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Occupational Risk of *Mycobacterium tuberculosis* Infection in Hospital Workers

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We conducted a 4-year (1/89–12/92) retrospective cohort study among employees at a large metropolitan hospital where a nosocomial outbreak of multidrug-resistant tuberculosis (TB) had occurred. We compared the risk of tuberculin skin test (TST) conversion among employees who worked on wards where patients with culture-confirmed TB were cared for ("exposed") with the risk among employees who worked on wards with no such patients ("unexposed"). Exposed employees had a higher 4-year risk of TST conversion (14.5%) than unexposed employees (1.4%) (adjusted relative risk 13.4; 95 percent confidence interval 5.1–35.2). Exposed employees had significantly higher risks of conversion than unexposed employees during 1989–91, but not for 1992. Among the exposed, ward clerks had a risk of conversion (15.6%) only slightly lower than nurses (18.2%). We conclude that employees who worked in areas where patients with active M. tuberculosis *infection were cared for, including workers who did not provide direct patient care, had a higher risk of TST conversion than employees who did not work in these areas. Reasons for the decline in risk over time include outbreak termination, fewer admissions of patients with TB, implementation of effective infection control measures, and possible resistance to infection in some members of the study population.* Am. J. Ind. Med. 32:528–534, 1997. *© 1997 Wiley-Liss, Inc.*

KEY WORDS: tuberculosis; occupational exposure; hospital workers; nosocomial transmission; infection control measures; tuberculin skin test

INTRODUCTION

The well-documented resurgence of tuberculosis (TB) in the United States [Rieder et al., 1989; MMWR, 1991, 1992; Barnes et al., 1993] has important implications for hospital employees caring for patients infected with *Mycobacterium tuberculosis*. The appearance of multidrug-resistance (MDR) strains of *M. tuberculosis* increases the need for primary prevention of infection as chemoprophylaxis against, and successful treatment of, active disease becomes more difficult. A review of reported occupationally acquired cases of active TB among health care workers (HCWs) identified five deaths due to this disease [Bowden et al., 1994].

Defining those at highest risk and devising means of protection against TB infection have become priorities for hospital infection control personnel and other public health professionals. Risks associated with caring for patients with TB have been reported for decades but, as a recent review of TB risk among health care workers points out, there have been no published cohort studies that have included an internal nonexposed control group and that have controlled for non-occupational, socio-economic risk factors [Menzies

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et al., 1995]. Further, much of the literature has focused on risks to physicians, nurses, technicians, and others with close patient contact. Several studies have included small numbers of ward clerks and others who do not have close patient contact, but these have typically been in the setting of a TB outbreak or in the presence of a particularly infectious patient [Ehrenkranz et al., 1972; Beck-Sagué et al., 1992; Catanzaro, 1982]. Such studies focus on contact investigation for the purpose of tracking outbreaks of disease. These studies have the advantage of clearly defining the exposure and of rapidly identifying potentially infected individuals so that they can be appropriately treated. However, multiple contact studies may be impractical in large institutions that have large numbers of active cases, each infectious for an unknown period of time prior to diagnosis. Furthermore, they cannot be used to study entire occupational groups potentially at risk. In addition, contact studies are usually cross-sectional studies of prevalence, and they often lack a group of nonexposed individuals to compare with the exposed.

Conversely, population-based studies such as ours have the advantage of including the entire population potentially at risk, and of considering as potential sources of infection all active cases among patients during a specified time period. Prospective studies of this nature permit the calculation of incidence rates, rate ratios and attributable risks. They may also reveal previously unknown associations between certain occupations and risk of infection. These findings can lead to interventions to prevent exposures in groups that might not have been considered in a contact investigation.

In this study, we examined the risk of infection with *M. tuberculosis* from 1989–1992 among a variety of hospital workers at a large, urban teaching hospital by comparing the risks of tuberculin skin test (TST) conversions among those who worked on wards with patients with culture-confirmed TB and those who did not. Although the study was initiated in response to a hospital outbreak of multidrug-resistant TB (MDR-TB) among patients on the HIV ward, the follow-up period extended well beyond the termination of this outbreak.

