years.

Compared with what was reported for the patients studied by Frieden et al., epidemiological linkages were identified in a much smaller proportion of patients in the present study (21% vs. 70%; $P < .001$). Nosocomial transmission could be documented in 25 (16%) of the 161 cases: as reported elsewhere, 12 patients were exposed in 1 facility [14]; the other 13 patients could be linked to 12 different facilities. Nine (6%) of the patients were known to have had a contact with another patient in the community who was known to have either strain W or

one of its variants. No epidemiological link could be identified in 127 (79%) of the 161 patients. Compared with patients without epidemiological linkages, the patients with documented epidemiological linkages were significantly less likely to be either HIV seropositive (41% vs. 65%; $P = .02$) or Hispanic (24% vs. 45%; $P = .018$). Fifteen (9%) of the 161 patients were HCWs (physicians, nurses, radiology technicians, morgue attendants, custodial staff, and home health aides), and 7 of these 15 patients had a documented link to a facility known to have had an outbreak of TB with strain W; these 7 patients were included as part of the nosocomial-transmission category.

Twenty (12%) of the 161 patients had cavitory pulmonary disease, and 131 (81%) had abnormal non-cavitory pulmonary lesions. One hundred sixteen patients (73%) were treated with an appropriate treatment regimen, which was started a median of 48 days (range, 9–420 days) after the date of diagnosis. There was no significant difference, by year of diagnosis, in either the proportion of patients placed on appropriate treatment or the time until initiation of such treatment. Of the 45 patients who were not placed on appropriate treatment, 43 (95%) died a median of 12 days (range, 0–92 days) after the date of diagnosis. One of the 2 remaining patients moved out of NYC before starting appropriate treatment and before culture conversion. In the other remaining patient, *M. tuberculosis* was cultured from sputum, but susceptibility testing was not performed on the isolate; sputum conversion was documented within 3 months, and, 7 months later, after an MDRTB isolate was recovered from synovial fluid, MDRTB treatment was initiated. As of 15 March 2001, relapse had not been identified in either of these 2 patients.

Of the 161 patients, 108 (67%) survived and were discharged from the facility at which they were diagnosed and thus were eligible for directly observed therapy (DOT); 79 (73%) of these 108 patients received DOT through a formal DOT program,

