OUTBREAK OF TUBERCULOSIS AMONG REGULAR PATRONS OF A NEIGHBORHOOD BAR

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Abstract *Background. Outbreaks of tuberculosis have been reported in prisons, nursing homes, urban homeless shelters, and other crowded settings. We report a nonresidential outbreak of tuberculosis that originated in a neighborhood bar.*

Methods. A homeless patient with highly infectious pulmonary tuberculosis was a regular patron of a neighborhood bar during a long symptomatic interval before diagnosis. We investigated 97 other regular customers and employees of the bar through interviews, tuberculin skin testing, and chest roentgenography. We performed DNA fingerprinting on isolates from the index patient and 11 other patients.

Results. The index patient apparently infected 41 of 97 contacts (42 percent), resulting in 14 cases of active tuberculosis and 27 cases of infection but no disease (indicated by positive tuberculin skin tests). Four other cases of active tuberculosis occurred among regular customers of the bar who were missed by the contact investigation. There were also two secondary cases. Radiographic findings in active cases included upper-lobe disease in seven cases (three cavitary) and negative chest films at the time of diagnosis in four cases. All 12 culture isolates we tested had the same chromosomal-DNA restriction pattern.

Conclusions. The spread of tuberculosis in a neighborhood bar can be a major public health problem. The high rate of infection and disease among the contacts was unexpected and was not due to coinfection with the human immunodeficiency virus. Possible explanations include heavy alcohol use among the contacts, high infectivity of the index case, or both. Sputum cultures must be performed in tuberculin-positive contacts who have symptoms, even if the chest films are normal. (N Engl J Med 1995;333:222-7.)

OUTBREAKS of tuberculosis often occur under crowded living conditions when there is prolonged close exposure to an infectious person. They have been reported from prisons, nursing homes, residential centers for persons infected with the human immunodeficiency virus (HIV), and urban homeless shelters.[1-6] We report an outbreak caused by nonresidential exposure at a neighborhood bar. A highly infectious person with cavitary tuberculosis spent much of his time at the bar for several months. He became increasingly symptomatic, yet remained untreated and without a diagnosis. Mental health problems and chronic alcoholism effectively blocked his access to health care. The result was an outbreak of tuberculosis among those who frequented the bar. The outbreak had a substantial impact on community health, contributing 35 percent of all new active cases of tuberculosis in Minneapolis during 1992.

METHODS

Contact Investigation

The index patient identified a neighborhood bar where he had spent most of his time during a long, highly symptomatic interval before diagnosis. All employees and regular customers were invited to participate in a contact investigation. An epidemiologic investigator conducted interviews at the bar between March 11 and April 15, 1992. Information was obtained on the participants' demographic characteristics, places of residence, and workplaces. They were asked about any history of tuberculosis, previous exposures to active tuberculosis, and previous results of tuberculin skin tests. Social and behavioral histories taken included questions about smoking, alcohol use, other drug use, and activity associated with a high risk for HIV infection. Data on their medical histories and all current symptoms were also collected.

All persons with previous positive tuberculin skin tests were offered chest roentgenography; those whose previous tuberculin status was negative or unknown were offered tuberculin skin tests. Skin tests were performed and read by one investigator. The test antigen was Tubersol (Connaught; Willowdale, Ont., Canada), and the dosage was 0.1 ml (5 tuberculin units). A positive test was defined as the presence of 5 mm or more of induration at 48 to 72 hours.

People who had negative tuberculin skin tests were not evaluated further unless they had one or more of the following: cough, fever, chills, night sweats, or weight loss. Chest films were recommended for people with negative skin tests who had symptoms and for all those with positive skin tests. Sputum cultures were recommended for participants with abnormal chest films and for all in the survey who had positive tuberculin tests and symptoms, even if their chest films were normal.

Because the contact investigation did not reach all the people at risk, all patients with active tuberculosis diagnosed in Minneapolis since the outbreak were also asked about the extent of their exposure to the bar during the second half of 1991 and the first half of 1992.

