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Cross-Matching TB and AIDS Registries: TB Patients with HIV Co-Infection, United States, 1993–1994

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SYNOPSIS

Objectives. Because of limited reporting of HIV status in case reports to the national tuberculosis (TB) surveillance system, the authors conducted this study to estimate the proportion of US TB cases with HIV co-infection and to describe demographic and clinical characteristics of co-infected patients.

Methods. The 50 states, New York City, and Puerto Rico submitted the results of cross-matches of TB registries and HIV-AIDS registries. The authors determined the number of TB cases reported for 1993–1994 that were listed in HIV-AIDS registries and analyzed data on demographic and clinical characteristics by match status.

Results. Of 49,938 TB cases reported for 1993–1994, 6863 (14%) were listed in AIDS or HIV registries. The proportions of TB-AIDS cases among TB cases varied by reporting area, from 0% to 31%. Anti–TB drug resistance was higher among TB-AIDS cases, particularly resistance to isoniazid and rifampin (multidrug resistance) and rifampin alone. In some areas with low proportions of multidrug-resistant TB cases, however, the difference in multidrug resistance between TB-AIDS patients and non-AIDS TB patients was not found.

Conclusions. The proportion of TB cases with HIV co-infection, particularly in some areas, underscores the importance of the HIV-AIDS epidemic for the epidemiology of TB. Efforts to improve HIV testing as well as reporting of HIV status for TB patients should continue to ensure optimum management of coinfected patients, enhance surveillance activities, and promote judicious resource allocation and targeted prevention and control activities.

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The HIV-AIDS epidemic has significantly influenced the epidemiology of tuberculosis (TB), particularly in locations with a high burden of TB patients.[1-3] From 1985 to 1992, TB morbidity became increasingly concentrated in the five states with the highest number of AIDS cases and in large urban centers with the highest AIDS rates; at least 50% of the difference between the actual number of TB cases in the US during this period and the number predicted following decades of decline is attributable to the HIV epidemic.[3] In 1993, based on the strong epidemiologic link between HIV infection and the development of TB, the Centers for Disease Control and Prevention (CDC) expanded the AIDS surveillance case definition to include all HIV-infected people with pulmonary TB.[4] (In the 1986 classification system, only extrapulmonary TB had been listed as one of 23 AIDS indicator diseases.)

With the cooperation of state health departments, CDC has conducted national TB surveillance since 1953. In 1993, CDC implemented electronic individual TB case reporting. Concurrently, CDC expanded the individual TB case report and began collecting information on TB risk factors, including HIV status, and clinical characteristics such as drug resistance.[5] Analysis of US TB cases by HIV status, however, has been limited due to incomplete reporting of HIV test results to the national surveillance system (for example, during 1993–1994, fewer than 40% of TB case reports for patients ages 25–44 included HIV test results[6,7]). Cross-matching of TB and AIDS registries has been used by CDC and state health departments to estimate the number of TB cases with HIV co-infection (TB-AIDS cases).[1,8-10] According to the results of cross-matches conducted by state health departments, TB-AIDS cases represented 9% of the US TB cases reported in 1990.[1] To update this estimate, we collected and compiled the results of more recent cross-matches of state TB and HIV-AIDS registries. In addition, using demographic and clinical data from the TB case reports, we compared the characteristics of TB-AIDS patients and non-AIDS TB patients.

METHODS

Registry matching. To determine the proportion of US TB cases with HIV co-infection in 1993–1994, CDC requested the results of TB and AIDS registry cross-matches from the 50 states, New York City, and Puerto Rico.

Name and birth date together were most commonly used to match cases. Thirty of the 52 reporting areas compared 1993 and 1994 TB cases to their historical AIDS registries, which included AIDS cases reported from the early 1980s through 1995 or 1996. The remaining areas conducted more limited comparisons; for example, 17 areas used 1993 and 1994 AIDS cases only.

Of the 26 states that had confidential HIV reporting, 21 cross-matched TB cases to their registries of individuals who were HIV-infected but did not have reported AIDS-defining illnesses.

