Healthcare workers with tuberculosis infected during work

G. de Vries^{*,#}, M.M.G.G. Šebek[†] and C.S.B. Lambregts-van Weezenbeek[†]

ABSTRACT: The risk for healthcare workers (HCWs) of tuberculosis (TB) attributable to occupational exposure is difficult to determine, as are the conditions contributing to this risk. The objective of the present study was to determine which TB cases among HCWs in the Netherlands were infected during work and to analyse factors which contributed to infection and subsequent disease.

The total study population consisted of 101 cases over a 5-yr period. In 67 (66%) subjects the route of infection could be determined by epidemiological and microbiological information. Of these cases, 28 out of 67 (42%) were due to infection at work, 19 (28%) were community acquired, and 20 (30%) were infected abroad.

The 28 cases infected at work were subject to an in-depth analysis. Delayed diagnosis of the index case, especially in the elderly patient, was the main cause of patient-to-HCW transmission. In some circumstances, inadequate infection-control measures also contributed to transmission.

In conclusion, a high suspicion of tuberculosis by the clinician, adequate infection control measures by hospital authorities, and early identification of latent tuberculosis infection by occupational and public-health specialists are necessary to prevent tuberculosis among healthcare workers.

KEYWORDS: DNA fingerprinting, epidemiology, nosocomial transmission, tuberculosis

Healthcare workers (HCWs) are at risk of nosocomial infection with *Mycobacterium tuberculosis* [1]. This risk was high in the pre-chemotherapy era, but declined rapidly after the introduction of effective treatment, which reduced the infectious period of tuberculosis (TB) patients, as well as the absolute number of TB patients in many countries [2]. Along with the declining risk, the attention for infection-control practices in hospitals has lessened [2]. Recognition of nosocomial transmission as a public-health issue was renewed when extensive HIV-related transmission of multidrug-resistant TB occurred in New York City hospitals (NY, USA), which also affected HCWs, some with fatal outcomes [3–5].

Several research methods, such as cohort studies and case-control studies, have been applied to study and estimate the extent of work-related TB among HCWs [2, 6–8]. These studies have methodological limitations in determining the excess risk for HCWs and the importance of conditions of exposure leading to this risk [7, 8]. Cohort studies and case-control studies are often unable to differentiate between occupational and nonoccupational risk, while outbreak reports may describe extraordinary situations with a

high number of infecting inocula, particular virulent strains or HIV comorbidity, making it difficult to extrapolate such results to nonoutbreak conditions [4, 6, 7, 9].

In the Netherlands, all TB cases are reported to the Netherlands Tuberculosis Register (NTR), which also includes information on risk-group status [10]. One of the variables within the register is “working in the healthcare/social-welfare sector”. Every year, on average 20–30 HCWs out of 1,500 cases are reported with TB. The objective of the present study was to determine which cases were really infected during healthcare work in the Netherlands and to analyse factors which contributed to infection and subsequent disease.

METHODS

The current study cohort comprised of all consecutive TB patients registered in the Netherlands during the period of January 1, 1995 to December 31, 1999, who were classified as “working in the healthcare/social-welfare sector”. After approval by the ethical committee of the NTR, all 37 Depts of Tuberculosis Control of the Municipal Health Services (MHSs) responsible for notification of the cases were identified

AFFILIATIONS

*Dept of Tuberculosis Control, Municipal Public Health Service, and #Dept of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, and †KNCV Tuberculosis Foundation, The Hague, The Netherlands.

CORRESPONDENCE

G. de Vries
Dept of Tuberculosis Control
Municipal Public Health Service
P.O. Box 70032
3000 LP Rotterdam
The Netherlands
Fax: 31 104339950
E-mail: devriesg@ggd.rotterdam.nl

Received:

March 21 2006

Accepted after revision:

June 14 2006

SUPPORT STATEMENT

The authors of the present study received no financial support and there is no conflict of interest to report.

and asked for their collaboration. This essentially meant that nurses who were involved in patient management and contact investigations related to these patients were interviewed to answer three basic questions as follows. 1) Was the patient really a HCW before or at the time of diagnosis? 2) What kind of work was the HCW involved in at the time of diagnosis or before diagnosis? 3) Does epidemiological or molecular information exist to prove or exclude infection during work in the Netherlands? Cases were excluded if the patient was not a HCW or the diagnosis of TB was withdrawn after notification.