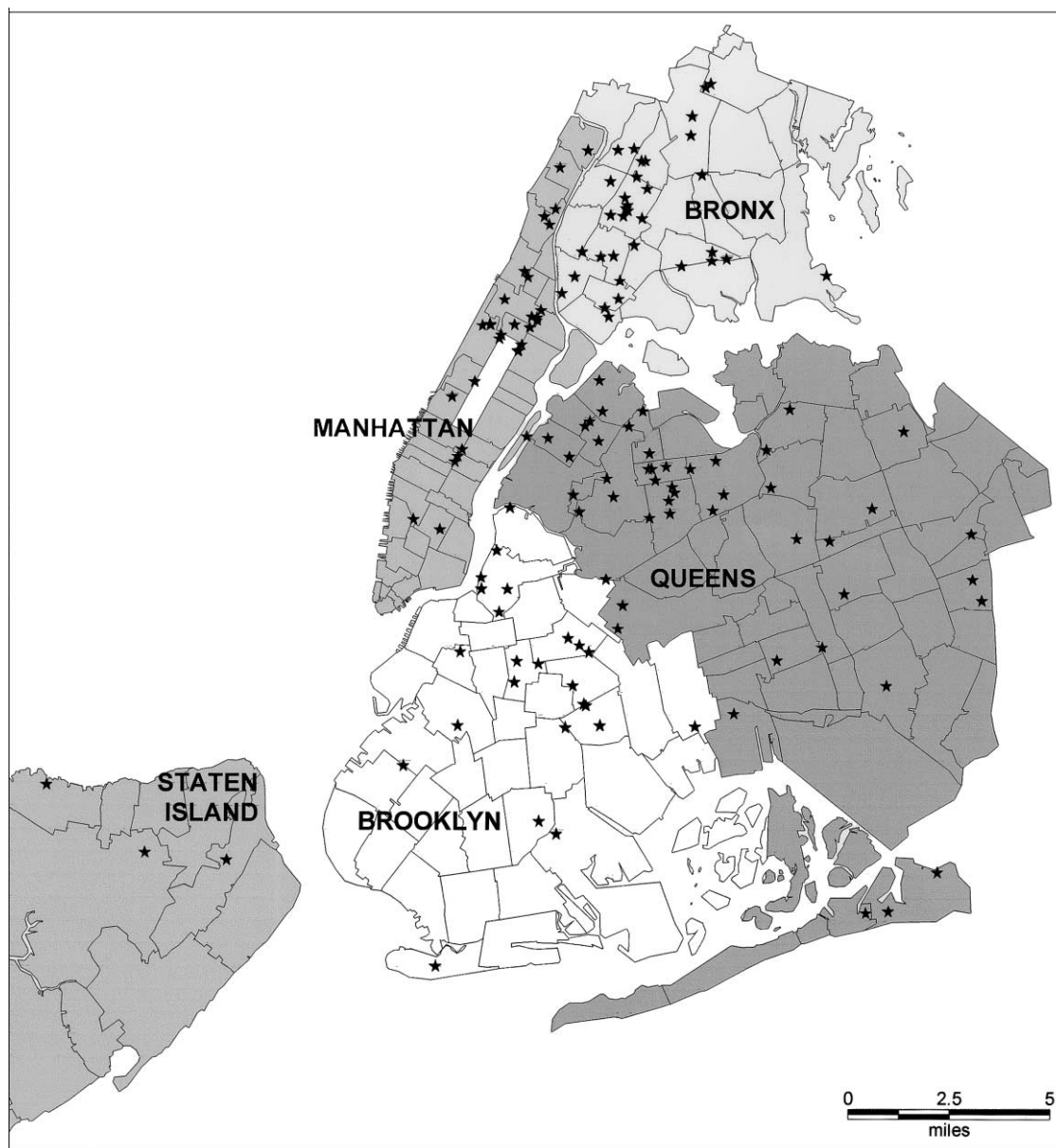


Figure 3. Geographic distribution of patients with strain W and its variants, in New York City during 1 August 1993–31 December 1999

in NYC, and an additional 9 (8%) received it at other sites—7 in long-term-care facilities, 1 in a correctional facility, and 1 (a HCW) through an agreement with the work-site infection-control office. Thus, 88 (81%) the 108 eligible patients received DOT, and 21 of these received some or all of their DOT after an order for mandatory observation was given. Because of persistent nonadherence, 12 patients were legally detained during their treatment, for a mean of 34 weeks each. After all other alternatives to improve adherence had been exhausted, these patients were hospitalized in a special unit at a long-term-care facility until they either completed treatment or were determined to be sufficiently educated to be able to resume DOT services as outpatients.

As of 15 March 2001, 89 (55%) of the 161 patients had died (median time until death, 5 weeks; range, 0–52 weeks) before completing treatment; 52 (59%) of these 89 deaths occurred while the patients were still hospitalized for the initial TB diagnosis, and, in 1 additional patient, TB was diagnosed at autopsy. All-causes mortality was significantly lower than that for cases from 1 January 1990–31 July 1993 (55% vs. 89%; $P < .001$). Of the 98 HIV-seropositive patients, 70 (71%) died, whereas 6 (15%) of the 41 HIV-seronegative patients died (table 3). As of 15 March 2001, 55 (34%) of the 161 patients had completed treatment (mean duration, 102 weeks; range, 40.1–193.1 weeks); the treatment outcomes in patients who received DOT did not differ from those in patients who did

Table 2. Demographic characteristics of patients with either strain W or one of its variants, in New York City during 1990–1999.

Characteristic	1 August 1993– 31 December 1999 (n = 161) ^a	1 January 1990– 31 July 1993 (n = 267) ^a	Change	P
Median age, years	41.2 years	39.0 years		.005
Sex			–10%	.03
Male	108 (67)	206 (77)		
Female	53 (33)	62 (23)		
Race/ethnicity				
Hispanic	64 (40)	120 (45)	–5%	NS
Black	54 (33)	91 (34)	0	NS
White	37 (23)	48 (18)	+4%	NS
Asian	6 (4)	8 (3)	+1%	NS
Country of birth				
United States/Puerto Rico	126 (78)	239 (90)	–12%	<.001
Foreign born	34 (21)	27 (10)	+11%	<.001
Unknown	2 (1)	1 (<1%)	0	NS
HIV serostatus				
Positive	98 (61)	230 (86)	–26%	<.001
Negative	41 (25)	19 (7)	+19%	<.001
Unknown	22 (14)	18 (7)	+7%	NS
History of injection drug use	37 (23)	146 (55)	–33%	.001
History of alcohol abuse	36 (22)	103 (39)	–17%	<.001
History of incarceration	7 (4)	78 (29)	–25%	<.05
History of homelessness	13 (8)	68 (26)	–17%	<.05
Health-care worker	15 (9)	20 (7)	+2%	NS

