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TRANSMISSION OF MULTIDRUG-RESISTANT *MYCOBACTERIUM TUBERCULOSIS* DURING A LONG AIRPLANE FLIGHT

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Abstract *Background.* In April 1994, a passenger with infectious multidrug-resistant tuberculosis traveled on commercial-airline flights from Honolulu to Chicago and from Chicago to Baltimore and returned one month later. We sought to determine whether she had infected any of her contacts on this extensive trip.

Methods. Passengers and crew were identified from airline records and were notified of their exposure, asked to complete a questionnaire, and screened by tuberculin skin tests.

Results. Of the 925 people on the airplanes, 802 (86.7 percent) responded. All 11 contacts with positive tuberculin skin tests who were on the April flights and 2 of 3 contacts with positive tests who were on the Baltimore-to-Chicago flight in May had other risk factors for tuberculosis. More contacts on the final, 8.75-hour flight from Chicago to Honolulu had positive skin tests than those on the other three flights (6 percent, as compared with 2.3, 3.8, and 2.8 percent). Of 15 contacts with positive tests on the May flight from Chicago to Honolulu, 6 (4 with skin-test conversions) had no other risk factors; all 6 had sat in the same section of the plane as the index patient ($P = 0.001$). Passengers seated within two rows of the index patient were more likely to have positive tuberculin skin tests than those in the rest of the section (4 of 13, or 30.8 percent, vs. 2 of 55, or 3.6 percent; rate ratio, 8.5; 95 percent confidence interval, 1.7 to 41.3; $P = 0.01$).

Conclusions. The transmission of *Mycobacterium tuberculosis* that we describe aboard a commercial aircraft involved a highly infectious passenger, a long flight, and close proximity of contacts to the index patient. (N Engl J Med 1996;334:933-8.)

A 1993 investigation of a flight attendant with infectious tuberculosis demonstrated transmission of the disease to other crew members, but evidence of transmission to passengers was inconclusive.[1] In June 1994, a state health department notified the Centers for Disease Control and Prevention (CDC) that a visitor from a foreign country had died of complications of pulmonary tuberculosis; her *Mycobacterium tuberculosis* isolate was resistant to isoniazid, rifampin, pyrazinamide, streptomycin, and kanamycin. Before the tuberculosis was diagnosed in May 1994, she flew from Honolulu to Chicago and from Chicago to Baltimore in April 1994 and returned one month later. Because of the extent of her disease, concern about the potential transmission of drug-resistant *M. tuberculosis*, and uncertainty regarding passenger-to-passenger transmission of *M. tuberculosis* on aircraft, an investigation of the passengers and flight crew was conducted. The results of this investigation prompted the CDC to issue recommendations concerning the notification of passengers and flight crews after exposure to tuberculosis on aircraft.[2]

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METHODS

Investigation of Index Patient and Household Contacts

Medical and laboratory records of the index patient were reviewed. State and local health departments investigated the contacts of the two households in the two states where the index patient had lived during her visit to the United States.

Investigation of the Flight Crew and Passengers

The passenger manifests and lists of flight-crew members for the four flights were obtained from the airline company. Information from the manifests and from frequent-flyer records was used to locate passengers and identify seat assignments. People who were not residents of the United States or Canada were excluded from the investigation. The passengers and members of the flight crews (contacts) were notified by certified letter of their potential exposure to tuberculosis, advised to have a Mantoux tuberculin skin test, and asked to complete a questionnaire. Data collected included demographic and epidemiologic information. Except for those of contacts with evidence of previous tuberculosis or previous positive tuberculin skin tests, skin-test results reported in this study are based on written records provided by health departments or by personal physicians.

Contacts with negative results on tuberculin skin tests performed less than 12 weeks after the flight were mailed a second letter advising them of the need for a final test at least 12 weeks after their exposure. A positive tuberculin skin test was defined as involving an induration

of 10 mm or larger. A skin-test conversion was defined as an increase of 10 mm or more in induration within the previous two years. Contacts with positive tuberculin skin tests or conversions were interviewed about other risk factors for tuberculosis. Results of tuberculin skin tests and interviews were reviewed independently by three tuberculosis experts, who assessed whether positive results were due to new infection or the booster effect.[3-5]

Data Analysis

Results of tuberculin skin tests were analyzed according to age, sex, race or ethnic group, flight, flight duration, and seat proximity to the index patient. Categorical variables were compared with the use of the chi-square or Fisher's exact test. Continuous variables were compared with the use of Student's t-test.[6]

Aircraft

Information about the type of aircraft flown on each flight was obtained from airline records. Airline-industry diagrams were used to map seat assignments and manufacturers' specifications of airflow, and air-distribution systems were reviewed for each type of aircraft. Aircraft-ventilation systems were not otherwise evaluated.