BACKGROUND

In April 1991, the National Institute for Occupational Safety and Health (NIOSH) received a request to investigate the risk of nosocomial transmission of TB among employees at a large, urban teaching hospital. This request was prompted by employees' concern that they were at an increased risk for TB infection due to an outbreak of TB in patients.

The hospital is a 1,500-bed facility that employs about 7,000 persons, including approximately 450 house staff. From October 1989 through September 1990, more than 66,000 inpatients were discharged; more than 300,000 patients were examined in the clinics; and approximately 108,000 persons were seen in the Emergency Care Center.

The numbers of patients hospitalized with TB during each year of our study period (January 1, 1989 through December 31, 1992) were 338 (18 MDR-TB), 339 (44 MDR-TB), 200 (10 MDR-TB), and 197 (9 MDR-TB), respectively. A nosocomial outbreak of MDR-TB occurred in patients on the Human Immunodeficiency Virus (HIV) ward between March 1988 and September 1990 [Beck-Sagué, 1992]. Hospital personnel recognized the outbreak in February, 1990 and began implementing new TB infection control measures throughout the hospital. These were incorporated to varying extents during our study period (Fig. 1). A more detailed description of the environmental control measures can be found in the NIOSH Health Hazard Evaluation report No. 91-0187-2544.

METHODS

Hospital management provided a copy of the microbiology laboratory's computer file of positive *M. tuberculosis* cultures for January 1988 through December 1989. In order to limit the study to personnel with exposures to patients with the highest infectious potential, we considered only those cultures that came from a pulmonary or laryngeal site. Thirty-seven wards had submitted at least one such culture during 1988–89. We chose to focus our study on wards that had submitted 15 or more of these cultures during this two-year period in order to maximize the potential for employee exposure. These ''exposed'' wards included the Medical Intensive Care Unit (18 cultures), five Medicine wards (32, 45, 108, 115, and 121 cultures, respectively), and the Emergency department (108 cultures).

For each of the above inpatient wards, the possibility existed that patients with cultures positive for *M. tuberculosis* may have been moved to another ward for treatment after their cultures were submitted. Therefore, a random sample of these patients' records was examined to confirm, with 95% confidence, that the patients were treated on the ward from which their cultures were sent. All the inpatient wards met this criterion.

Wards with no positive cultures during 1988–1989 were considered ''nonexposed.'' All the nonexposed wards whose employees had age and race characteristics similar to employees from the exposed wards were chosen for the study. These wards included Post Partum, Labor and Delivery, Newborn Intensive Care Unit, Newborn Intermediate Care Unit, and Well Newborn.

Persons eligible for inclusion in the study were those full-time employees listed in the computerized hospital payroll database as either working on one of the exposed or unexposed wards at the time the wards were being chosen (May 31, 1991), or whose job had been terminated while