^a Data are no. (%) of cases, unless otherwise indicated.

not receive DOT. Seven patients moved out of NYC before completing anti-TB treatment, and 1 patient refused medications after 1 year of treatment. As of 31 March 2001, 9 patients were still on treatment. (Because of failure to convert, as evidenced by smear or culture, 1 of these 9 patients has been on treatment for 7 years, and 1 other has been on treatment for 5 years; these 2 patients have acquired additional resistance to second-line drugs.)

One hundred thirty-two (82%) of the 161 patients were hospitalized for the initial MDRTB diagnosis (median period, 34 days; range, 2–385 days). The total hospitalization days for the initial diagnosis were 6523. During the course of treatment for MDRTB, a minimum of 207 additional hospitalizations occurred, comprising 8627 days.

DISCUSSION

This is the first report based on molecular epidemiological tools that has tracked the course of a strain of *M. tuberculosis* in a community. After the outbreak period of 1990–1993, strain W and its variants continued to cause disease in NYC. Strain W has continued to evolve during prolonged treatment, reactivation,

and transmission, generating variations in both the W fingerprint pattern and the drug-susceptibility profile. Some isolates have acquired additional IS6110 insertions (e.g., W1, W31, or W34) and/or have developed additional drug resistance to second-line drugs such as capreomycin and the fluoroquinolones [6]. Each new variant has the potential to continue to disseminate and evolve further. An example of this would be W1, which is believed to have evolved in a noncompliant patient at a single medical facility and to have spread from there [14,15]. In agreement with the epidemiological observation, molecular data indicate that W1 evolved from strain W only once and then spread. All 32 W1 cases reported in this investigation share the identical array of IS6110 chromosomal insertions that is found in strain W but are distinguished by having an additional copy of it [1,8]. All genetic alterations (i.e., *rpoB*, *rpsL*, *embB*, and *katG*) associated with drug resistance in strain W were also confirmed in isolates recovered since 1 August 1993.

The control measures instituted in response to the TB crisis in NYC during the early 1990's have led to a significant decline in TB [16, 17]. Although the absolute numbers of cases with either strain W or one of its variants has decreased along with

Table 3. Outcome of cases with either strain W or one of its variants, diagnosed in New York City during 1 August 1993–31 December 1999.

Status	Total (n = 161)	HIV status		
		Infected (n = 98)	Negative (n = 41)	Unknown (n = 22)
Died before completion of treatment	89 (55)	70 (71)	6 (15) ^a	13 (59)
Completed treatment	55 (34)	21 (22)	29 (71) ^a	5 (23)
Refused treatment	1 (<1)	0	0	1 (4.5)
Moved out of New York City before completion of treatment	7 (4)	3 (3)	3 (7)	1 (4.5)
Being treated as of 15 March 2001	9 (6)	4 (4)	3 (7)	2 (9)

NOTE. Data are no. (%) of cases. HIV, human immunodeficiency virus.

^a $P < .001$, for comparison with HIV-infected cases.

the overall MDRTB incidence, the proportion of MDRTB cases that are caused by strain W and its variants has remained 25%–34%. Nosocomial outbreaks associated with other MDRTB strains also occurred during the time of the outbreak of the W strain, but they were much less frequent [18]. In their investigation of the multi-institutional outbreak, Frieden et al. [1] have suggested that HIV-negative contacts, including HCWs, who had been reported to have converted during the outbreak could be expected to develop TB with strain W and its variants. In support of this, we found that a smaller percentage of the patients in the present study had HIV infection. It has been estimated that, during the outbreak period, several hundred people were likely to have been infected in the hospital or in the community. Of the cases diagnosed since 1 August 1993, only relatively few could be identified as being due to nosocomial or community exposure. Unlike the earlier investigation, the present study did not attempt to identify potential nosocomial exposures by reviewing medical records of patients' hospitalizations before diagnosis of MDRTB; thus, we may have underestimated the number of cases with nosocomial epidemiological links.