Since 1993, all *M. tuberculosis* isolates in the Netherlands are subject to standardised insertion sequence (IS) 6110-based restriction fragment length polymorphism (RFLP) typing, so-called DNA fingerprinting [11]. Clusters are defined as groups of patients having isolates with fully identical RFLP patterns or, if strains harbour less than five IS6110 copies, with identical sub-typing by use of the polymorphic GC-rich sequence probe [12]. The fingerprints of all culture-confirmed cases in the cohort were cross-checked with the National DNA fingerprint database.

With the information from the interviews, the NTR and DNA fingerprints, patients were classified into four categories as follows. Category 1: HCW infected during healthcare work in the Netherlands. Cases were included if an epidemiological nosocomial link was confirmed by matching DNA fingerprints, or TB was diagnosed during a contact investigation carried out at the workplace, or a well-documented epidemiological link was present without bacteriological confirmation of the diagnosis in the HCW. Category 2: HCW infected in the community. These cases had either matching DNA fingerprints with a close contact in the community or, if culture negative, were considered infected in the community based on convincing epidemiological evidence, such as contact investigation among household contacts and friends. Category 3: HCW infected abroad. This category includes Dutch HCWs who worked for a long period in a hospital within a TB-endemic country, as well as foreign-born HCWs. Classification was also based on tuberculin skin test (TST) conversion after leaving the Netherlands and on DNA fingerprints (e.g. a unique fingerprint). Category 4: HCW place of infection unknown, including the remaining cases which could not be classified into one of the above categories.

Cases belonging to category one were investigated in more detail by contacting the TB departments of the MHSs and other health institutions involved. Patient and disease characteristics of both the HCW and the index case were obtained from patient records. In addition, information was collected about the circumstances under which transmission occurred. The results were discussed with involved professionals working in these settings. The study design did not allow for collection of standardised information about the airflow (ventilation) in relevant rooms.

RESULTS

In the 5-yr study period, 123 patients were recorded as working in the healthcare/social-welfare sector. Eight cases were misclassified as having TB, seven had a latent TB infection and one case had disease caused by *M. avium*. Another 21 cases were workers/volunteers involved in the social services in asylum seekers centres, penitentiary institutions and homeless centres who did not have a HCW status. In total, these 29 (24%) cases were excluded from the analysis, leaving a total of 94 eligible HCWs with active TB. However, during the field research, seven additional cases were identified, which were not (yet) included in the present study. The box on the registration form was either not ticked or information was wrongly copied into the national TB register. These cases were included in the current study, giving a total study population of 101 HCWs.

The incidence of TB among HCWs was calculated for hospital workers involved in patient care, since they are at greatest risk for nosocomial infection and their denominator can be more accurately determined. In 1997, 126,500 persons were involved in patient care in Dutch hospitals [13]. During the 5-yr study period, 50 cases were hospital-employed HCWs involved in patient care, resulting in a TB incidence of 7.9 per 100,000 per annum. The other 51 cases were employed in nursing homes, home-care organisations or were general practitioners, physiotherapists, student doctors or not employed in the healthcare setting at the time of diagnosis.