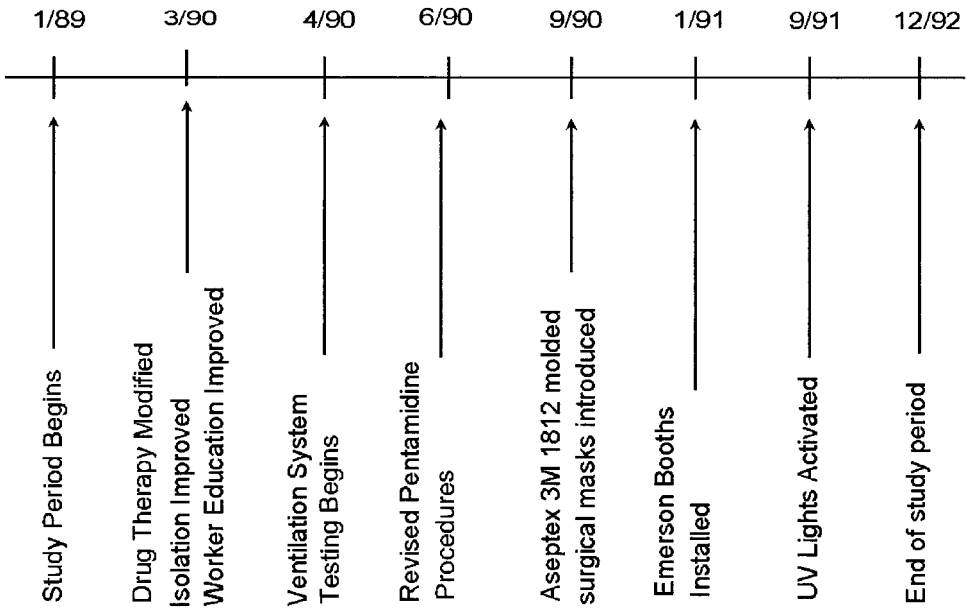

FIGURE 1. Time line of TB control measures implemented during study period at the study hospital, January 1989–December 1992.

working on one of those wards any time between January 1, 1989 and May 31, 1991.

We followed this cohort of employees through December 1992 to assess the risks of TST conversion over time during the changing conditions at the hospital, including the termination of the outbreak of MDR-TB and implementation of TB infection control measures. The microbiology laboratory culture data for 1990–1992 showed that the exposed wards continued to submit cultures positive for *M. tuberculosis,* and the nonexposed wards submitted no cultures positive for *M. tuberculosis* through 1992.

TSTs were administered, evaluated, and recorded in the employee's health record by the hospital's Employee Health Office staff. A TST result was recorded as positive if there was a reaction at 48–72 hr of ≥10 mm to a Mantoux skin test using 5 tuberculin units of purified protein derivative (PPD) tuberculin. At the time of our study, the hospital did not keep track of whether Aplisol® or Tubersol® was used. Positive results were verified by one of the Employee Health Office staff. A TST result was recorded as negative for any observed reaction of less than 10 mm; however, size of reactions less than 10 mm was not recorded. In addition, employees were instructed as to the signs of a positive test and, because Health Office staff resources were limited, were told that they needn't return if there was no reaction. Skin tests were therefore also recorded as negative in the health record for those who did not return for TST assessment within 48–72 hr.

Skin testing was performed approximately once every 4 months on employees on the exposed wards, and once per year on employees on the unexposed wards. During our study period, the hospital changed its policy for workers who had received bacillus Calmette-Guérin (BCG) vaccine. Before fall 1990, TSTs were not given to BCG vaccine recipients; after that, they were given only if at least seven years had elapsed since the last BCG vaccination.

We defined a TST converter as any person whose employee health record documented a positive TST result and a previous negative TST result during the study period. Since conversion could have occurred any time between the positive and prior negative TST, a random date between the negative and positive result dates was assigned using a computerized random-date generator with all dates during the period having an equal probability of selection. This random date was used as the date of conversion for our analyses.

Characteristics of the study population, including age, race, gender, and hourly wage, were obtained from the hospital's computerized personnel records. Work histories from the personnel department were directly reviewed to determine the time period of employment at the hospital, the ward(s) on which employees worked during the study period, and the employee's job title.

STATISTICS

Unadjusted relative risks of TST conversion and chi-square statistics were computed based on simple two-by-two contingency tables [Dean et al., 1990]. Multivariate analysis of the risk of conversion of the TST from a negative to a positive result was performed using stepwise logistic regression with a p-value of 0.10 as the inclusion criterion [SAS,

1988]. This analysis tested the effect of exposure on the risk of conversion, with adjustment for age, race, gender, and salary. Gender was the only covariate that remained in the model with exposure. The population attributable risk was calculated using the method of Kleinbaum et al. [1992]. Person-time analyses were also conducted. However, rates and rate ratios obtained from these analyses were virtually identical to risks and relative risks, and are not presented.

RESULTS

There were 1,371 employees listed in the hospital's payroll database as having worked on one of the wards chosen for the study. Of these, 590 worked exclusively on exposed wards, and 704 worked exclusively on unexposed wards during the study period; these employees did not move between wards within their exposure category. Seventy-seven employees who worked on both exposed and unexposed wards were excluded from the study.

We excluded 132 (22.4%) of the 590 exposed employees because they had a positive TST prior to the beginning of the study period or at the time they were hired, if hired during the study period. We also excluded 69 employees (11.7%) for whom we were unable to obtain a detailed work history and 140 people (23.7%) who had received BCG vaccination. The remaining 249 exposed workers were included in the data analysis.