Bacteriology

Sputum smears were obtained, and cultures and tests for drug sensitivity were performed in the mycobacteriology laboratory of the Hennepin County Medical Center. Smears were examined with a fluorescent microscope after being stained with rhodamine–auramine. Cultures and tests for sensitivity were performed with a liquid BacTec system.[7] After each vial was sampled, the sampling needle was heated to 170°C for 84 seconds to sterilize it. We guarded further against laboratory cross-contamination of vials by tracking the processing dates of all positive cultures and the sequence of positive vials on the counter, and, in one case, by clinical correlation. Isolates were tested for drug sensitivity to isoniazid, rifampin, ethambutol, and streptomycin.

Isolates from the index patient and 11 other patients with active tuberculosis were sent to the Centers for Disease Control and Prevention in Atlanta for analysis of restriction-fragment–length polymorphisms (RFLPs).[8,9] DNA was extracted, digested, and electrophoresed. The membranes were hybridized with a fragment of the insertion sequence IS6110 to provide a characteristic DNA "fingerprint" established by the frequency and location of repeats of the insertion sequence.[8,9] DNA fingerprinting was performed on the isolate from the index patient, on eight isolates from people who participated in the contact investigation, and on three isolates from other people with tuberculosis in the community who had exposure to the bar during the period of risk.

All participants with active tuberculosis were strongly encouraged to have serum HIV-antibody tests. In addition, all subjects who started isoniazid prophylaxis were tested blindly for HIV antibodies as part of a community testing program.

RESULTS

Index Case

A 48-year-old man presented to Hennepin County Medical Center (a public teaching hospital in Minneap-

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olis) on March 7, 1992, with progressive weakness and weight loss of 31 kg over a period of six months. He could not walk without assistance. Other symptoms included fever and chills, nausea, vomiting, diarrhea, and a chronic productive cough with intermittent scanty hemoptysis. He smoked one pack of cigarettes per day and was a heavy alcohol user. He had been homeless for six months. He spent most of his days in one neighborhood bar and slept under a bridge, in shelters, and occasionally in a rooming house next to the bar. He had no history of tuberculosis and no known exposure to anyone with active tuberculosis.

He weighed 49 kg, had a temperature of 39°C, and had a respiratory rate of 36 breaths per minute. There were extensive crackles over the upper anterior lung fields. Abdominal examination was normal. There was no lymphadenopathy. The fingers and toes were clubbed.

A chest film showed extensive bilateral cavitary infiltrates in the upper lobes (Fig. 1). A serum HIV-antibody test was negative. Skin tests using tuberculin and mumps and candida antigens were negative. Smears of unconcentrated sputum were positive for tubercle bacilli and were graded 4+ (more than 9 organisms per oil-immersion field [magnification, ×1000]). Sputum culture was positive for *Mycobacterium tuberculosis* and was sensitive to isoniazid, rifampin, ethambutol, and streptomycin. DNA fingerprinting of the isolate, by RFLP analysis, showed a pattern with 15 bands, representing separate repeats of the insertion sequence.

Figure 1. Posteroanterior Chest Film of the Index Patient at Presentation, Showing Extensive Bilateral Cavitary Infiltrates.

Contact Investigation

The patient was interviewed about possible contacts. He was able to supply few names but reported that most of his time, especially as he was getting sicker, had been spent at the bar and the adjacent rooming house. A contact investigation was initiated, centering on the bar and the rooming house and targeting all bar workers and all regular bar customers, including five who were staying in the rooming house.

Ninety-seven contacts (4 bartenders and 93 regular customers) were interviewed at the bar between March 11 and April 15, 1992. Figure 2 gives an overview of the entire contact investigation.

None of the participants had previously been given a diagnosis of active tuberculosis or treated with antimycobacterial therapy. Eight of them had had positive tuberculin skin tests at least one year earlier, confirmed in six cases by medical records or family members. Chest films were negative in seven of the eight. The eighth person had a dense peripheral infiltrate in the right upper lobe. A chest film obtained two years earlier showed only minimal fibrosis in the right upper lobe, in a slightly different location. The patient had a chronic cough and a weight loss of 5 kg. Sputum smears were negative for *M. tuberculosis,* but sputum cultures were positive. The clinical features suggested endogenous reactivation of tuberculosis, but DNA fingerprinting demonstrated that the culture isolate from this patient was of the same strain as that from the index patient, indicating exogenous reinfection.