CDC collected the results of the registry cross-matches in aggregate format from each reporting area, including the numbers of TB cases reported for 1993 and 1994, the numbers of AIDS cases reported for 1993 and 1994, and the numbers of TB cases listed in HIV-AIDS registries.

In addition, the participating health departments (with the exception of California) reported TB cases with matches in either the AIDS or HIV registries by filling in the AIDS case registry number on the standard TB case report submitted electronically to CDC for routine surveillance or (in four cases) by identifying the TB-AIDS cases by TB case number in a separate electronic or hard copy file. California submitted aggregate data for specific demographic and clinical characteristics by match status.

Data analysis. We analyzed the individual-level data from the national TB surveillance system and added in the aggregate data for California to compare demographic and clinical characteristics of TB-AIDS patients and non-AIDS TB patients.

We determined the number and proportions of patients by age group, sex, and country of birth (US-born versus foreign-born). We also calculated the numbers and proportions of patients with the following clinical characteristics: a previous TB episode, deceased at the time of TB diagnosis, pulmonary TB, extrapulmonary TB, smear-positive and culture-positive pulmonary TB, abnormal chest radiograph findings of those with pulmonary TB, and initial drug resistance patterns of those with culture-positive TB. We calculated rates of resistance to anti-TB drugs by dividing the number of cases with isolates resistant to at least the specified drug(s) by the total number of culture-positive cases with isolates tested for resistance to the drug(s). We determined rifampin mono-resistance (resistance only to rifampin) for cases in which isolates were tested to at least isoniazid, rifampin, ethambutol, and streptomycin,

Fifteen percent of TB cases reported in the US in 1993 and 12% of TB cases reported in 1994 were also listed in AIDS or HIV registries.

defined as the number of cases with isolates resistant to rifampin but susceptible to other drugs tested.

We used chi-square tests to compare the proportions of demographic and clinical characteristics by match status in the univariate analyses. We used unconditional logistic regression (excluding cases from California) to model selected clinical characteristics. We used separate models adjusted by age, previous TB disease, and US versus foreign birth to determine whether TB-AIDS patients with pulmonary TB were more likely than non-AIDS patients to have sputum smear-positive TB, sputum culture-positive TB, an abnormal chest radiograph, and, among those with abnormal radiographs, cavitation by chest radiograph.

RESULTS

Registry matching. Of 25,392 TB cases reported in the US in 1993, 3841 (15%) were listed in an AIDS or HIV registry; of 24,546 TB cases reported in 1994, 3022 (12%) were listed in an AIDS or HIV registry. Across the 52 reporting areas, the median difference between 1993 and 1994 in the proportion of TB cases with HIV co-infection was zero. Excluding the 17 areas with fewer than 10 matched TB cases over the two-year period, the difference ranged from a 19% decrease from 1993 to 1994 for New York City to a 2% increase for Michigan.

Table 1 shows the numbers of TB cases, AIDS cases, and TB cases with matches in AIDS or HIV registries by reporting area for 1993–1994 and the rankings of reporting areas by number of TB, AIDS, and TB-AIDS cases. The reporting areas with the largest burdens of TB-AIDS cases were California, Florida, Georgia, Illinois, New Jersey, New York (excluding New York City), New York City, and Texas (see Table 1). These areas accounted for 80% of all TB-AIDS cases and 63% of all TB cases reported for 1993 and 1994.

TB-AIDS cases as a percentage of all reported TB cases varied by reporting area, from 0% to 31%, with the highest proportions found in Connecticut, Florida, New Jersey, New York City, and Puerto Rico (see Figure).

Comparison of TB-AIDS cases and non-AIDS TB cases.

Demographic characteristics. Selected demographic characteristics of TB patients by HIV status are shown in Table 2. TB-AIDS patients were more likely than non-AIDS TB patients to be 25–44 years of age, to be male, and to be US-born.