Table 1 shows the classification of the cases in the four categories. Of the 47 cases infected in the Netherlands, 28 were work-related (category one) and 19 community acquired (category two). The attributable risk (AR) of healthcare work in the Netherlands can be derived directly by dividing the

TABLE 1 Classification of healthcare workers with tuberculosis (TB) in all four categories according to information from interviews, the Netherlands TB Register and DNA fingerprints 1995–1999

	Category 1	Category 2	Category 3	Category 4	Total
Cases n	28	19	20	34	101
Born in the Netherlands	28 (100)	15 (79)	11 (55)	27 (79)	81 (80)
Age yrs	30 (21–65)	30 (21–56)	33 (24–87)	37 (17–84)	33 (17–87)
Pulmonary TB	13 (46)	13 (68)	16 (80)	28 (82)	70 (69)
Bacteriological confirmation	18 (64)	14 (74)	10 (50)	8 (24)	50 (50)
Clustered cases	16 (89)	13 (93)	1 (10)	5 (63)	35 (70)

Data are presented as n (%) and median (range), unless otherwise stated.

number of cases in category one by all cases infected in the Netherlands (categories one and two) and is 0.6 (28 out of 47). The relative risk (RR) for healthcare work in the Netherlands can be calculated by $AR = (1 - 1/RR)$ and is 2.47.

Of the 11 HCWs infected abroad (category three) and born in the Netherlands, all but one case was involved in patient care in developing countries, often for many years. One Dutch HCW had a negative TST when leaving the Netherlands to work in a refugee camp in Kenya and on returning the TST was 6 mm. No treatment for latent TB infection was prescribed in accordance with Dutch guidelines. The patient developed pleural TB within 1 yr of returning, with a *M. tuberculosis* strain identical to a strain prevalent among Somali TB patients in the Netherlands.

In-depth investigation focused on the 28 cases infected during work in the Netherlands. Among them, 16 cases were classified based on both an epidemiological link and a matching DNA fingerprint, two cases had an epidemiological link and a unique fingerprint which could be explained (see below), eight cases had culture-negative TB diagnosed in a contact investigation at work, and two HCWs with culture-negative TB had a well-documented contact in the hospital, but were diagnosed after they reported with symptoms. However, five cases were excluded from analysis below since they had no identified patient contact: two HCWs were infected by a regular visitor of the hospital; two HCWs by another HCW; and one laboratory assistant developed cutaneous TB with a unique fingerprint after injuring herself with a needle in a laboratory.

Characteristics of HCWs and index patients

The median (range) age of the HCWs was 28 (21–65) yrs with the majority being female (18 out of 23). The following professions were involved: nurses (n=14); doctors (n=4); ward assistants (n=2); bronchoscopy assistants (n=2); and an assistant of an outpatient department (n=1). In total, 21 were infected in the hospital and two outside the hospital. The hospital workers were deployed at the following departments: a pulmonology ward (n=9); an internal medicine (including AIDS) department (n=5); a bronchoscopy unit (n=2); an outpatient department (n=2); and at other wards (n=3). In total, 10 cases had pulmonary TB (among them two cases were smear positive), 12 had pleural TB and one had TB of the skin. None of the cases reported a previous history of TB. There were no HCWs with HIV co-infection. However, as the HCWs were not systematically tested for HIV, this information is incomplete. All isolates were drug susceptible and all 23 HCWs completed treatment.

In 21 out of the 23 patients, the infection could be attributed to a specific index case, while in two cases only incomplete information of the presumed index patient could be obtained. Of the known sources, 16 index patients each caused one secondary case among HCWs, one index case was the source of two secondary cases and one index case caused three secondary cases among HCWs. Almost all index patients had smear-positive pulmonary TB, except for two cases: one with disseminated TB with chest radiography abnormalities, a negative sputum culture and a positive stool culture for *M. tuberculosis*; and one case with a TB abscess of the knee joint that was surgically managed and drained. The median (range)

age of the index patients was 45 (25–87) yrs, with 44% of the index patients (eight out of 18) aged >60 yrs. Two index cases were HIV infected.