RESULTS

Index Patient

The index patient was a 32-year-old Korean woman, who according to relatives was taking no antituberculous medication but had previously been treated for tuberculosis — twice as an adolescent in Korea and once within the past two years in Japan — with unknown medication. She arrived in Honolulu in April on a tourist visa and was reportedly coughing and lethargic while staying with friends (Household 1) for five days. She then flew from Honolulu to Chicago and from Chicago to Baltimore, where she remained with friends (Household 2) for one month. Members of Household 2 reported a worsening of her symptoms, including progressive cough, lethargy, shortness of breath, fever, night sweats, and the eventual onset of scant hemoptysis. In May she returned to Honolulu, flying from Baltimore to Chicago and from Chicago to Honolulu. Eight days after returning to Household 1, she had an acute episode of hemoptysis, described as consisting of approximately 1 liter of bright red blood. Hospital evaluation revealed extensive pulmonary disease (Fig. 1), and her sputum was highly positive (3+) for acid-fast bacilli and was culture-positive for *M. tuberculosis*. The patient died of pulmonary hemorrhage and respiratory failure five days after being hospitalized.

Figure 1. Chest Film of the Index Patient Eight Days after Flight 4, Showing Extensive Bilateral Pulmonary Disease with Cavitary Lesions.

Household Contacts of the Index Patient

Both Korean-born adults in Household 1 had positive tuberculin skin tests in June 1994. Their two children, three and seven years of age, had negative skin tests 14 weeks after exposure. The mother in Household 2 had had a positive skin test in 1977, and her chest film was normal in May 1994. The father's test showed 12 mm of induration at the end of May, and his chest film was normal. Their 21-month-old, U.S.-born child had a skin-test conversion from 0 mm of induration in May and early June (2 and 8 weeks after the index patient departed, respectively) to 22 mm of induration 17 weeks after her departure. As of December 1995, the child remained free of signs and symptoms of active tuberculosis.

Flight Crew and Passengers

Of 1042 passenger and crew contacts identified on the four flights, 117 (11.2 percent) were not notified: 24 were residents of foreign countries, and for 93 no information on their whereabouts was available. The remaining 925 (88.8 percent) resided in 41 states, Puerto Rico, the District of Columbia, and Canada and were notified of their possible exposure. Of these, 802 (86.7 percent) provided results of a final tuberculin skin test (at least 12 weeks after exposure). Forty-two contacts were excluded from the analysis: 40 had had tuberculosis previously or had evidence of a previous positive tuberculin skin test, 1 died of cancer, and 1 died of the acquired immunodeficiency syndrome (AIDS) with documented anergy. Neither contact who died had signs or symptoms compatible with tuberculosis. The passenger

Table 1. Results of Tuberculin Skin Tests for the 760 Passengers and Crew Members, According to Flight.*

Test Result	Flight 1 (N = 298)	Flight 2 (N = 104)	Flight 3 (N = 109)	Flight 4 (N = 249)	Total (N = 760)
			number (percent)		
Positive	7 (2.3)	4 (3.8)	3 (2.8)	15 (6.0)	29 (3.8)
No previous test†	7 (2.3)	4 (3.8)	3 (2.8)	9 (3.6)	23 (3.0)
Conversion	0	0	0	6 (2.4)	6 (0.8)
Negative‡	291 (97.7)	100 (96.2)	106 (97.2)	234 (94.0)	731 (96.2)

*Flight 1 was from Honolulu to Chicago in April, flight 2 from Chicago to Baltimore in April, flight 3 from Baltimore to Chicago in May, and flight 4 from Chicago to Honolulu in May.

†These contacts had no results of previous skin tests in their medical records.

‡All 10 contacts who were exposed on two connecting flights had negative tuberculin skin tests.

with AIDS was already receiving rifabutin prophylaxis and had smears and cultures negative for acid-fast bacilli after exposure.