Tuberculin skin tests were performed in the remaining 89 participants, 81 of whom returned to have the skin tests read and recorded. Forty-two of the 81 had negative tests; 34 of these 42 were asymptomatic and were not investigated further. However, the remaining 8 of the 42 had chronic coughs (most were long-term smokers). Six of them had normal chest films, 1 had a small granuloma but failed to report for follow-up, and 1 tuberculin-negative subject with cough had an isolated nodule, 1 cm in diameter, in the right upper lobe. The last-mentioned subject failed to return for two months but reappeared in June 1992, when another tuberculin skin test was positive. He refused both a second chest film and prophylactic therapy with isoniazid. He next appeared four months later with a worsening cough. A chest film showed a dense peripheral infiltrate in the right upper lobe, located closer to the apex than the nodule had been. Sputum smears and cultures were positive for *M. tuberculosis.*

Thirty-nine people in the survey had positive tuberculin skin tests (38 had ≥10 mm of induration). Of 34 who agreed to have chest films, 3 had radiologic abnormalities consistent with active tuberculosis (2 had upper-lobe infiltrates, of which one was cavitary). In all 3, sputum smears and cultures were positive for *M. tuberculosis.* Analysis of RFLPs showed that these 3 isolates had the same 15 bands as the isolate from the index patient. Four other people in this group of 34 had negative chest films but had coughs and, in 2 cases, weight loss. None had fever or night sweats. Computed tomography of the chest was negative in 3 of the 4. All had negative sputum smears, but the sputum cultures were positive for *M. tuberculosis.* In each case,