Interval between infection and diagnosis of TB in HCW

The date of infection was determined as the date of admission of the index case to the hospital or, for nonhospitalised patients, the date of first contact with the HCW. The date of TB diagnosis of the HCW was the date of admission to the hospital, or for nonhospitalised HCWs, the date of specimen collection for TB examination or the first date of presenting with symptoms at a health post. For two HCWs, both infected by the same index patient, the interval could not be determined because the index patient was undiagnosed for a long time, probably >1 yr. One of these HCWs even developed pleural TB 4 months before the index patient was diagnosed.

The interval between infection and disease of TB cases among HCWs is presented in figure 1. The median interval was 32 weeks for all 21 secondary cases and 34 weeks for the 13 culture-confirmed secondary cases. The factors that contributed to infection are summarised in table 2. In 10 index cases, mostly elderly patients with comorbidity, TB was initially not suspected and, thus, adequate isolation was delayed. This diagnostic delay was the main cause of patient-to-HCW transmission, while in some circumstances inadequate isolation measures contributed to infection.

Screening for TB or latent TB infection

Eight HCWs were diagnosed with TB in a contact investigation or pre-employment screening. Three HCWs developed TB despite treatment for latent TB infection (LTBI) with 6 months isoniazid (one was diagnosed later in a pre-employment screening). In three HCWs, LTBI was missed due to a false-negative TST. Results are shown in table 3.

FIGURE 1. Interval between contact and diagnosis of 19 tuberculosis (TB) cases among healthcare workers. Pulmonary TB was diagnosed after 10, 12, 18, 23, 29, 31, 32, 75, 78 weeks and 4 yrs (last case not shown). In six cases, TB was confirmed by a positive culture. Pleural TB was diagnosed after 17, 23, 24, 26, 31, 32, 33, 45, 65, 85 weeks and 9 yrs (last case not shown). In seven of these cases, TB was confirmed by a positive culture. Two cases (pleural TB and TB of the skin) had an undetermined interval due to a long delay in diagnosis of the index patient (both infected by the same source case). ■: culture confirmed; □: culture negative.

TABLE 2 Underlying factors for patient-to-healthcare worker (HCW) transmission of tuberculosis (TB)

HCW with TB	
Failure to identify and isolate index case	
For some days after admission	4
For 3 weeks	4 [#]
During outpatient consultation	3
During irrigation of an abscess at home for several months	1
Total delay in diagnosis	12
Inadequate infection control	
Surgical masks used during isolation period	3
Adequate protective masks used, but not all the time	2
Total inadequate infection-control practices	5
High-risk procedures[†]	2
No underlying factors identified	2
Incomplete information of the index patient⁺	2

Data are presented as n. [#]: One 80-yr-old index patient, with chronic obstructive pulmonary disease, was diagnosed with smear-positive pulmonary TB 2 months after a previous hospital admission of 3 weeks and caused three secondary cases among HCWs: two among other elderly hospitalised patients (one died) and one in a visitor. The four bacteriologically confirmed cases had identical DNA fingerprints as the index case. [†]: i.e. bronchoscopies. ⁺: one HCW developed pleural TB 15 months after being diagnosed and treated for a latent TB infection (LTBI) after exposure in a hospital. The other HCW had pleural TB with a unique fingerprint. She was treated for LTBI 9 yrs previously after exposure to a highly infectious case, before DNA fingerprinting was carried out in the Netherlands. This case was included in the study population because no other risk factors were identified.

Seven HCWs with TB were not enrolled in a contact investigation or periodical screening. Two of them should have been included in a periodical screening, both employed at a pulmonology ward. Another two should have been included in a contact investigation, but in one situation the index patient

refused to mention contacts with health professionals. In the remaining three cases, contact investigation or periodical screening for TB was not indicated and the link with the index patient was only determined by matching DNA fingerprints retrospectively.

DISCUSSION

In the present study, a case series of HCWs with TB, information from a comprehensive national DNA fingerprinting database and detailed epidemiological information from TB departments was used to distinguish nosocomial and non-nosocomial routes of transmission. In 67 out of 101 (66%) HCWs with TB, the route of infection could be determined. Among them, 28 out of 67 (42%) were infected during work in the Netherlands, 19 (28%) were community acquired and 20 (30%) were infected abroad. In 34% of cases, the route of transmission could not be determined, mainly due to lack of bacteriological confirmation.