Of the 760 contacts for whom data were analyzed, 95 percent were passengers and 5 percent were crew members. Only 10 contacts (1.3 percent) were exposed on two connecting flights. Fifty-five percent of the contacts were male, 94 percent were U.S.-born, 86 percent were white, and the median age was 43 years (range, 6 months to 86 years). There were no statistically significant differences in the demographic characteristics of contacts among the four flights. Previous vaccination with bacille Calmette–Guérin (BCG) was reported by 2.6 percent of all the contacts, and exposure to a family member or friend with tuberculosis by 7.5 percent.

The results of tuberculin skin tests of the contacts are shown in Table 1. In the six contacts on flight 4 who had conversions to positive skin tests, the first test was performed a median of 8 weeks after exposure (range, 34 weeks before exposure to 10 weeks after exposure), and the second test was administered a median of 23 weeks after exposure (range, 8 to 29). All the contacts with negative tuberculin skin tests had final tests performed at least 12 weeks after exposure (median, 16; range, 13 to 32).

All 11 contacts on flights 1 and 2 who had positive tuberculin skin tests had other risk factors, including birth in a country where tuberculosis is highly endemic[7] or receipt of BCG (5 contacts), exposure to tuberculosis in a family member (3), residence overseas (2), and occupational exposure (1). Passengers on flights 1 and 2 who had positive tuberculin skin tests had not been seated near the index patient. On flight 3, three people had positive tuberculin skin tests, but none had conversion. Of these, two were born in countries where tuberculosis is highly endemic and had received BCG. The third person with a positive test, who had been seated three rows away from the index patient, reported having no other risk factors for tuberculosis.

The characteristics of the 15 contacts on flight 4 who had positive tuberculin skin tests are shown in Table 2, and their seat assignments in relation to that of the index patient are shown in Figure 2. The index patient had been seated next to the aisle in the next-to-last row of the rear cabin section of the aircraft. Nine contacts with positive tuberculin skin tests, who had been seated throughout the aircraft, had other risk factors for tuberculosis. Six contacts with positive tuberculin skin tests, including four with conversions, had no other identified risk factors.

Table 3 summarizes the association between the results of tuberculin skin tests and seating proximity to the index patient for contacts on flight 4 who had no other identified risk factors. Contacts with positive tests, including four with conversions, were more likely to have been seated in the same cabin section of the aircraft as the index patient than contacts with negative tests ($P = 0.001$). In fact, all six contacts with positive tuberculin skin tests and no risk factors, including all four with conversions, had been seated in the same cabin section of the aircraft as the index patient. Those seated within two rows of her were 8.5 times more likely to have positive tuberculin skin tests or conversions than those seated elsewhere in the same cabin section.

Table 2. Characteristics of the Passengers and Crew Members on Flight 4 Who Had Positive Tuberculin Skin Tests.

Contact No.	Age	Race or Ethnic Group*	Sex	Rows from Index Patient	Tuberculin Skin Test		Risk Factors†	Infection Status‡
					first	second		
	yr				*mm*			
1	55	W	M	49	10	—	Uncle with tuberculosis	Previous
2	43	A	M	31	11	—	Foreign-born	Previous
3	76	W	M	26	10	—	Lived in Southeast Asia	Previous
4	30	W	M	24	4	18	Friend with tuberculosis	Previous
5	28	W	F	24	20	—	Friend with tuberculosis, health care worker	Previous
6	57	W	M	13	0	20	Foreign-born	Previous
7	51	W	F	13	18	—	Foreign-born	Previous
8	55	W	F	13	0	11	None identified	New
9	37	W	F	12	0	12	None identified	New
10	38	A	M	9	14	—	Foreign-born, received BCG	Previous
11	29	H	M	6	20	—	Foreign-born, received BCG	Previous
12	47	W	F	2	11	—	None identified	New
13	41	W	M	1	0	15	None identified	New
14	36	W	M	1	0	19	None identified	New
15	41	W	M	0	17	—	None identified	New

*W denotes white, A Asian, and H Hispanic.

†Foreign-born denotes birth in a country where the rate of tuberculosis is at least 10 times higher than in the United States and where bacille Calmette–Guérin (BCG) vaccine is routinely used.

‡The investigators' determinations were based on the results of the skin tests and on the risk factors.