We excluded 130 (18.5%) of the 704 unexposed employees because they were TST positive at entry, 82 (11.7%) for whom there was no work history available, and 137 (19.5%) because they had received vaccination with BCG. The remaining 355 unexposed employees were included in the data analysis.

When we examined the demographic and other characteristics of exposed and unexposed employees, there were significantly fewer females and significantly more whites (than nonwhites) in the exposed group (Table I). Although hospital personnel recorded the TST as negative if individuals did not return to the Employee Health Office for evaluation, the proportion of employees with an evaluated PPD reaction was similar in the exposed and unexposed employees; the characteristic "PPD Read" in Table I refers to this variable.

The cumulative incidence of TST conversion was significantly higher in the exposed than in the unexposed group (36/249 [14.5%] vs. 5/355 [1.4%], relative risk, 10.3; 95% CI = 4.1–25.8). After adjustment for age, race, gender, and salary, the relative risk was 13.4 (95% CI = 5.1–35.2). If we excluded employees who worked on the MDR-TB outbreak ward, the cumulative incidence of TST conversion remained significantly higher in the exposed group (31/232 [13.4%] vs. 5/355 [1.4%], relative risk, 9.6; 95% CI = 3.8–24.4). In this study population, the risk of conversion attributable to occupational exposure was 83%. The population attributable risk (or etiologic fraction) is p(RR-1)/[p(RR-1) + 1]. For "p" we used 249/604 (41%), which was the percentage exposed in our study population. This therefore reflects the attributable risk in our study population. Alternatively, if 20% of the entire hospital staff were exposed, the attributable risk for the hospital staff would be 71%, based on our RR of 13.4.

Table II shows annual risks and relative risks for TST conversion. The relative risk was undefined in 1992 because there were no conversions in the unexposed group during that year.

Table III shows the risk of TST conversion for nurses and ward clerks. The majority (32/36 [89%]) of the converters in our study were employed in one of these job categories. The other four converters were emergency department technicians. They are not included in Table III because they worked only in the emergency department;

TABLE I. Characteristics of the Exposed and Unexposed Employees at Study Hospital, January 1989–December 1992

Characteristic	Exposed (n = 249)	Unexposed (n = 355)
Female (%)[a]	79.5	94.7
Mean age ± SD	37.3 ± 8.7	40.5 ± 9.7
Ethnicity		
White (%)[a]	43.4	35.5
Black (%)	36.1	47.9
Other (%)	20.5	16.6
Mean wage ± SD	14.0 ± 5.0	14.9 ± 5.3
PPD read (%)	41.2	45.9

[a]$P < 0.05$.

TABLE II. Secular Trend in Health Care Worker Rate of Tuberculin Skin Test Conversion at Study Hospital, January 1989–December 1992

Year	Exposed	Unexposed	Relative risk	95% CI
1989	6.2 (13/209)	0.6 (2/324)	10.1	2.3–44.2
1990	7.5 (16/212)	0.7 (2/309)	11.7	2.7–50.2
1991	3.2 (6/189)	0.4 (1/282)	9	1.1–73.8
1992	0.6 (1/158)	0 (0/251)	Undefined	Undefined

TABLE III. Rate of Tuberculin Skin Test Conversion by Job Title in Study Hospital, January 1989–December 1992

Job title	Exposed	Unexposed	Relative risk	95% CI	*P*
Nurse	18.2 (27/148)	1.5 (4/269)	12.3	4.4–34.4	<0.001
Ward clerk	15.6 (5/32)	0 (0/39)	Undefined	Undefined	<0.02[a]

[a]Fisher's exact test.

TABLE IV. Rate of Tuberculin Skin Test Conversion for the Exposed Workers by Job Title and Hospital Location at Study Hospital, January 1989–December 1992

Job title	Medicine ward	Emergency department	Medical intensive care unit
Nurse	32.7 (17/52)	8.3 (5/60)	13.9 (5/36)
Ward clerk	7.7 (1/13)	22.2 (4/18)	0 (0/1)

therefore, there were no employees with the same job title on other wards with whom their risk could be compared.