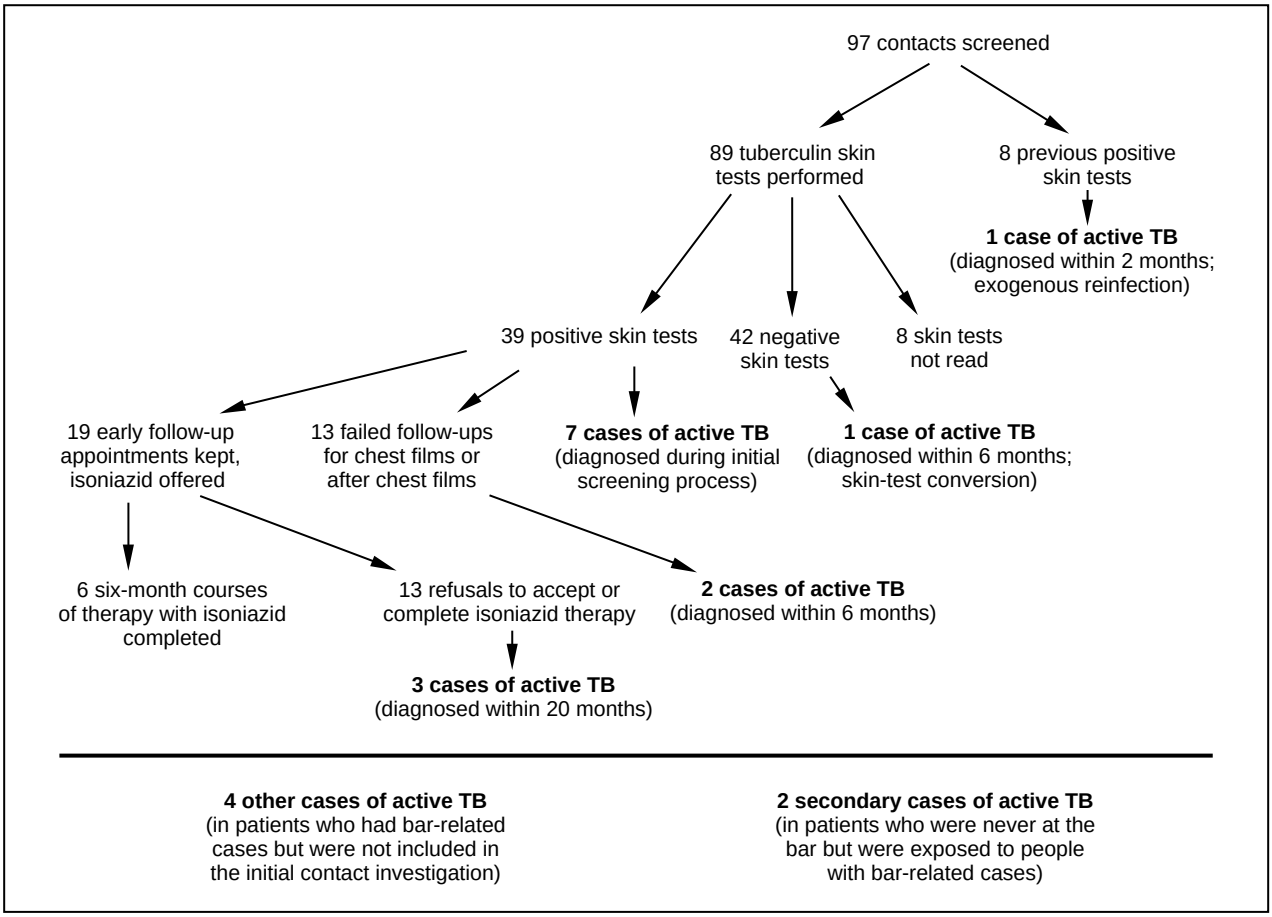

Figure 2. Flow-Chart Overview of the Contact Investigation and Origin of the 20 Active Cases of Tuberculosis That Resulted from Infection in the Index Patient.

RFLP analysis showed the same pattern as that of the isolate from the index case.

Thirteen tuberculin-positive subjects refused any further appointments: the five who refused chest films plus eight others with normal chest films. None of these 13 had sputum cultures, and none were offered preventive therapy with isoniazid. Two of them returned within six months with fever, cough, and lymphocytic pleural effusions. Pleural-fluid cultures were negative. The subjects were treated empirically for tuberculosis and had good clinical and radiographic responses.

The remaining 19 tuberculin-positive participants kept their initial series of appointments and were offered isoniazid prophylaxis. Six completed six months of isoniazid therapy and remained well (three of them were bartenders; the fourth bartender had a negative skin test and a negative chest film). Thirteen refused isoniazid therapy or were noncompliant. One returned six months later with a cough, weight loss, night sweats, and bilateral cavitary upper-lobe infiltrates. Sputum smears and cultures were positive. A second person returned 10 months later with pulmonary symptoms and right-upper-lobe consolidation. She did not tolerate triple therapy with isoniazid, rifampin, and pyrazinamide and then did not accept an alternative regimen. Her disease progressed to smear-positive cavitary tuberculosis. Another woman returned 20 months later with a chronic cough, dyspnea, and depression. A chest film showed extensive bilateral infiltrates. Direct smears of bronchial washings were positive for tubercle bacilli, and cultures of this fluid grew *M. tuberculosis.* Lumbar puncture revealed tuberculous meningitis. She was started on triple therapy with isoniazid, rifampin, and pyrazinamide and was also given high doses of glucocorticoids. Despite this therapy, she died within two weeks, of brain-stem herniation.

Two people with secondary tuberculosis — one a 7-month-old child, the second a 36-year-old man — presented 6 and 7 months after the contact investigation. They had no direct exposure to the index patient or to the implicated bar, but they had been exposed to people with active tuberculosis who frequented the bar.

Four other cases of active tuberculosis were not identified by the contact investigation but were linked to the bar. Two were diagnosed synchronously with the contact investigation, and two others were diagnosed in 1994. These four patients had severe chronic alcoholism and had spent much time at the bar during the high-risk period. They were aware of the contact investigation but had been unwilling or unable to participate.

One patient with pleural tuberculosis had a positive HIV-antibody test. However, 18 people with active tuberculosis and 15 others who started isoniazid prophylaxis all had negative tests for HIV antibodies. Those

who started isoniazid prophylaxis were HIV-negative by inference. In 1992 only 6 of 582 patients who were started on isoniazid prophylaxis at the Tuberculosis Control Clinic in Minneapolis were HIV-positive, and these 6 could all be excluded from the outbreak demographically.

Geographic Distribution of Cases

Addresses were obtained for 16 patients with active tuberculosis (not including the index patient) and for 19 others in the investigation who were tuberculin-positive but who did not have active disease. Figure 3 shows where these 35 infected people lived in relation to the implicated bar. All the participants with active tuberculosis lived in Minneapolis, all but one within two miles of the bar. Five of them lived in the rooming house adjacent to the bar; three lived together at another rooming house. In each of three other locations, two participants lived together. Twenty-one participants did not live with another infected person. In most cases the bar was the only site where there was any contact with the index patient. The map in Figure 3 shows the wide distribution of new cases of active tuberculosis around the bar in the adjacent community.

