High Rate of Transmission of Tuberculosis in an Office: Impact of Delayed Diagnosis

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We identified two cases of tuberculosis (TB) in office co-workers in Melbourne, Victoria, Australia; the *Mycobacterium tuberculosis* isolates were found to be identical with use of restriction fragment length polymorphism. Contact tracing was performed for 195 of 210 workers by means of the tuberculin skin test. Risk of infection was assessed according to a number of variables. Office contacts were exposed to infectious TB for 4 months; at least 24% of employees were infected. There was an association between sitting in proximity to the case during the period of exposure (OR, 4.24; 95% CI, 1.06–19.67). On-site workers had a higher risk of being infected (OR, 5.48; CI, 1.51–23.54) than did visiting workers. Workers in this office were exposed to open pulmonary TB for prolonged periods. The prevalence of TB infection (24%) among these workers was high compared with the infection rate (2%–7%) in the general community. Delay in diagnosis was the major factor responsible for the spread of TB in this office.

We investigated an outbreak of tuberculosis (TB) in an office in Melbourne, Victoria, Australia. Outbreaks of TB typically occur in high-risk settings such as hospitals, prisons, and other institutions [1–5]. However, sporadic outbreaks have been described in other closed environments such as office buildings [6, 7], schools [8], and aircraft [9]. Although less common, these outbreaks are associated with infection rates of ≤40% [6–9] and emphasize the importance of contact screening in the workplace. When a case with infectious TB is notified, close contacts should be screened for evidence of infection. Close contacts comprise household contacts and immediate social and work contacts, all of whom are at the highest risk of acquiring infection with TB. The principle of contact screening is to first screen close contacts. Screening should be extended to more-remote contacts if the prevalence of infection among close contacts is higher than expected [10]. The tuberculin skin test (TST), despite its varying positive predictive value, is the best screening tool available for detecting asymptomatic infection with TB [11]. The aim of this study was to quantitate and describe transmission of TB infection within the office in question and to determine the relationship between the cases.

On 18 April 1993 the State Health Department of Victoria, Victoria, Australia, was notified of two cases of pulmonary TB in employees in a Melbourne office. The first case was diagnosed in January 1993. Routine contact tracing of domestic, social, and work contacts by the TB Unit of the Health Department was carried out. On 18 April 1993, a second case was diagnosed in a woman in another state who had worked at the same Melbourne office until 25 September 1992. Following notification of the second case, the members of the TB Unit returned to the office and conducted further screening of employees. We interviewed case 1, but case 2 refused to be interviewed. Her history was obtained from the physicians who treated her. Details of her symptomatic period, which may have occurred as early as September 1992, are therefore unclear.

Case Reports

Case 1. A 24-year-old Australian-born female employee was found to have pulmonary tuberculosis in January 1993. She had had a productive cough and night sweats and had noted weight loss since the end of September 1992. Despite multiple visits to her physician, the diagnosis was delayed. She was treated with several courses of erythromycin, amoxicillin, and inhalation high-dose corticosteroids. No chest radiograph or sputum examination was done until she consulted another physician in January 1993. She was infected with a fully drug-susceptible strain of *Mycobacterium tuberculosis;* a sputum smear was positive (3+) for acid-fast bacilli. Her chest radiograph showed a large right mid-zone cavity and widespread nodules.

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Informed consent was obtained in writing from all employees who were screened.

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Members of the TB Unit screened 21 household, work, and social contacts of case 1. All were screened with a chest radiograph, and 17 of 21 underwent a TST. Of these, 59% (10 of 17) were infected, and one contact converted from a negative reaction to a positive reaction (induration, 30 mm) during the test period.

Case 2. In April 1993, an Australian-born woman in another state who had been employed at the same office as case 1 until 25 September 1992 was found to have pulmonary TB. She had a 6- to 12-month history of cough and a positive TST reaction (induration, 13 mm), and a right upper-lobe cavity was apparent on a chest radiograph. She was not a close work contact of case 1 and was not screened during the initial contact screening.