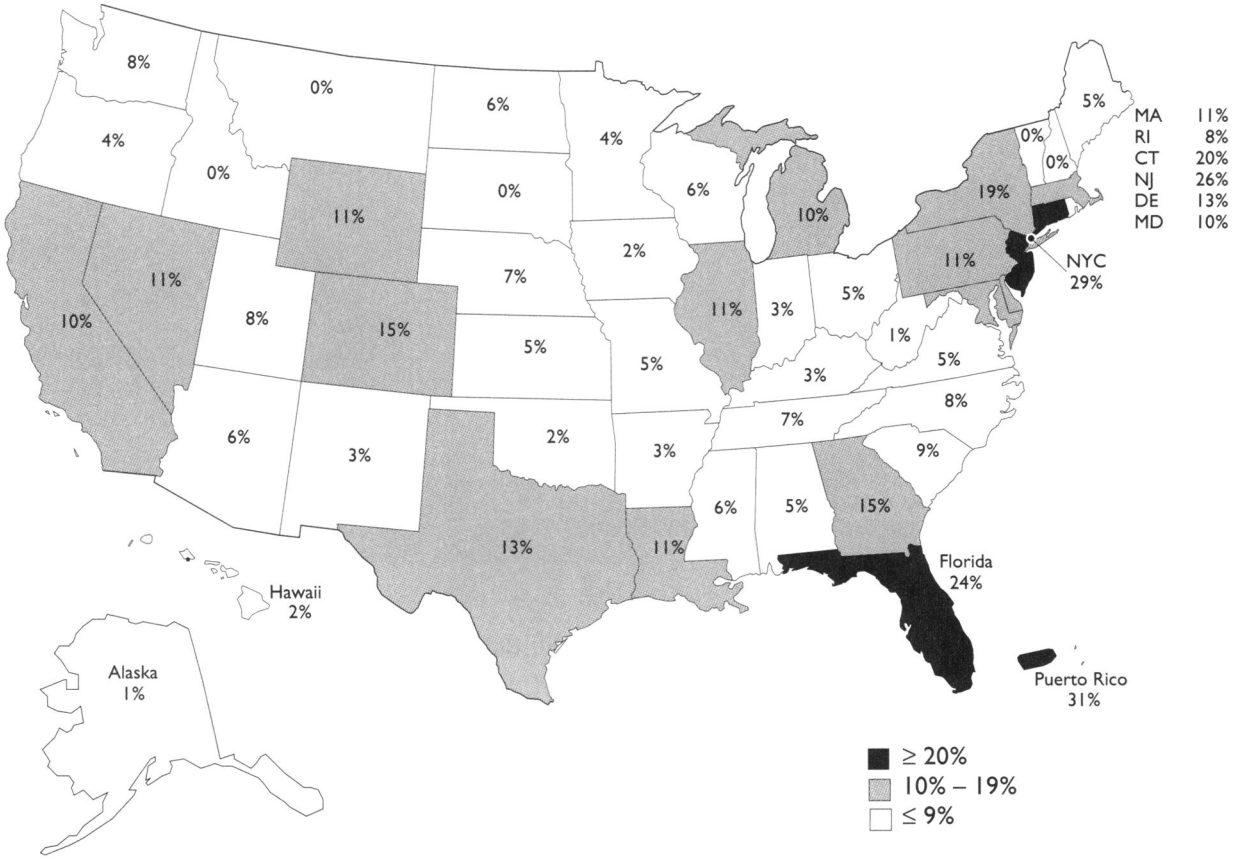
Clinical characteristics. Clinical characteristics of TB patients by HIV status are shown in Table 3. Extrapulmonary TB disease (either alone or with pulmonary TB) was more common among TB-AIDS patients than among non-AIDS TB patients, although more than 80% of patients, regardless of HIV status, had pulmonary involvement. Logistic regression models of cases with pulmonary TB either alone or with extrapulmonary disease (excluding cases from California, for which individual-level data were not available) were adjusted for age, previous TB, and US versus foreign birth. With the adjusted models, we found that TB-AIDS patients were more likely than non-AIDS TB patients to have culture-positive sputum (odds ratio [OR] 1.96, 95% confidence interval [CI] 1.74, 2.21), although they were not more likely to have a sputum smear positive for acid fast bacilli

