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TUBERCULOSIS AND AIDS - CONNECTICUT

The incidence of tuberculosis in Connecticut had steadily declined for several decades until 1983. In 1982, the incidence of tuberculosis reached a nadir of 5.0 cases per 100,000 population. Since then, tuberculosis incidence has fluctuated above that level, at 6.2 in 1983, 5.6 in 1984, 5.1 in 1985, and 5.6 in 1986.

The failure of tuberculosis incidence to decline led to an evaluation of data on acquired immunodeficiency syndrome (AIDS) and tuberculosis in Connecticut. The AIDS case register was linked to the tuberculosis case register back to 1970 to determine the proportion of tuberculosis patients known to have AIDS, the proportion of AIDS patients known to have had tuberculosis, the interval between the diagnosis of tuberculosis and AIDS, and selected demographic characteristics of those with both diagnoses. Demographic characteristics examined included age, sex, race/ethnicity, geographic location by city size, and risk factors for a diagnosis of AIDS. In order to estimate the relative risk of tuberculosis in persons with AIDS compared to those without AIDS, the incidence of tuberculosis was calculated and compared for persons with and without AIDS in subgroups by each of these characteristics. The 3-year incidence of tuberculosis was used for these comparisons, because most diagnoses of tuberculosis in AIDS patients were made in the 3-year period beginning 30 months before to 6 months after the diagnosis of AIDS.

Demographic Features of Tuberculosis in AIDS Cases.

As of September 1, 1986, 18 cases of tuberculosis had been diagnosed in the 299 reported AIDS cases in Connecticut. Sixteen tuberculosis cases (89%) had been diagnosed since January 1, 1982. This represents 5.4% of AIDS cases and 2.0% of all 816 TB cases diagnosed and reported during the 1982-1986 time period. The number of tuberculosis cases with AIDS (TB/AIDS) by year of tuberculosis diagnosis has shown no trend thus far (1, 0, 5, 3, 0, 5, and 3 cases, for the years 1980-1986, respectively). The remaining patient was diagnosed in 1973. The 18 TB/AIDS patients ranged from 24-53 years of age, with a median of 33 years. Fourteen (78%) were male, 11 (61%) were black, 13 (72%) were from the six cities with a population of 100,000 or greater, and seven (39%) were intravenous drug users.

Compared to tuberculosis patients without AIDS, TB/AIDS cases were more likely to be younger, male, black, and come from a large city. Compared to AIDS patients without tuberculosis in Connecticut, TB/AIDS patients were more likely to be black, come from big cities, and have intravenous drug abuse as an AIDS risk factor. Age and sex distribution were similar in the two groups.

The interval between the diagnosis of tuberculosis and diagnosis of AIDS ranged from 10 years before to 19 months after the diagnosis of AIDS, with a median of four months before the diagnosis of AIDS. In 14 TB/AIDS cases (78%), the diagnosis of tuberculosis was made within 3 years of the diagnosis of AIDS (2.5 yrs. before to 0.5 yrs. after).

Incidence of TB/AIDS and TB/non-AIDS

Table 1 shows crude and adjusted 3-year incidence of tuberculosis in AIDS patients and in the general population without AIDS according to sex, race, and city size, as well as adjusted for these factors and age. In all groups, the incidence of tuberculosis (risk ratio) in AIDS patients was more than 100 times the incidence in the general population.

Editorial Note: The demographic features of TB/AIDS cases in Connecticut are similar to those found elsewhere; individuals are most likely to come from groups that have both a higher incidence of tuberculosis and which are at risk for AIDS (1,2).

An association between tuberculosis and AIDS in Connecticut is suggested by several factors; the 5.5% incidence of tuberculosis in AIDS cases, the clustering of development of tuberculosis and AIDS cases within a distinct time period (within 3 years of the diagnosis of AIDS), and the 100-fold or

greater risk of tuberculosis in AIDS cases than in the general population. The risk that persons with latent tuberculous infection who develop AIDS will develop clinically active tuberculosis cannot be determined from these data. However, to the extent that individuals with AIDs are representative of the general population in prevalence and incidence of tuberculous infection, this risk could be as much as 100-200 fold greater than that of their non-HIV infected counterparts.

These data further support recently published guidelines (3) that as part of the evaluation of persons with tuberculous infection, risk factors for HIV infection should be identified. HIV antibody testing should be offered and where tuberculosis infection and HIV infection positivity coexist, isoniazid preventive therapy be offered. Conversely, persons initially found to be HIV antibody positive should be offered tuberculin skin testing, and isoniazid preventive therapy should be offered for reactors (3). These guidelines are presented in the next article.