The TB incidence rate for hospital-employed HCWs with patient contacts (7.9 per 100,000) was approximately two times higher than the incidence rate for Dutch citizens during the study period (average 4.4 per 100,000), but still lower than the rates for all citizens in the Netherlands (average 9.8 per 100,000 with immigrants accounting for >50% of all cases) [10]. The present authors also calculated the relative risk for healthcare work in the Netherlands by classifying cases into categories. The RR of 2.47 compares with findings in England and Wales where TB rates in HCWs were two to three times higher than those in similar occupational groups [14]. The fact that in one-third of cases the route of transmission could not be determined (category four) probably does not influence the distribution of cases among the three categories and the RR in a significant manner.

Only 20% of all HCWs with TB were foreign born. This differs from studies in low-incidence countries with high percentages of foreign-born HCWs with TB [14–17]. Almost all HCWs with work-related TB in the present study developed early

TABLE 3 Enrolment of healthcare workers (HCWs) with tuberculosis (TB) in active case finding activities

In a contact investigation	
TB diagnosed six times	
LTBI missed twice, TST false negative [#]	
Two HCWs developed TB despite treatment with 6 months isoniazid for a latent TB infection	
In a pre-employment screening	
TB diagnosed twice [†]	
In periodical screening	
LTBI missed once, TST false negative [#]	
Two HCWs were infected and developed TB within the screening interval	
One BCG-vaccinated HCW was screened by periodical chest radiography, no TB found	
Not enrolled in a contact investigation or periodical screening⁺	

LTBI: latent TB infection; TST: tuberculin skin test; BCG: bacille Calmette–Guérin. [#]: two HCWs had a negative TST in a contact investigation and one in a periodical screening, but later developed pleural TB with the same strain as the presumed index cases. Retrospectively, TSTs were false negative 7, 8 and 10 weeks after contact with the index patient, while they were 10 mm, 19 mm and “strongly positive” at the time of diagnosis, 31, 32 and 24 weeks after infection. [†]: One was diagnosed with LTBI before contact investigation at work. The HCW completed 6 months isoniazid preventive treatment, but had chest radiography abnormalities 4 yrs later at pre-employment screening. TB was confirmed by a positive culture of material obtained by video-assisted thoracoscopy and the restriction fragment length polymorphism pattern matched with the index patient. ⁺: n=7.

manifestations of TB, such as primary pulmonary TB, pleural TB or TB of the skin. Although active-case finding activities such as pre-employment screening and contact investigation detect TB in an early stage, often without bacteriological confirmation, the current authors also found a relatively short interval between infection and disease for HCWs who presented with symptoms. In these cases, awareness of the HCW and a high suspicion of the physician might have limited diagnostic delay, as has been observed elsewhere [14], although in one other study the health-seeking behaviour was similar for HCWs and controls [16].

The reported TB cases among HCWs are the tip of the iceberg of nosocomial transmission of *M. tuberculosis* bacteria. After all, only 10% of TB infections will eventually lead to active TB [18], so many more infections have occurred. Furthermore, through pre-employment screening, contact investigation and periodical screening of HCWs, a number of latent TB infections are identified (250 annually in the Netherlands) and treated in the majority of cases [10]. However, as the present data show, a significant proportion of these infections have been acquired outside the hospital, as has been observed in other studies [19–21]. Furthermore, other patients (and visitors) might be at even greater risk if TB is not suspected and diagnosis is delayed. This is well illustrated by the transmission of *M. tuberculosis* from one index case to three HCWs, two other hospitalised patients and one visitor.