Table IV shows the risks of TST conversion for nurses and ward clerks according to the ward on which they were employed during the study. We found that, in the emergency department, ward clerks were nearly three times more likely to convert their TST than were nurses.

DISCUSSION

Our data show that nurses and ward clerks who worked in areas where patients with culture-positive TB were cared for had a significantly greater risk of becoming infected with *M. tuberculosis* than were nurses and ward clerks who worked in areas where there were no such patients. Prior studies have shown that workers who provide direct patient care were at greater risk for infection than workers who did not provide direct patient care [Mikol et al., 1952]. The high risk in ward clerks in our study is particularly disturbing, as these workers are not involved in direct patient care.

In the emergency department, the risk of TST conversion for the ward clerks was almost three times higher than for the nurses. Ward clerks in the emergency department are responsible for clerical processing of patients after triage, handling specimens for the laboratory, and gathering clothing and valuables from admitted patients. During these interactions, there may have been less strict adherence to infection control measures (such as wearing a mask) than during typical interactions between nurses and patients.

The decrease in TST conversions over time in the exposed group is encouraging. Several factors may have contributed to this decrease. First, since an outbreak of MDR-TB occurred among hospital patients during the first two years of our study period, the decrease in risk of TST conversion could be due in part to the termination of this outbreak. In addition, the total number of TB patients decreased over the course of our study period and this also could have contributed to the decline in TST conversions.

A second factor that may have contributed to the decrease in TST conversion risks in the exposed group is the implementation of tuberculosis infection control measures by the hospital over the course of our study period. Our study was not designed to test the specific impact of individual control measures. Discussion continues regarding the effectiveness of various control measures available to hospitals to reduce transmission of TB, including general ventilation, directional air flow, air filtration, ultraviolet air disinfection, patient isolation, and personal respiratory protection for staff. To date, studies demonstrating a decrease in risk of infection coincident with institution of control measures have been unable to separate the effect of the control measures from the effects of other factors, such as changes in the number and infectiousness of TB patients. The Centers for Disease Control and Prevention (CDC) is currently funding several studies designed in part to investigate these issues.

A third factor that may have contributed to the reduction in TST conversion risks may be natural immunity to TB infection in some of the individuals in our cohort. Several studies suggest that genetic factors may play a role in resistance to mycobacteria [Lurie, 1964; O'Brien, 1991; Comstock, 1978; Schurr et al., 1991; Radzioch et al., 1991; Malo et al., 1991]. Some of the employees in our cohort may have had a greater resistance to infection with *M. tuberculosis* than others. Those with a lower resistance may have become infected sooner and then dropped out of the pool of people eligible for infection. A less susceptible group of people would have remained, resulting in a decreasing risk of conversion.

Our study has a number of limitations. First, several characteristics of the TST program in place at the hospital during our study period did not meet current CDC recommendations [MMWR, 1994]. For example, two-step testing was not used and the size of *negative* TSTs was not recorded, so the issue of the ''booster'' phenomenon could not be addressed [Thompson et al. 1979]. In addition, the hospital's definition of a positive TST (any reaction of 10 mm or greater) differed from the current CDC guidelines which recommend that only specific *increases* in induration (the magnitude of which depends on a variety of risk factors) be considered evidence of a newly-acquired infection with *M. tuberculosis* [MMWR 1994]. However, a chi-square analysis of only the TSTs 20 mm or larger (which would eliminate the TSTs that exhibited less than a 10 mm increase) revealed that the relative risk of a positive TST was still significantly greater in the exposed than the unexposed workers (relative risk 13.5; 95 percent confidence interval, 3.2 to 57.6). Figure 2 shows the size distribution for the positive TSTs.

A second limitation is that many employees did not have their TST evaluated by a trained individual, and we included these unevaluated TSTs as negative in our analyses. If some of these employees had positive TSTs, then our results could have underestimated the TST conversion risks, in either or both groups.

A third limitation of our study is that TST data were not available for house staff or for recipients of BCG vaccine.