Table 1. TB cases, AIDS cases, and TB-AIDS cases, numbers and national rankings, by reporting area, United States, 1993–1994

Reporting area	TB		AIDS		TB-AIDS	
	Number	Rank	Number	Rank	Number	Rank
Alabama	920	13	1264	27	49	19
Alaska	149	39	100	47	2	44
Arizona	476	26	1081	29	28	25
Arkansas	473	27	903	31	14	30
California	10,033	1	30,826	1	992	2
Colorado	200	35	2151	22	29	24
Connecticut	301	31	2685	16	59	18
Delaware	122	41	640	34	16	29
Florida	3399	4	18,286	3	806	3
Georgia	1549	7	4385	11	240	8
Hawaii	498	25	612	36	10	35
Idaho	23	49	128	46	0	48
Illinois	2505	5	5951	6	284	6
Indiana	459	29	1521	24	12	32
Iowa	125	40	326	41	3	41
Kansas	167	36	586	37	8	37
Kentucky	751	18	453	39	21	28
Louisiana	806	15	2537	19	85	13
Maine	63	44	272	43	3	41
Maryland	779	17	5235	8	80	14
Massachusetts	695	19	4180	12	76	15
Michigan	947	12	2956	13	91	11
Minnesota	281	32	1084	28	11	34
Mississippi	557	21	663	33	34	22
Missouri	516	24	2393	20	25	26
Montana	47	45	66	49	0	48
Nebraska	45	46	276	42	3	41
Nevada	227	33	1002	30	24	27
New Hampshire	43	48	212	44	0	48
New Jersey	1767	6	10,291	5	461	5
New Mexico	165	37	466	38	5	40
New York (excluding New York City)	1343	9	4768	9	256	7
New York City	6177	2	28,044	2	1787	1
North Carolina	1159	10	2362	21	90	12
North Dakota	17	52	17	52	1	47
Ohio	654	20	2690	15	32	23
Oklahoma	470	28	704	32	8	37
Oregon	318	30	1365	25	14	30
Pennsylvania	1369	8	4434	10	147	10
Rhode Island	120	42	614	35	9	36
South Carolina	788	16	2674	17	69	17
South Dakota	44	47	29	51	0	48
Tennessee	1074	11	1734	23	76	15
Texas	4901	3	13,201	4	633	4
Utah	101	43	397	40	8	37
Vermont	18	51	84	48	0	48
Virginia	830	14	2834	14	42	20
Washington	550	22	2564	18	42	20
West Virginia	155	38	194	45	2	44
Wisconsin	212	34	1295	26	12	32
Wyoming	19	50	54	50	2	44
Puerto Rico	531	23	5905	7	162	9
Total	49,938		179,494		6863	

NOTE: A TB-AIDS case is defined as a TB case with a match in a reporting area's AIDS or HIV registry.

Figure. TB cases with matches in AIDS or HIV registries (TB-AIDS cases) as percentage of all TB cases, by reporting area, United States, 1993–1994



(OR 1.05, 95% CI 0.98, 1.13). TB-AIDS patients with pulmonary TB were less likely to have an abnormal chest radiograph (OR 0.32, 95% CI 0.28, 0.36), and among those with an abnormal chest radiograph, TB-AIDS patients were also less likely to have cavitary disease (OR 0.33 95% CI 0.30, 0.36).

Anti-TB drug resistance. We calculated resistance to anti-TB drugs for US-born patients ages 25–44 years without a previous history of TB. Drug resistance was higher for TB-AIDS patients, particularly to isoniazid and rifampin (multidrug resistance) and rifampin alone (see Table 3). When we excluded cases from New York City from the analysis, drug resistance remained higher among TB-AIDS patients than among non-AIDS TB patients, particularly multidrug resistance (2.9% for TB-AIDS patients vs 1.4% for non-AIDS TB patients, $P < 0.001$) and rifampin mono-resistance (3.2% vs 0.4%, $P < 0.001$). However, in some areas with low proportions of cases with multidrug-resistant TB (for example, California and Texas), the difference between the two groups in multidrug resistance was not found.