Since 1993, nosocomial transmission of strain W and its variants has waned; only 3 cases from 1998–1999 have been confirmed (NYC Department of Health, unpublished data). Enhanced engineering controls in hospitals, as well as stricter compliance with infection-control and administrative protocols, likely contributed to decreased transmission at these facilities [19].

Preventive therapy for persons exposed to multidrug-resistant TB has not been well studied, although the Centers for Disease Control and Prevention (CDC) has published guidelines for the management of such contacts [20]. Potential regimens include either pyrazinamide and ethambutol or pyrazinamide and a fluoroquinolone, for 6–12 months. However, most patients with either strain W or one of its variants have isolates resistant to ethambutol, and almost half (43%) of the patients in the present study had isolates resistant to pyrazinamide. Alternative prophylactic regimens for these strains have unproven efficacy and are poorly tolerated [21].

In the present study, the majority of patients with either strain W or one of its variants were treated with a regimen appropriately tailored to the susceptibility pattern of the infecting strain. The increasing attention on TB and MDRTB, after the well-publicized outbreaks during the early 1990s, may have contributed to HCWs' increased awareness of proper treatment. There was no difference seen in the time to initiate appropriate treatment by year of diagnosis; efficient utilization of laboratory diagnostic methods during the early 1990s may have resulted in the more timely availability of both first- and second-line-susceptibility-test results during this period.

Although the relative number of patients with MDRTB—and, in particular, those with either strain W or one of its variants—is decreasing annually, the burden that this disease places on the health-care system remains substantial. In 1991 dollars, the initial hospitalization for these patients is estimated to have cost \geq \$18,588/hospitalization. The total-cost estimate, \$3.0 million, is likely an underestimate, since the median duration of hospitalization for the study patients was 34 days, compared with the 20 days reported by Brown et al. [22]. In addition, during the course of TB treatment, there were an additional 207 hospitalizations comprising 8627 days. Although we did not identify how many of these hospitalizations were TB related, many patients were rehospitalized because they did not respond adequately to MDRTB treatment. In addition, CDC guidelines recommend that, even if they are culture negative, patients known to have MDRTB be hospitalized in airborne-pathogen-isolation rooms, if available, until treatment is completed [23]. It is thus likely that most of these patients were kept in airborne-pathogen isolation during all these admissions. This would substantially increase the cost of hospitalizations. The treatment of this disease is also expensive. In 1991 dollars, the estimated cost of the outpatient part of the treatment is \sim \$8000/patient, compared with \sim \$2300/patient for treatment of drug-susceptible TB [22]. The total-cost estimate also does not take into account the cost of either clinic and field DOT (some patients received DOT twice a day) or 12 patients' civil detention in a medical facility for several months.

Despite the fact that most MDRTB cases can be treated within 18–24 months after culture conversion, the Bureau of Tuberculosis Control is treating several strain-W cases 2–7 years after initial diagnosis. These are patients whose acid-fast bacilli (AFB) smears and/or cultures either continuously revert to positive or have not converted—despite excellent adherence to DOT and, in some cases, surgical excision. Some of these patients have acquired additional resistance to second-line medications and are currently taking experimental treatment. Infection-control requirements for these patients with persistently positive AFB smears who are in the community pose many challenging ethical dilemmas.

The CDC's own surveillance system for strain W and its variants uses a variety of sources [7]. During 1992–1997, 23 cases of strain W were diagnosed in 9 states; 8 (35%) of these 23 cases had been exposed in NYC. Eighty-six personal contacts of these patients are presumably infected with strain W. MDRTB, including strain W and its variants, has spread to areas where the level of expertise and care necessary to treat this disease is inadequate. Although the programmatic measures adopted during the past decade have produced a steep decrease in the incidence of TB and MDRTB, in both NYC and the rest of the country, they may not be sufficient to forestall the continued spread, via these infected contacts, of strain W and its variants. Since preventive treatment of these strains has not been proven to be effective, we can expect to see active cases of strain W and its variants anywhere in the United States. Despite extensive experience with MDRTB treatment, NYC is still struggling with the consequences of the initial outbreaks during the early 1990s.

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