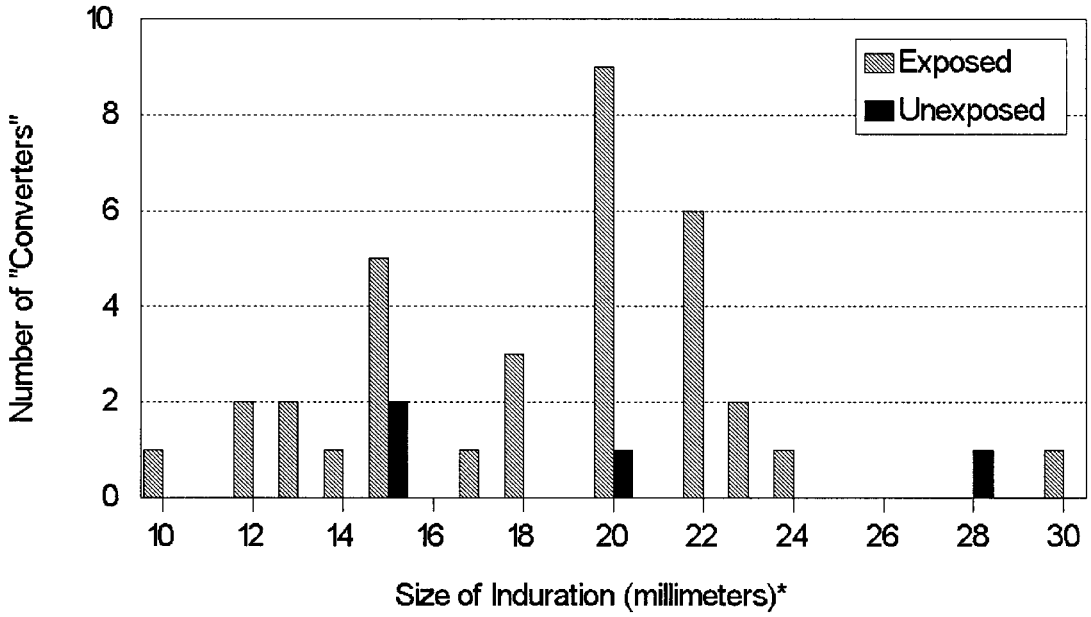

FIGURE 2. Size of tuberculin skin test reactions in ''Converters'' at the study hospital, January 1989–December 1992. *Size results missing for 2 exposed and 1 unexposed.

Therefore, our results do not provide information regarding the occupational risk in these groups. The CDC recommends tuberculin skin testing of all health-care facility personnel, including those with a history of BCG vaccination [MMWR, 1994]. As these recommendations are adopted, data on conversion risks in groups such as those missing from our study should become available. Data were also not available for respiratory therapists, bronchoscopists and employees working in autopsy areas because these occupations were not represented in the exposed or unexposed wards chosen for our study. Future studies should try to incorporate these potentially exposed groups.

A fourth limitation involves quantifying exposure. The number of positive *M. tuberculosis* cultures submitted from each ward only reflects potential for exposure. It is limited in representing actual exposure since risk of infection with *M. tuberculosis* is thought to be related, at least in part, to the concentration of airborne organisms and to the duration of exposure [Nardell, 1993]. In addition, the number of positive cultures does not necessarily reflect the number of patients with *M. tuberculosis*, since more than one culture may have been submitted for each patient. More accurate measures of airborne tubercle bacilli are needed in order for exposure to be defined more reliably. NIOSH is currently developing an air sampling method for *M. tuberculosis.*

Our study's demonstration of a high risk for *M. tuberculosis* infection among workers with and without close patient contact has important implications for the development and implementation of strategies to prevent occupational transmission of TB. Effective TB transmission control is needed not only in areas of hospitals where direct patient care is taking place, but in all areas where employees may be exposed to infectious individuals. The results of our study also emphasize the importance of including all workers in TST programs, not just those providing direct patient care. In all areas in which there is potential for exposure, ongoing evaluation of the effectiveness of various environmental and administrative control measures, as well as the use of personal protective equipment, should be undertaken as recommended in the CDC Guidelines [MMWR, 1994].

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