Methods

Investigation of the outbreak. A TST (with use of the Mantoux method [11] and 10 TU of PPD) was performed on all available work contacts. Those with a positive reaction were screened with a chest radiograph. If TST reactions were negative at the initial screening in February 1993, a second TST was performed 3 months later. Negative reactions at first testing in April–May 1993 were not repeated, since 3 months had elapsed since the last exposure. We defined a case of infection with TB as an employee working at the office between September 1992 and January 1993 with any of the following characteristics: a TST reaction of $\geq$10 mm and no history of receiving a BCG vaccine; documented conversion from a negative to a positive TST reaction of $\geq$10 mm within 3 months of an initial negative test; or a TST reaction of $\geq$15 mm, regardless of the BCG vaccine history.

The Australian National Health and Medical Research Council recommends these cutoff points and used BCG status in the interpretation of the TST [12]. These criteria are used because universal BCG vaccination was performed in the State of Victoria until 1985, the prevalence of atypical mycobacterial infection in some states of Australia is high, and the TST is administered with use of 10 TU in Australia [12]. Nevertheless, analysis was also performed by using the lower cutoff points of 10 mm and 5 mm recommended by the Centers for Disease Control and Prevention [13]. The BCG vaccine history was ascertained from the employee's medical history and by examination of the employee's arms for a scar consistent with BCG vaccination.

In plotting TST reactions we used 3-point averages of PPD reaction values to minimize the effect of observer bias. The office space was a rectangle of ~2,000 m^2. We divided this space arbitrarily into four equal parts for the purpose of analysis: A, B, C, and D (from the front to the back of the office). During the period she was infectious, case 1 was seated in area A, at the front of the office. All employees who underwent a TST were also surveyed by questionnaire to ascertain demographic details, where they had worked within the office during the period of exposure, whether they had rotated to more than three sites during the same period, and other risk factors for TB.

Table 1. Demographic characteristics of office workers with tuberculosis in Melbourne, Victoria, Australia.

Characteristic	Percent with indicated characteristic
Male sex	53
Smoker	31
History of overseas travel	62
Testing for antibodies to HIV	19
Region of birth	
Australia and New Zealand	80
Europe	16
Asia	2
Middle East	2

NOTE. The mean age of the subjects was 33 years.

Restriction fragment length polymorphism typing and case investigations. Typing of specimens from the two clinical cases was done by restriction fragment length polymorphism (RFLP) with use of the probe pTBN12 [14] at the Victorian Mycobacteria Reference Laboratory at Fairfield Hospital for Infectious Diseases. This probe is used in preference to IS6110 because the latter has a lower sensitivity in distinguishing between common subtypes in Australia [14].

Results

The office is located in a western suburb of Melbourne. It has 210 employees; of these, 150 work on site permanently, and 60 work at other sites but visit the office for at least 1 day a week. We screened 195 of the 210 employees and read the TST in 189 of 195 cases.

Inspection of the work environment. The majority of on-site employees (85 of 150) are customer service representatives who work in a large, unpartitioned office area and answer telephone calls from customers. These employees rotate to different desks at regular intervals. Inspection of the office revealed that it is spacious and clean, with an air space of roughly 6,100 m^3. The office is air-conditioned with an air-cooled chiller-boiler system. There had been long-standing problems with air distribution and with maintenance of the system. The system was upgraded in April 1993 to make 10 air changes per hour.

Molecular typing of M. tuberculosis isolates. Typing by RFLP revealed that cases 1 and 2 were infected with an identical type, which has been designated by Fairfield Infectious Diseases Hospital as "147799."