DISCUSSION

Registry matching. From the results of this study, we estimate that 14% of US TB cases reported for 1993–1994 were TB-AIDS cases. Although the majority of TB-AIDS cases were found in reporting areas with large burdens of TB cases, the proportion of TB cases with co-infection varied among these areas, probably reflecting geographic variations in characteristics of the

Table 2. Selected demographic characteristics of TB patients by HIV status, United States, 1993–1994

Characteristic	TB-AIDS patients n = 6833		Non-AIDS TB patients n = 42,828	
	Number	Percent	Number	Percent
Age group				
0–14	33	< 1	3316	8
15–24	211	3	3457	8
25–44	5139	75	13,586	32
45–64	1334	20	11,078	26
≥65	98	1	11,312	26
Sex				
Male	5527	81	26,728	62
Female	1306	19	16,094	38
Country of birth				
United States	5731	85	28,066	66
Outside US	1020	15	14,149	34

NOTES: These totals do not include patients for whom information was unavailable for a given data item. For age group, sex, and country of birth, information was lacking for ≤ 1% of both TB-AIDS patients and non-AIDS TB patients. The *n*'s differ from those in Table 1 because individual case data sent to CDC were used for this analysis instead of aggregated data. Individual TB case reports are periodically updated, and these *n*'s reflect updates as of April 1997. All chi-square comparisons between TB-AIDS and non-AIDS TB patients were statistically significant at the $P < 0.05$ level.

HIV-AIDS epidemic and in TB epidemiology.

Our findings may have underestimated the proportion of TB-AIDS cases for several reasons. First, 17 areas conducted limited matches of 1993–1994 TB cases only to AIDS cases reported for 1993 and 1994 rather than using historical AIDS registries for the 1980s through 1995 or 1996. Matching only to AIDS cases reported in 1993–1994 misses people reported with AIDS-defining illnesses who were included in AIDS registries before 1993. Also missed with this approach are co-infected patients reported to TB registries in 1993–1994 whose AIDS case reports were delayed until after 1994. However, for more than 90% of TB-AIDS patients found in a previous state registry match (which used historical registries for both TB and AIDS), TB was diagnosed within the two years prior to and one year after the diagnosis of AIDS.[10] Furthermore, seven of the eight areas reporting the highest number of TB-AIDS cases in the current study (accounting for 70% of TB-AIDS cases and 54% of TB cases) did match to historical AIDS registries.

Second, because TB and AIDS registries were cross-matched within a reporting area, coinfected patients reported as an AIDS case in one area and a TB case in a different area could not be identified. Third, due to reporting lags, AIDS case reports may follow TB case reports of coinfected patients, which may result in missed matches even when historical AIDS registries are used. Reporting lags (despite use of the historical AIDS registry through early 1996) appear to account for the substantial decrease in the proportion of TB-AIDS cases in New York City detected in this study—from 38% in 1993 to 19% in 1994. We concluded this after examining HIV test results reported to the national TB surveillance system from New York City. For TB cases reported in New York City in 1994, we calculated that as a minimum estimate, 34% were in people coinfected with HIV (Unpublished data, Division of TB Elimination, CDC). This estimate of coinfection for 1994 using surveillance data was more consistent with the 1993 New York City estimate based on registry cross-matching than with the 1994 estimate. This led us to believe that the substantial decrease in the proportion of TB-AIDS cases in New York City from 1993 to 1994 found by registry cross-matching was artificial. This apparently artificial decrease in New York City resulted in the observed decrease from 1993 to 1994 in the estimated proportion of all US TB cases with coinfection in the present study.

Finally, 21 of the 26 areas with HIV reporting also matched TB cases to their HIV registries; however, HIV registries were not used in the cross-matches for seven of the eight areas that reported the highest number of TB-AIDS cases (accounting for 73% of the TB-AIDS cases and 61% of the TB cases reported during 1993–1994).