Early recognition of TB and adequate isolation of cases remain the most important interventions to prevent transmission [2, 8, 22, 23]. In the current study, diagnostic delay was the main cause of patient-to-HCW transmission in 50% of the cases, often in an elderly Dutch patient with comorbidity. The association between initially missed diagnosis and older age has been described by others [23]. Greater experience in TB management, with increased TB suspicion and compliance with diagnostic algorithms, has the potential to reduce diagnostic delay and nosocomial transmission [23]. In some cases in the present study, failure to apply with infection-control procedures, such as the use of appropriate masks, contributed to infection. Hospital infection-control measures are relevant to prevent transmission of TB to healthcare workers [18, 23, 24]. Although the study design did not allow for a standardised assessment of ventilation during the study period, the relevance of airflow is also well known [21]. Four cases in the current study were infected during high-risk procedures, *i.e.* two HCWs while assisting with bronchoscopies, one laboratory attendant due to a needle stick injury and one HCW during irrigation of a TB abscess (syringing). The occupational risk of these procedures, as well as autopsies, has previously been described in case reports and reviews [2, 8, 23, 25–27]. Adequate personal protection measures should be taken during these procedures.

In spite of adequate infection-control measures, transmission of TB might still occur in healthcare institutions, and early diagnosis of latent TB infection or active TB in HCWs is needed in high-risk settings. In the present study, 70% of cases (16 out of 23) had been examined at least once because of high-risk activities or unprotected exposure to a patient at work. The reasons for not detecting and/or effectively treating LTBI were related to the inability of screening procedures to identify

infections, the limitations of the TST and failure of (unsupervised) preventive treatment. However, the current study focused on a relatively limited number of HCWs in which infection control measures failed. It needs to be emphasised that a much greater number of infected HCWs have benefited from screening and preventive treatment.

In conclusion, DNA fingerprint surveillance can be used to confirm expected and reveal unexpected cases of nosocomial transmission, thus providing the necessary evidence for policy makers and professionals to take appropriate action. High suspicion of tuberculosis by the clinician, adequate infection-control measures by the hospital authorities and early identification of latent tuberculosis infection in healthcare workers by occupational specialists form the essential components of a comprehensive package to prevent tuberculosis in healthcare workers.

ACKNOWLEDGEMENTS

The authors would like to thank the public-health nurses and physicians of the Depts of Tuberculosis Control of the Municipal Health Services who participated in this study.

REFERENCES

- 1 Sepkowitz KA. Tuberculosis and the health care worker: a historical perspective. *Ann Intern Med* 1994; 120: 71–79.
- 2 Menzies D, Fanning A, Yuan L, Fitzgerald M. Tuberculosis among health care workers. *N Engl J Med* 1995; 332: 92–98.
- 3 Sepkowitz KA, Friedman CR, Hafner A, *et al.* Tuberculosis among urban health care workers: a study using restriction fragment length polymorphism typing. *Clin Infect Dis* 1995; 21: 1098–1101.
- 4 Fennelly KP, Iseman MD. Health care workers and tuberculosis: the battle of a century. *Int J Tuberc Lung Dis* 1999; 3: 363–364.
- 5 Nosocomial transmission of multidrug-resistant tuberculosis among HIV-infected persons—Florida and New York, 1988–1991. *MMWR Morb Mortal Wkly Rep* 1991; 40: 585–591.
- 6 Diel R, Seidler A, Nienhaus A, Rusch-Gerdes S, Niemann S. Occupational risk of tuberculosis transmission in a low incidence area. *Respir Res* 2005; 6: 35.
- 7 Markowitz SB. Epidemiology of tuberculosis among health care workers. *Occup Med* 1994; 9: 589–608.
- 8 Seidler A, Nienhaus A, Diel R. Review of epidemiological studies on the occupational risk of tuberculosis in low-incidence areas. *Respiration* 2005; 72: 431–446.
- 9 Iseman MD, ed. *A Clinician's Guide to Tuberculosis*. Philadelphia, Lippincott Williams & Wilkins, 1999.
- 10 KNCV. Index tuberculosis 1999 the Netherlands. Netherlands Tuberculosis Register. The Hague, KNCV Tuberculosis Foundation, 2001.
- 11 van Embden JD, Cave MD, Crawford JT, *et al.* Strain identification of *Mycobacterium tuberculosis* by DNA fingerprinting: recommendations for a standardized methodology. *J Clin Microbiol* 1993; 31: 406–409.
- 12 van Soolingen D, de Haas PE, Hermans PW, Groenen PM, van Embden JD. Comparison of various repetitive DNA elements as genetic markers for strain differentiation and