A total of 49 new cases of active tuberculosis were diagnosed in Minneapolis in 1992, including 17 bar-related cases (35 percent). Two bar-related cases were diagnosed in 1993, and two more in 1994.

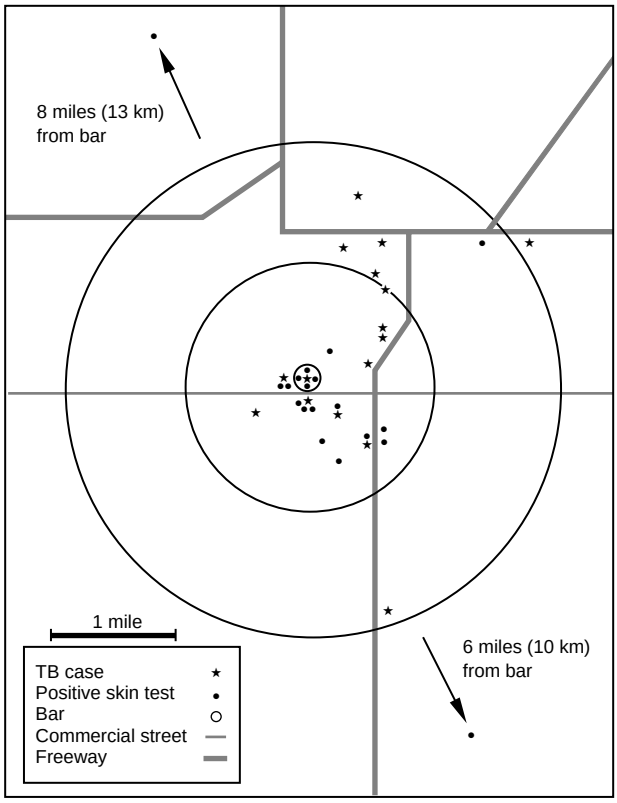

Figure 3. Schematic Map of the Neighborhood.
The bar is in the center, with the two larger circles indicating a one-mile (1.6-km) radius and a two-mile (3.2-km) radius. The residences of people with active tuberculosis (not including the index patient) are indicated by stars. The residences of people with positive tuberculin skin tests (either new or of unknown duration) but no active disease are indicated by dots. The symbols within the smallest circle represent the five subjects who lived in the rooming house adjacent to the bar.

Bacteriology

Fifteen of the 21 people with active tuberculosis had positive sputum cultures. In one of the 1994 cases, a resected pulmonary nodule that proved to be a tuberculoma had a positive culture. The remaining cases, including four of pleural tuberculosis and one of tuberculous pneumonia in a seven-month-old child, were diagnosed on strong clinical grounds that included symptoms, positive tuberculin skin tests, relevant findings on chest films, and resolution of the illness with appropriate therapy. All isolates were fully susceptible to antituberculous drugs. The first 10 isolates and 2 late isolates from 1994 were referred to the mycobacteriology laboratory of the Centers for Disease Control and Prevention for analysis of RFLPs. All had the same chromosomal-DNA restriction pattern of 15 bands.

Results of Therapy

Most, if not all, of the participants (except the seven-month-old child) used alcohol excessively, and all but four required directly observed therapy. One patient died before diagnosis, and another died of tuberculous meningitis within two weeks of diagnosis. Two patients had good initial responses to therapy but moved out of the state and were lost to follow-up. Seventeen cases of active tuberculosis were successfully treated, including the index case and the two 1994 cases. To date, there have been no relapses.

Discussion

This outbreak demonstrates that tuberculosis can spread in a neighborhood bar if one of the regular patrons is highly infectious. The index patient had a progressively worsening cough, and over a period of six months his weight declined from 80 to 49 kg. There was no intervention, however, even though he was eligible for health care under government programs. There was a public clinic within six blocks of the bar and a public hospital within three miles, yet he did not seek health care, nor did any of the bar's employees or customers intervene. Instead, the patient went untreated until he could barely stand unassisted, had extensive destruction of lung tissue, and had infected numerous others. His alcoholism and mental health problems were a highly effective barrier to health care. Though it would have been difficult, early intervention would probably have reduced the extent of the outbreak.