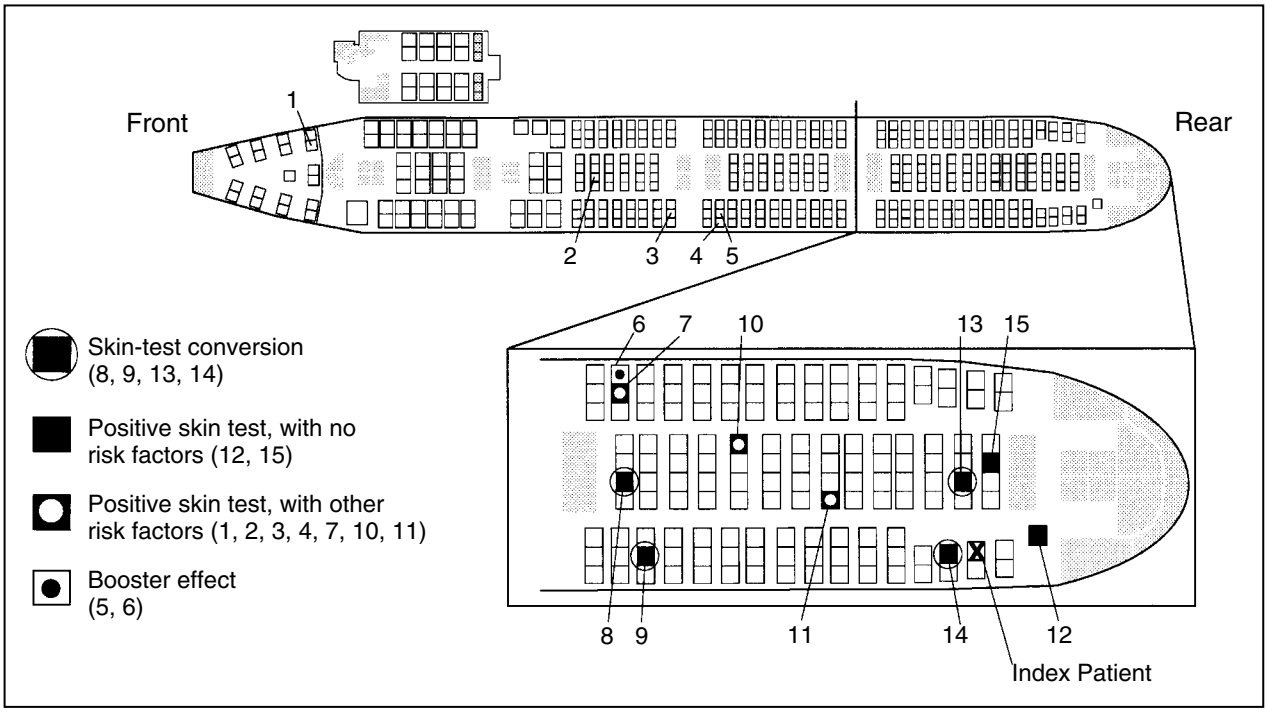

Figure 2. Diagram of the Boeing 747-100, with Seat Assignments of the Passengers and Flight Crew on Flight 4 Who Had Positive Tuberculin Skin Tests.

Numbers refer to the contacts listed in Table 2. Contact 12 was a member of the flight crew.

Among the six persons with positive tuberculin skin tests, four had been seated within two rows of the index patient, and the two seated toward the front of the rear cabin section reported having frequently visited friends seated very near the index patient and having used the lavatory close to her seat. As of February 1996, all six remained free of signs and symptoms of active tuberculosis.

Aircraft and Ventilation Systems

For both transoceanic flights, flights 1 and 4, Boeing 747-100 aircraft were used. Flight 1 took place in April and lasted 8 hours; flight 4 was in May and lasted 8.75 hours. The Chicago-to-Baltimore and Baltimore-to-Chicago flights, flights 2 and 3, were both on Airbus 320-200 aircraft and were 1.75 and 2 hours long, respectively. No flight delays were reported to have occurred on any of the flights. Both the B747-100 and A320-200 aircraft had air-recirculation systems with high-efficiency particulate air (HEPA) filtration. The B747-100 aircraft recirculates air through one common reservoir for the entire aircraft. Approximately 50 percent of the air is recirculated, and rates of air exchange reported by the manufacturers of these types of aircraft range from 6 to 20 times per hour. Smoking was prohibited on all four flights.

Discussion

This incident provided a unique opportunity to investigate the transmission of *M. tuberculosis* on aircraft. A high proportion of U.S. residents among the passengers, repeated notification, and national media attention led to a high response rate among contacts. Prompt notification by a state tuberculosis-control program allowed us to assess the development of tuberculous infection among the May 1994 passengers and flight crew prospectively.