TABLE 1. Three-year incidence* of tuberculosis in 20-to-49 year-olds with AIDS and without AIDS (general population) by selected demographic characteristics, Connecticut, October 1986

	Tuberculosis Incidence (n)		
Demographics	AIDS Patients	General Population	Risk Ratio**
Sex			
Male	6,250 (10)	18.8 (119)	333
Female	7,692 (2)	12.7 (84)	605
Race			
Black	12,121 (8)	102.8 (95)	118
White	3,670 (4)	5.4 (63)	677
City Size			
≥100,000	9,677 (9)	44.7 (111)	216
<100,000	3,226 (3)	8.8 (92)	367
Adjusted***	2,671 (12)	15.7 (203)	170

* Incidence per 100,000 at risk. Incidence of TB/AIDS is for the period 2.5 years before to 0.5 years after the diagnosis of AIDS in all AIDS cases as of April 1, 1986; incidence of TB/non-AIDS is for the 3-year period, 1982-1984.

** Ratio of 3-year incidence of TB/AIDS to TB/non-AIDS

*** Adjusted for age (5-year intervals), race, sex, and city size according to 1980 census.

References

1. CDC. Tuberculosis and acquired immunodeficiency syndrome - Florida. MMWR 1986; 35: 587-590.

2. Sunderam G, McDonald RJ, Maniatis T, et al. Tuberculosis as a manifestation of the acquired immunodeficiency syndrome (AIDS). JAMA 1986; 256:357-61.

3. CDC. Diagnosis and management of mycobacterial infection and disease in persons with human T-lymphotropic virus type III/lymphadenopathy-associated virus infection. MMWR 1986; 35:448-52.

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DIAGNOSIS AND MANAGEMENT OF MYCOBACTERIAL INFECTION AND DISEASE IN PERSONS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION

In 1985, the number of new tuberculosis cases reported to CDC was essentially the same as that reported in 1984 (1). In contrast, the average annual decline in morbidity during the past 32 years has been 5%. The failure of tuberculosis morbidity to decline as expected in 1985 is probably related to the occurrence of tuberculosis among persons with acquired immunodeficiency syndrome (AIDS) or human immunodeficiency virus (HIV) infection. Several reports have indicated that mycobacterial disease is common among AIDS patients and among persons at risk for AIDS (2-9). The most common mycobacterial species isolated from patients with diagnosed AIDS is Mycobacterium avium complex (MAC), although in some groups in which tuberculous infection is highly prevalent, disease caused by M. tuberculosis is more common (10-12). Even among groups in which MAC is the most common mycobacterial pathogen, M. tuberculosis accounts for a substantial proportion of the mycobacterial isolates. The association between mycobacterial disease and AIDS raises several important clinical and public health issues that are addressed below.

Diagnosis of Tuberculosis in Patients Likely to Have HIV Infection

Clinicians should consider the diagnosis of tuberculosis in patients with, or at risk of, HIV infection, even if the clinical presentation is unusual (4,13,14). Available data indicate that extrapulmonary forms of tuberculosis, particularly lymphatic and disseminated (miliary), are seen much more frequently among patients with HIV infection than among those without such infection. Pulmonary tuberculosis in patients with HIV infection cannot readily be distinguished from other pulmonary infections, such as Pneumocystis carinii pneumonia,

on the basis of clinical and radiographic findings. Patients with tuberculosis may have infiltrates in any lung zone, often associated with mediastinal and/or hilar lymphadenopathy. Cavitation is uncommon. Appropriate specimens to establish a culture-confirmed diagnosis of tuberculosis include respiratory secretions, urine, blood, lymph node, bone marrow, liver, or other tissue or body fluid that is indicated clinically. All tissue specimens should be stained for acid-fast bacilli and cultured for mycobacteria. In the presence of undiagnosed pulmonary infiltrates, bronchoscopy with lavage and transbronchial biopsy (if not contraindicated) may be needed to obtain material for both culture and histologic examination. A tuberculin skin test should be administered, but the absence of a reaction does not rule out the diagnosis of tuberculosis because immunosuppression associated with HIV infection may cause false-negative results.

Treatment of Mycobacterial Disease in a Patient with HIV Infection

Chemotherapy should be started whenever acid-fast bacilli are found in a specimen from a patient with HIV infection and clinical evidence of mycobacterial disease. Because it is difficult to distinguish tuberculosis from MAC disease by any criterion other than culture, and because of the individual and public health implications of tuberculosis, it is important to treat patients with a regimen effective against tuberculosis. With some exceptions, patients with tuberculosis and HIV infection respond relatively well to standard antituberculosis drugs (15); however, their treatment should include at least three drugs initially, and treatment may need to be longer than the standard duration of 9 months (16). The recommended regimen is isoniazid (INH), 10-15 mg/kg/day up to 300 mg/day; rifampin (RIF), 10-15 mg/kg/day up to 600 mg/day; and either ethambutol (EMB), 25 mg/kg/day, or pyrazinamide (PZA), 20-30 mg/kg/day. The last two drugs are usually given only during the first 2 months of therapy. The addition of a fourth drug may be indicated in certain situations, such as central nervous system or disseminated disease or when INH resistance is suspected. An initial drug-susceptibility test should always be performed and the treatment regimen revised if resistance is found to any of the drugs being used. The appropriate duration of treatment for patients with tuberculosis and HIV infection is unknown; however, it is recommended that treatment continue for a minimum of 9 months and for at least 6 months after documented culture conversion. If INH or RIF is not included in the treatment regimen, therapy should continue for a minimum of 18 months and for at least 12 months following culture conversion. After therapy is completed, patients should be followed closely, and mycobacteriologic examinations should be repeated if clinically indicated.