Table 3. Clinical characteristics of TB patients by HIV Status, United States, 1993–1994

Characteristic	TB-AIDS patients n = 6833		Non-AIDS TB patients n = 42,828	
	Number	Percent	Number	Percent
Previous TB[a]	328	5	2436	6
Deceased at diagnosis[a]	417	6	1570	4
Extrapulmonary TB[a,b]	2077	30	9070	21
Pulmonary TB[c]				
Smear-positive[d]	2965	59	15,407	53
Culture-positive[e]	4631	91	24,358	83
Abnormal X-ray[f]	4565	89	32,992	97
Cavitary X-ray[g]	617	15	8660	28
Non-cavitary X-ray	3629	85	22,710	72
Drug-resistant TB[h]				
Isoniazid (INH)[i]	376	12	426	7
INH + rifampin[j]	193	6	130	2
Rifampin only[k]	81	3	30	< 1

NOTES: The *n*'s differ from those in Table 1 because individual case data sent to CDC were used for this analysis instead of aggregated data. All chi-square comparisons between TB-AIDS and non-AIDS TB patients were statistically significant at the $P < 0.05$ level.

[a]Excludes cases without information for this data item (≤ 1% of both TB- AIDS patients and non-AIDS TB patients)

[b]Includes patients with only extrapulmonary disease and those with both pulmonary and extrapulmonary TB

[c]Includes patients with only pulmonary disease and those with both pulmonary and extrapulmonary TB (5567 TB-AIDS patients; 35,599 non-AIDS TB patients)

[d]Excludes cases without information for sputum smear (2% of TB-AIDS patients, 3% of non-AIDS TB patients) and cases in which sputum smear was not done (8% of TB-AIDS patients, 15% of non-AIDS TB patients)

[e]Excludes cases without information for sputum culture (3% of TB-AIDS patients, 3% of non-AIDS TB patients) and cases in which sputum culture was not done (6% of TB-AIDS patients, 14% of non-AIDS TB patients)

[f]Excludes cases without information on an initial chest X-ray (4% of TB-AIDS patients, 3% of non-AIDS TB patients) and cases in which an initial chest X-ray was not done (3% of TB-AIDS patients, 2% of non-AIDS TB patients)

[g]Excludes cases without information on the type of chest X-ray abnormality (7% of TB- AIDS patients, 5% of non-AIDS TB patients)

[h]Includes US-born patients ages 25-44 with no previous TB who had culture-positive TB (3673 TB-AIDS patients, 6505 non-AIDS TB patients)

[i]Excludes cases without susceptibility test results for isoniazid (12% of TB-AIDS patients, 10% of non-AIDS TB patients).

[j] Excludes cases without susceptibility test results for isoniazid and rifampin (13% of TB-AIDS patients, 11% of non-AIDS TB patients)

[k]Excludes cases without susceptibility test results for isoniazid, rifampin, ethambutol, and streptomycin (25% of TB-AIDS patients, 25% of non-AIDS TB patients)

Temporal comparison. Our findings also suggest an apparent increase in the proportion of TB patients with HIV co-infection since 1990, when 9% of TB cases were estimated to have been co-infected based on the results of TB and AIDS registry cross-matches conducted by the 50 states, New York City, and Puerto Rico.[1] Several considerations must be taken into account, however, in evaluating this apparent increase. Perhaps most important, the revision of the AIDS case definition in 1993 increased the likelihood that co-infected TB patients reported as TB cases in 1993 or 1994 would also have been reported as AIDS cases. Increased communication between TB and AIDS surveillance programs as a result of the revision of the AIDS case definition and the addition of HIV status to the TB case report may have also improved detection. Second, the proportions of TB-AIDS cases in the earlier[1] and present studies may not be directly comparable because reporting areas may have used different methods for the cross-matches. For example, in providing data for the current study, some areas are likely to have used technically improved matching algorithms, some areas matched to only two years of AIDS case reports rather than historical registries, and some areas matched TB cases to HIV registries in addition to AIDS registries. Overall, however, we think that the effect of this variation was likely to have been minimal.