Epidemiology. Demographic characteristics of the office workers are shown in table 1. The majority of employees (75%; 141 of 189) had received the BCG vaccine; 19% (36 of 189) had not received the vaccine, and 6% (12 of 189) were unsure

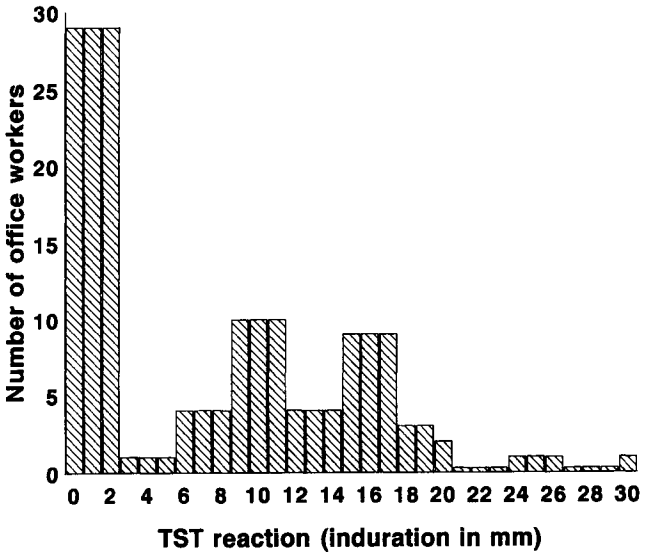

Figure 1. Distribution of tuberculin skin test reactions among Australian office workers in Melbourne, Victoria, based on a 3-point average.

of their BCG vaccine status. The distribution of TST reactions among the workers is shown in figure 1.

We found, based on Australian standards, that 46 (24%) of the 189 employees were infected [12]. Of these, one converted from a negative reaction to a positive reaction during the test period (he was among those initially screened on 9 February 1993 and again in April 1993), 36 had a history and/or evidence of BCG vaccination, five had no history and/or evidence of BCG vaccination, and five were unsure of their BCG vaccine status. Of the 46 infected employees, 45 had reactions of ⩾15 mm, including 16 who had reactions of ⩾20 mm. In addition, of the infected employees, 33 (72%) of 46 were born in Australia, 11 (24%) were born in Europe, one was born in Asia, and one was born in the Middle East. With use of different TST cutoff points, we found that 46% (87 of 189) had reactions of ⩾10 mm, and 54% (102 of 189) had reactions of ⩾5 mm.

Table 2 shows associations between certain factors and infection among the workers. Workers seated in areas A or B (the front half of the office) between September 1992 and January 1993 were significantly more likely to be infected than were workers seated in areas C or D (36% vs. 11%; OR, 4.24; 95% CI, 1.06–19.67; $P < .05$). The prevalence of infection among workers who rotated to three or more desks during the period of exposure was 38%, as opposed to 19% among workers who remained at the same desk during that period. This difference was not significant ($P = .2$). The prevalence of infection among Australian-born employees was 22%, and that among foreign-born employees was 35%. This difference was not significant ($P = .1$). The risk of infection was significantly higher for on-site workers than for visiting workers (OR = 5.48; 95% CI, 1.51–23.54). There was no significant association between infection and lunch place (in the staff canteen, at the desk, at the local cafés, or other sites), smoking (and smoking site), BCG vaccination, or a history of overseas travel. Radiographic screening was carried out for 48 employees, and no abnormalities were detected.

Discussion

Results of molecular typing of the isolates from the two cases described confirmed that they were infected with the same *M. tuberculosis* subtype. It is likely that the infections in these cases were directly related and that case 1 was the index case in the office. Because case 2 was reluctant to be interviewed, we cannot clearly ascertain whether or not she was symptomatic during her time at this office. It is possible (but less probable) that case 2 was the index case.

Case 1 had smear-positive pulmonary TB that remained undiagnosed for at least 4 months. This delay resulted in prolonged exposure of her co-workers, of whom at least 46 became infected with TB. The distribution of TST reactions in figure 1 is clearly bimodal, suggesting that the influence of BCG vaccination and infection with atypical mycobacteria (false positive reactions) was minimal. In a population with high exposure to BCG and other mycobacteria, the distribution of reactions would be more even, approaching a unimodal curve [11]. Our results support the use of a more sensitive cutoff point, such as 10 mm, when testing persons in Victoria. However, even a prevalence of 24% based on a 15-mm cutoff is higher than the expected baseline prevalence of infection, which should be between 1% and 4% in Australia. A TST survey of 8th graders in Sydney (New South Wales) revealed a prevalence of infection of 1.6% among Australian-born children and an unadjusted prevalence of 10% among the whole group [15]. In this study, however, probability sampling was not used, and the adjusted prevalence of infection may have been closer to 4% in that age group [16]. A study of Australian police recruits that was conducted between 1987 and 1990 showed a point prevalence of 7% TST reactivity [17]. Studies in the United States showed a point prevalence of 2.5% TST reactivity among young naval recruits in 1990; this prevalence varied from 26% among Asian-born recruits to 5.2% among