Our investigation provides evidence of the transmission of *M. tuberculosis* from passenger to passenger and from passenger to flight crew aboard commercial aircraft. Although the possibility of transmission from the index patient to other passengers on flights 1, 2, and 3 cannot be excluded, the evidence is most compelling for flight 4. This includes evidence of recent transmission (i.e., skin-test conversions), an association between transmission and proximity to the index patient, and a dose–response effect. All but one of the contacts who had no risk factors for tuberculosis and had positive skin tests, including all those with conversions, were seated in the same section as the index patient. Those seated within two rows were at greatest risk. The skin-test conversions on flight 4 but not on flight 3, although the flights took place on the same day, suggest that prolonged exposure to aerosol droplets from the index patient played a part. The apparent absence of transmission on flight 1 may have been due to the varying infectiousness of the index patient, who had long-standing disease. She was more symptomatic in May than in April. The timing of the skin-test conversion of the child in Household 2 suggests that transmission occurred just before flights 3 and 4. The children in Household 1 may have escaped infection because the

index patient was less infectious in April, because they were not in close proximity to her when she returned in May, or because of chance alone, since many household contacts of people with infectious tuberculosis are known to remain uninfected.[8,9] Since there are no clinical data on the risks and benefits of preventive therapy that does not include isoniazid and rifampin, clinicians of the infected contacts had two options: to administer no preventive therapy and watch carefully for the appearance of signs and symptoms of tuberculosis,[10] or to consider six months of preventive therapy with rifabutin, to which the isolate was fully susceptible.

These findings are consistent with previous reports of the transmission of other airborne pathogens on commercial aircraft, such as measles, influenza, and smallpox viruses.[11-13] Our results are also consistent with the previous finding that the risk of transmission of *M. tuberculosis* from a flight-crew member with infectious tuberculosis to other crew members increased with the duration of in-flight exposure.[1] Previous investigations involving closed environments, including naval ships, also showed an association between proximity to a person with infectious tuberculosis and transmission of *M. tuberculosis*.[14] In our investigation, the absence of passengers with skin-test conversions in other cabin sections of the aircraft on flight 4 is further evidence that *M. tuberculosis* was not transmitted through the aircraft's air-recirculation system.

Domestic air travel in the United States increased by 62 percent from 1980 through 1993 — from 275 million to 445 million passengers per year.[15] Air travel from foreign countries to the United States increased by 182 percent, from 12.6 million passenger arrivals during 1975 to 35.5 million in 1991.[15] The projections of the World Health Organization for the worldwide tuberculosis epidemic include 90 million new cases during the present decade.[16] Increased air travel, the presence of tuberculosis worldwide, and immigration to the United States from countries with high rates of tuberculosis increase the probability that passengers on commercial aircraft will be exposed to persons with tuberculosis.[15-17]

After the national media reported this incident in July 1994, the CDC received unsolicited reports of another 30 airline passengers with tuberculosis, including 10 whose diagnosis was already known at the time of travel, who were on commercial flights from July through December 1994. Assuming approximately 260 million airline passengers during that period, the 30 passengers with tuberculosis are estimated to represent approximately 1 of every 9 million passengers.[15] This probably underestimates the risk of exposure to tuberculosis on aircraft, since the reporting was unsolicited and probably incomplete. Assuming 300 passengers per international flight and 150 per domestic flight, however, as many as 10,000 passengers may have been exposed to *M. tuberculosis* on these flights, or approximately 1 of every 26,000 passengers who flew during that period. Furthermore, in our investigation less than 1 percent of all the contacts had skin-test conversions as a result of exposure to the index patient on the aircraft. Although limited by underreporting, these data suggest that passengers and flight crews have a relatively low risk of exposure to and transmission of *M. tuberculosis* on commercial aircraft in the United States.

Table 3. Seat Locations in Aircraft and Results of Tuberculin Skin Tests of Passengers and Crew Members on Flight 4 Who Had No Risk Factors.*

Seat Location	No. with Positive Skin Tests/No. Tested (%)	Rate Ratio (95% CI)†	P Value
Not same cabin section as index patient	0/136	Reference value	—
Same cabin section as index patient	6/68 (8.8)	Undefined	0.001
Within 2 rows	4/13 (30.8)	8.5 (1.7–41.3)	0.01
Elsewhere in same section	2/55 (3.6)	Reference value	

*Data for the flight crew exclude seven flight attendants who could not recall their work assignments on flight 4; all had negative tuberculin skin tests. Risk factors for a positive tuberculin skin test included having been born or having lived in a country where the rate of tuberculosis is at least 10 times higher than in the United States,[7] having had possible occupational exposure, having received the bacille Calmette–Guérin vaccine, or having had exposure to a family member or friend with tuberculosis.