The absolute increase in the number of TB-AIDS cases may also reflect the HIV-infected population's having had more person-time exposure to TB and more opportunity for TB infection to become disease. The pre-

Drug resistance, particularly multidrug resistance and rifampin mono-resistance, was higher among TB patients with AIDS than among other TB patients.

vious analysis of data from registry matches performed by state health departments found a steady increase in the proportion of US TB cases with HIV co-infection from 1980 through 1990.[1] The 1993–1994 data may reflect a continued rise of the HIV-AIDS epidemic curve; however, further data are needed to assess temporal trends during the 1990s. The decrease in US TB cases since 1993 will be an additional consideration in evaluating these temporal trends.[11]

Comparison of TB-AIDS cases and non-AIDS TB cases.

Demographic and clinical characteristics. The demographic and clinical characteristics of TB-AIDS patients found in our study are consistent with those reported elsewhere.[1,10,12–13] National surveillance data have shown that the proportion of TB patients who are foreign-born has increased over the past decade, from 22% in 1986 to 39% in 1997.[11] The findings of the present study show that the proportion of TB-AIDS patients who were foreign-born (15%) was less than half the proportion of non-AIDS TB patients who were foreign-born (34%). Similarly, the proportion of foreign-born TB patients found to be coinfected with HIV (6.7%) was less than half the proportion of US-born patients who were coinfected (17%). The lower rate of co-infection among the foreign-born with TB may reflect several factors, including legal processes that generally exclude those with HIV from entering the United States and lower prevalences of risk factors (such as injection drug use) among the foreign-born communities accounting for the largest numbers of TB cases reported in the US. However, without vigilant attention to HIV prevention efforts in the US, the overlap of TB and HIV in the foreign-born living in the US is likely to increase.

Anti-TB drug resistance. The finding of higher drug resistance, particularly multidrug resistance and rifampin mono-resistance among TB-AIDS patients than among other TB patients, persisted after adjustment for other strong risk factors for drug resistance (previous TB, younger age, foreign birth).[14] This likely reflects several factors, including a higher proportion of disease resulting from recent infection among those co-infected with HIV[15,16] and thus a higher risk of infection with drug-resistant strains in areas in which transmission of drug-resistant strains has recently occurred.[17] The rapid progression from infection to disease among people with HIV infection also contributes to the higher proportion of cases resulting from recent infection.[2] The potential for re-infection among those with HIV co-infection, and thus infection with drug-resistant strains, is a further consideration.[18] Additional factors appear to contribute to higher rates of rifampin mono-resistance in HIV-infected patients. Reports of both primary and acquired rifampin mono-resistance have suggested that unique characteristics among HIV-infected patients may predispose to this unusual type of resistance.[19–23] Possible explanations include problems with malabsorption or drug interactions and the use of rifamycin derivatives for other HIV-related infections in the context of unrecognized TB disease.[19–23]

Public health importance of HIV testing for TB patients.

Surveillance. In 1993, the first year that information on HIV status was collected for TB cases reported to the national TB surveillance system, HIV test results were reported for only 33% of TB cases in patients ages 25–44.[6] Since then, reporting of HIV test results has improved overall and for most states, particularly for the target age group. In 1997, however, HIV test results were

reported for only 39% of all TB cases (Unpublished data, Division of TB Elimination, CDC) and for 53% of those ages 25–44.[11] National estimates based on this level of reporting may be unreliable. Efforts are currently underway by CDC in conjunction with state and local health departments to address barriers in both testing for HIV infection and reporting of these test results for TB patients.

Patient care. The management of TB disease in patients with HIV co-infection requires attention both to basic principles of TB therapy and to special issues such as the concurrent use of other medications (for example, protease inhibitors) and the potential for primary and acquired resistance to anti-TB drugs.[24] It is also essential to prevent active TB disease among patients with HIV infection through aggressive efforts to identify those infected with *M. tuberculosis* and to ensure that they complete a full recommended course of preventive therapy, unless therapy is contraindicated.[24,25]

State and local health departments should continue to work toward better communication between TB and AIDS programs in order to achieve both improved HIV testing and reporting of HIV status for TB patients. These efforts will help ensure optimum management of coinfected patients, enhance the completeness and accuracy of surveillance activities, and promote judicious resource allocation and targeted prevention and control activities.

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