Table 2. Factors associated with TB infection among workers in an office in Melbourne (Victoria, Australia), 1992–1993.

Factor	OR	95% CI	*P* value
Seating in area A or B	4.24	1.06–19.67	<.05
Rotation to three or more desks	1.85	0.68–5.01	.2
Foreign born	1.95	0.84–4.54	.1
History of overseas travel	1.22	0.48–3.15	.05
Smoking	0.72	0.26–1.58	.6
History of BCG vaccination	2.10	0.70–6.69	.2
Working on site	5.48	1.51–23.54	.005

black recruits and 0.8% among white recruits [18]. These data show that the prevalence of TB infection in a developed-world setting with a largely Caucasian population is low. In view of this finding, the prevalence of infection in the office population under study was much higher than can be explained by incidental (remote) infection. Studies of infection rates among household contacts of infectious cases of TB have reported rates of ~21% [19], which is similar to the infection rate among the workers in this office; this highlights the importance of the workplace (which is often overlooked) as a site of transmission of TB and the need to screen the work contacts of cases of infectious TB. A worker may spend at least half of his or her waking hours in the workplace, making this as important a site as is the home.

In retrospect, members of the TB Unit should have expanded the extent of their contact survey in January 1993. Of the initial contacts of case 1 who were screened with a TST in January 1993, nearly 60% (10 of 17) were infected. This is higher than the expected 21% rate of infection and therefore is an indication of the need to expand the contact survey.

Direct spread was the most important route of transmission in this outbreak, as evidenced by the association with proximity to case 1. Other studies have implicated air conditioning in the transmission of TB in a closed environment [20], but there was no evidence of such transmission in this study. We did not find associations with known community risk factors such as birth in a country with a high prevalence of TB, which emphasizes that the pattern of association we found is unusual and consistent with transmission within the office. The fact that there was no significant difference between the prevalence of infection among Australian-born and foreign-born workers is further evidence that the infections occurred at the workplace. If these had been community-acquired infections, we would expect a significantly higher prevalence of infection among foreign-born workers [21].

The major factor associated with the spread of infection, however, was the delay in diagnosis of the first case, which resulted in inadvertent spread over several months. In particular, smear-positive cases of pulmonary TB (as was case 1) are associated with increased risk of infection in contacts [22]. Case 1, who acted responsibly and had sought medical attention on several occasions, had the typical clinical presentation of pulmonary TB, yet a chest radiograph and sputum examination were not performed until she had been symptomatic for at least 4 months. Awareness on the part of her treating physician and prompt diagnosis would have reduced the risk of transmission of TB. An important but often underplayed element of TB control is early diagnosis of the disease. In a study of delay in the diagnosis of TB, it was found that only 31% of patients with TB received treatment within 1 month of the onset of symptoms [Pirkis JE, Speed BR, Dunt DR, Yung A, MacIntyre CR, Plant AJ, submitted for publication]. Results of studies that have attempted to quantify patient and physician delay have varied—one study found that the duration of physician delay was significantly longer than that of patient delay (5 weeks vs. 4.3 weeks) [24], while another found that patient delay was longer [25]. In the United States, >5% of cases of TB are diagnosed after death [26]. Regardless of the cause, delay in initiation of treatment does occur and must be acknowledged, since this is the first possible point at which transmission of TB can be prevented. The education of medical practitioners, whose aim is the raising of awareness about the possibility of TB, should be a part of TB control programs. Specifics regarding public health programs for the control and prevention of infectious diseases such as TB should also be an integral part of undergraduate medical education.

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