†CI denotes confidence interval.

In this investigation, the passenger with tuberculosis was a tourist from a region of the world where tuberculosis is highly endemic.[7,16] Screening for active tuberculosis is required for immigrants and refugees applying for legal residency in the United States but not for tourists, visitors on business, or students.[18] During 1993, 79 percent of the 21.4 million nonimmigrants who arrived in the United States were tourists.[19] Screening such large numbers of nonimmigrants, even from selected countries with high rates of tuberculosis, would be impractical and very costly and, unless performed just before their flights, would not necessarily prevent exposure to persons with active tuberculosis.

To develop recommendations based on the available scientific evidence, in February 1995 officials of the CDC met with representatives from the Federal Aviation Administration, the Air Transport Association, the Council of State and Territorial Epidemiologists, and the National Tuberculosis Controllers Association, as well as medical consultants from major airline companies. In March 1995, the CDC summarized six investigations of possible transmission of *M. tuberculosis* on aircraft and provided guidance for notifying passengers and flight crews in the event of exposure to tuberculosis during travel on commercial aircraft.[2] Four investigations found no conclusive evidence of the transmission of *M. tuberculosis* to other passengers.[2,20,21] Table 4 shows suggested criteria and procedures for the notification of contacts that were distributed nationally to airline companies, state health departments, and tuberculosis-control programs in March 1995. The decision to notify passengers and crew members potentially exposed to tuberculosis should be guided by three criteria: the flight duration, the infectiousness of the index patient (e.g., whether he or she has smear-positive, cavitary pulmonary tuberculosis or laryngeal tuberculosis and whether there has been documented transmission to contacts), and seating proximity to the index patient, depending on the

Table 4. Suggested Criteria and Procedures for Notifying Passengers and Flight Crews after Exposure to Tuberculosis on Commercial Aircraft.

1. When a health department determines that a passenger with tuberculosis was probably infectious at the time of a flight,[2] it should consult the airline company to verify that the person with tuberculosis was on the flight in question and to ascertain the duration of the flight.
2. Health departments and airline medical consultants may consider limiting notification to flights longer than eight hours. Health departments may consider notification after shorter flights when patients are considered to be particularly infectious, such as those with laryngeal tuberculosis, which has been reported to result in transmission after only five hours of classroom exposure.[22]
3. Depending on the design of the aircraft, notification of only the passengers seated in the same cabin area as the person with tuberculosis, and the crew working there, may be adequate. Collaboration between the health department and the airline is essential in determining who should be notified and how notification will occur.
4. The airline should notify passengers and flight crews in writing, in cooperation with the health department.

aircraft design.[2] In cases in which the airline is informed first, it should provide the name of the passenger's physician to the state health department in the state where the patient resides or is being treated for tuberculosis so that the health department can make a determination of infectiousness. Applying these criteria to instances of exposure to tuberculosis on aircraft will make it easier to decide when to inform those who may potentially benefit from preventive therapy, while averting the expenditure of resources in circumstances in which the transmission of *M. tuberculosis* is highly unlikely. The top priority of tuberculosis-control programs is still to identify and ensure the complete treatment of all patients with active tuberculosis.[23]

These suggested procedures apply to all domestic and foreign airlines. They were developed in the context of tuberculosis control in the United States, however, and may not be directly applicable to countries where strategies of tuberculosis prevention and control are different. The Global Tuberculosis Program of the World Health Organization, in collaboration with the CDC, has suggested these procedures to carriers that are not U.S.-based through the International Airline Transportation Association.

We are indebted to the staffs of more than 40 state and local health departments, the airline company, and the physicians of the exposed passengers and crew for their assistance and support in conducting the investigation; to the staffs of the tuberculosis-control programs of the states of Hawaii and Maryland for sharing information about the index patient and the results of contact investigations; and to the representatives of the Federal Aviation Administration, the Council of State and Territorial Epidemiologists, the Airline Transport Association, the National Tuberculosis Controllers Association, and the airline companies for their participation in the development of recommendations for notifying passengers and crew after possible exposure to tuberculosis on aircraft.

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