The index patient proved highly infectious. Forty-one of 97 contacts (42 percent) interviewed at the bar were infected. Active tuberculosis developed in 14 of 97 (14 percent). These numbers are higher than expected. In a typical contact investigation, approximately 20 to 30 percent of the close contacts have positive tuberculin skin tests and in only 1 or 2 percent does active tuberculosis develop. Also higher than expected was the proportion of the people we surveyed who were infected but without disease initially (i.e., they had positive tuberculin skin tests, normal chest films, and no symp-

toms), yet who later progressed to active disease. Nineteen such people were offered isoniazid prophylaxis. Six completed therapy and remained well, but 13 refused preventive therapy or were noncompliant. In 3 of these 13 (23 percent), active tuberculosis developed within two years. Typically, in approximately 5 percent of the people who convert to positive tuberculin skin tests, active tuberculosis develops in one year, and in an additional 5 percent it develops at some time during their lives.[10] A higher rate of active disease after conversion of the tuberculin test is expected among people infected in infancy, during puberty and adolescence, and in senescence, and those infected with HIV.[10,11] However, all the contacts at the bar in whom active tuberculosis developed were adults, and only one was HIV-positive.

Several factors could explain the high rate of tuberculosis among the contacts. One is heavy alcohol use, although it is not known whether this is because people who drink heavily have greater exposure to infectious tuberculosis, a greater susceptibility to infection, a higher frequency of progression from initial infection to active disease, or a higher rate of late reactivation.[12-14] Perhaps a combination of these elements accounts for the association. Studies by Friedman and colleagues suggest that late reactivation may not be the chief problem.[15,16] The late-reactivation rate among alcohol abusers who were tuberculin-positive (for an unknown length of time) in those studies was only 0.75 percent over a seven-year period — a normal rate and far less than that in HIV-infected cohorts who are tuberculin-positive.[17] Our study suggests that initial infection may progress to active disease more frequently in heavy alcohol users. Another factor contributing to the high incidence of both infection and active disease at the bar may have been the high infectivity of the index patient.

RFLP analysis can provide a highly characteristic fingerprint of an outbreak strain of *M. tuberculosis*. This tool is powerful because of the remarkable diversity of RFLP patterns of isolates from cases that are not linked epidemiologically.[18,19] RFLP analysis proved very useful in our investigation and supplemented standard epidemiologic procedures. The same 15 repeats of the insertion sequence were found in all the isolates we tested. The genetic fingerprint of the outbreak strain helped prove linkage among the infected people, including one person with exogenous reinfection, four with upper-lobe disease that resembled endogenous reactivation, and two who were missed by the contact investigation and presented more than two years later. A study of a tuberculosis outbreak in a residence for HIV-infected patients also showed that RFLP analysis enhances the investigation of known outbreaks.[5] RFLP analysis can even identify clusters of tuberculosis cases that traditional contact tracing by public health agencies cannot detect.[20]

In a study of an outbreak of tuberculosis in a homeless shelter, Nardell and colleagues also identified cases of exogenous reinfection and of upper-lobe disease resembling endogenous reinfection.[2] They used phage typing and the resistance patterns of culture isolates to link cases to the outbreak. Our findings support their conclusion that the radiographic pattern of disease may not distinguish reactivation tuberculosis from primary infection acquired during an outbreak.

Four symptomatic participants had positive sputum cultures but negative chest films. Active pulmonary tuberculosis in patients with negative chest films, an underappreciated combination, has been reported, particularly in immunocompromised patients.[17,21-30] In the context of a contact investigation, a negative chest film in a tuberculin-positive subject does not rule out active tuberculosis.

The cost of failing to complete prophylactic treatment was very high. Of 13 tuberculin-positive contacts who refused isoniazid prophylaxis or did not comply with the regimen, 3 had their conditions progress to active tuberculosis within two years. Our experience suggests that chronic alcoholism is such a high-risk factor for progression to active disease that major efforts to ensure completion of six months of isoniazid therapy are worthwhile for tuberculin-positive heavy drinkers who are close contacts of people with active disease. Since this outbreak, the Hennepin County Tuberculosis Control Clinic has begun using directly observed therapy, not only for multidrug therapy of selected cases of active tuberculosis but also for single-drug isoniazid prophylaxis of persons at high risk for early progression to active disease, including those with severe chronic alcoholism.

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