- epidemiology of *Mycobacterium tuberculosis*. *J Clin Microbiol* 1993; 31: 1987–1995.
- 13 Hingstman L, Kenens R, van der Windt W, Talma HF, Meihuizen HE, Josten EJC. Rapportage Arbeidsmarkt Zorg en Welzijn 2002. [Care and Welfare Labour Market Report, Annexes, 2002]. Tilburg, OSA, Nivel and Prismant, 2002; pp. 1–148.
 - 14 Meredith S, Watson JM, Citron KM, Cockcroft A, Darbyshire JH. Are healthcare workers in England and Wales at increased risk of tuberculosis? *BMJ* 1996; 313: 522–525.
 - 15 Ho TB, Rayner CF, Lindfield T, Young Y, Whitfield RJ. Prevalence of TB in healthcare workers in south west London. *Thorax* 2004; 59: 1002–1003.
 - 16 Pleszewski B, FitzGerald JM. Tuberculosis among health care workers in British Columbia. *Int J Tuberc Lung Dis* 1998; 2: 898–903.
 - 17 Hill A, Burge A, Skinner C. Tuberculosis in National Health Service hospital staff in the west Midlands region of England, 1992–5. *Thorax* 1997; 52: 994–997.
 - 18 American Thoracic Society. Targeted tuberculin testing and treatment of latent tuberculosis infection. *Am J Respir Crit Care Med* 2000; 161: 16–23.
 - 19 Bailey TC, Fraser VJ, Spitznagel EL, Dunagan WC. Risk factors for a positive tuberculin skin test among employees of an urban, midwestern teaching hospital. *Ann Intern Med* 1995; 122: 580–585.
 - 20 Panlilio AL, Burwen DR, Curtis AB, et al. Tuberculin skin testing surveillance of health care personnel. *Clin Infect Dis* 2002; 35: 219–227.
 - 21 Menzies D, Fanning A, Yuan L, FitzGerald JM. Hospital ventilation and risk for tuberculous infection in Canadian health care workers. Canadian Collaborative Group in Nosocomial Transmission of TB. *Ann Intern Med* 2000; 133: 779–789.
 - 22 Kent RJ, Uttley AH, Stoker NG, Miller R, Pozniak AL. Transmission of tuberculosis in British centre for patients infected with HIV. *BMJ* 1994; 309: 639–640.
 - 23 Greenaway C, Menzies D, Fanning A, Grewal R, Yuan L, FitzGerald JM. Delay in diagnosis among hospitalized patients with active tuberculosis—predictors and outcomes. *Am J Respir Crit Care Med* 2002; 165: 927–933.
 - 24 Stead WW. Management of health care workers after inadvertent exposure to tuberculosis: a guide for the use of preventive therapy. *Ann Intern Med* 1995; 122: 906–912.
 - 25 Frampton MW. An outbreak of tuberculosis among hospital personnel caring for a patient with a skin ulcer. *Ann Intern Med* 1992; 117: 312–313.
 - 26 Skodric V, Savic B, Jovanovic M, et al. Occupational risk of tuberculosis among health care workers at the Institute for Pulmonary Diseases of Serbia. *Int J Tuberc Lung Dis* 2000; 4: 827–831.
 - 27 Hutton MD, Stead WW, Cauthen GM, Bloch AB, Ewing WM. Nosocomial transmission of tuberculosis associated with a draining abscess. *J Infect Dis* 1990; 161: 286–295.