Some clinicians would take a different approach to treatment than that outlined above to cover the possibility of MAC disease. Although the clinical significance and optimal therapy of MAC disease in these patients is not well defined, and there are no definitive data on the efficacy of treatment, one regimen commonly used to treat MAC disease substitutes rifabutin (ansamycin LM 427) for rifampin, combined with INH, EMB, and clofazimine. Rifabutin and clofazimine are experimental drugs available to qualified investigators only under investigational new drug protocols. Rifabutin is distributed by the CDC Drug Service (telephone: 404-329-3670), and clofazimine, by Ciba-Geigy: (telephone: 201-277-5787). If M. tuberculosis is isolated from a patient receiving this four-drug regimen, treatment should be switched to one of the three-drug regimens outlined above (INH, RIF, and EMB or PZA). If MAC is isolated from a patient who has been started on a three-drug regimen, the clinician may continue the three-drug regimen or switch to the four-drug regimen of INH, EMB, rifabutin, and clofazimine. Although experience is very limited, patients with disease due to M. kansasii should respond to INH, RIF, and EMB. Some clinicians advocate the addition of streptomycin (SM), 1 gram twice weekly, for the first 3 months. Therapy should continue for a minimum of 15 months following culture conversion.

Monitoring for toxicity of antimycobacterial drugs may be difficult for patients who may be receiving a variety of other drugs and may have other concomitant conditions. Because hepatic and hematologic abnormalities may be caused by the mycobacterial disease, AIDS, or other drugs and conditions, the presence of such abnormalities is not an absolute contraindication to the use of the treatment regimens outlined above.

Infection Control

Recommendations for preventing transmission of HIV infection to health-care workers have been published (17). In addition, infection-control procedures applied to patients with HIV infection who have undiagnosed pulmonary disease should always take the possibility of tuberculosis into account. This is especially true when diagnostic procedures, such as sputum induction or bronchoscopy, are being performed. Previously published guidelines for preventing tuberculosis transmission in hospitals should be followed (18).

Contact Investigation for Tuberculosis

Patients with pulmonary tuberculosis and HIV infection should be considered potentially infectious for tuberculosis, and standard procedures for tuberculosis contact investigation should be followed (19). Specific data on the infectiousness of tuberculosis in patients with HIV infection are not yet available.

Examining HIV-infected Persons for Tuberculosis and Tuberculosis Infection

Individuals who are known to be HIV seropositive should be given a Mantoux skin test with 5 tuberculin units of purified protein derivative as part of their clinical evaluation. Although some false-negative skin test results may be encountered in this setting as a result of immunosuppression induced by HIV infection, significant reactions are still meaningful (20). If the skin test reaction is significant, a chest radiograph should be obtained, and if abnormalities are detected, additional diagnostic procedures for tuberculosis should be undertaken. Patients with clinical AIDS or other Class IV HIV infections (21) should receive both a tuberculin skin test and a chest radiograph because of the higher probability of false-negative tuberculin reactions in immunosuppressed patients.

Examining Patients with Clinically Active Tuberculosis or Latent Tuberculosis Infection for HIV Infection

As part of the evaluation of patients with tuberculosis and tuberculous infection, risk factors for HIV should be identified. Voluntary testing of all persons with these risk factors is recommended (22). In addition, testing for HIV antibody should be considered for patients of all ages who have severe or unusual manifestations of tuberculosis. The presence of HIV infection has implications regarding treatment (see above), alerts the physician to the possibility of other opportunistic infections, and allows for counselling about transmission of HIV infection (23). Testing for HIV antibody is especially important for persons over age 35 with asymptomatic tuberculous infection, because INH would not usually be indicated for persons in this age group unless they are also HIV seropositive.

Preventive Therapy

HIV seropositivity in a person of any age with a significant tuberculin reaction is an indication of INH preventive therapy (16). Although it is not known whether INH therapy is as efficacious in preventing tuberculosis in HIV-infected persons as in other groups, the usually good response of HIV-infected persons with tuberculosis to standard therapy suggests that INH preventive therapy would also be effective. Before instituting preventive therapy, clinically active tuberculosis should be excluded.

(Adapted from the MMWR 1986; 35:448-52. References available on request.)

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AIDS STATISTICS

Table 1. Adult AIDS cases by risk group and sex, Connecticut, 1980 - February 25, 1987

Risk Group	Male (%)	Female (%)	Total (%)
Homo/bisexual men	172 (55)	0 (0)	172 (46)
IV drug abusers	86 (27)	34 (57)	120 (32)
Homo/bi + IV drug	27 (9)	0 (0)	27 (7)
Hemophiliac	4 (1)	0 (0)	4 (1)
Heterosex. contact	3 (1)	14 (23)	17 (5)
Born NIR country	4 (1)	1 (2)	5 (1)
Transfusion	5 (2)	6 (10)	11 (3)
None above/other	14 (4)	5 (8)	19 (5)
Total	315 (100)	60 (100)	375 (100)

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