ERJ Express. Published on June 28, 2006 as doi: 10.1183/09031936.06.00039906

Health care workers with tuberculosis infected during work in the Netherlands.

G. de Vries[1], M.M.G.G. Šebek[2], C.S.B. Lambregts-van Weezenbeek[2]

[1] Department of Tuberculosis Control, Public Health Service Rotterdam, The Netherlands.

[2] KNCV Tuberculosis Foundation, The Hague, The Netherlands

Author for correspondence and requests for reprints:

Gerard de Vries MD, MSc

Department of Tuberculosis Control

Public Health Service

P.O. Box 70032

3000 LP Rotterdam

The Netherlands

T: + 31 10 4339657

F: + 31 10 4339950

E: devriesg@ggd.rotterdam.nl

Disclaimer: No financial support received. No conflict of interest to report.

Running head: Tuberculosis among health care workers

Keywords: DNA fingerprinting; epidemiology; nosocomial transmission; tuberculosis

Copyright 2006 by the European Respiratory Society.

Abstract

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

The total study population consisted of 101 cases over a five-year period. In 67 (66%) the route of infection could be determined by epidemiological and microbiological information. Of these cases, 42% (28/67) were due to infection at work in the Netherlands, 28% (19/67) community acquired and 30% (20/67) 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 contributed to transmission.

A high suspicion of TB by the clinician, adequate infection control measures by hospital authorities and early identification of latent TB infection by occupational and public health specialists are relevant to prevent tuberculosis among health care workers.

Introduction

Health care 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]. With the declining risk the attention for infection control practices in hospitals lessened as well [2]. Recognition of nosocomial transmission as a public health issue was renewed when extensive HIV-related

transmission of multidrug-resistant tuberculosis occurred in New York City hospitals, also affecting 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 not able to differentiate between occupational and non-occupational risk, while outbreak reports may describe extraordinary situations with a high number of infecting inocula, particular virulent strains or HIV co-morbidity making it difficult to extrapolate such results to non-outbreak 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 in the register is 'working in the health care/social welfare sector'. Every year on average 20-30 HCWs are reported with TB out of 1,500 cases. The objective of our study was to determine which cases were really infected during health care work in the Netherlands and to analyse factors that contributed to infection and subsequent disease.

Methods

The study cohort comprised all consecutive TB patients registered in the Netherlands during the period 1/1/1995 to 31/12/1999, who were classified as 'working in the health care/social welfare sector'. After approval of the ethical committee of the NTR, all 37 Departments of Tuberculosis Control of the Municipal Health Services (MHSs) responsible for notification of the cases were identified 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: i) was the patient really a HCW before or at the time of diagnosis, ii) what kind of work was the HCW involved in at the time of diagnosis or before diagnosis, and iii) does epidemiological or molecular information exist which allows 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 standardized IS6110-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 5 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 Netherlands Tuberculosis Register and DNA fingerprints we classified the patient in four categories:

- Category 1: 'HCW, infected during health care 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 time in a hospital in a TB endemic country and foreign born HCWs. Classification was also based on tuberculin skin test conversion after leaving the Netherlands and on DNA fingerprints (e.g. a unique fingerprint).

- Category 4: ‘HCW, place of infection unknown’ includes the remaining cases which could not be classified in one of the above categories.

Cases belonging to category 1 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 air flow (ventilation) in relevant rooms.

Results

In the five-year study period 123 patients were recorded as 'working in the health care/social welfare sector'. Eight patients were misclassified as TB: seven had a latent TB infection and one case had disease caused by *Mycobacterium avium*. Another 21 cases were workers/volunteers involved in the social services in asylum seekers centres, penitentiary institutions and homeless centres and did not have a HCW status. These 29 (8+21) cases (24%) were excluded from the analysis, leaving a total of 94 eligible HCWs with active TB. However, during our field-research we identified seven additional cases, which were not (yet) included in our 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 our study, leaving 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 five-year 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 e.g. general practitioners, physiotherapists, student doctors or not employed in health care settings anymore at the time of diagnosis.

Table 1 shows the classification in four categories. Of the 47 cases infected in the Netherlands, 28 were work-related (category 1) and 19 community acquired (category 2). The attributable risk (AR) of health care work in the Netherlands can be derived directly by dividing the number of cases in category 1 by all cases infected in the Netherlands (category 1 and 2) and is 0.6 (28/47). The relative risk (RR) for health care work in the Netherlands can be calculated from AR = (1-1/RR) and is 2.47.

Of the 11 HCWs infected abroad (category 3) and born in the Netherlands, all but one case were involved in patient care in developing countries, often for many years. One Dutch HCW had a negative tuberculin skin test (TST) when she left the Netherlands to work in a refugee camp in Kenya and TST was 6 mm after return. No treatment for latent TB infection was prescribed in accordance with Dutch guidelines. She developed pleural TB within one year after return with a *M. tuberculosis* strain identical with a strain prevalent among Somalian TB patients in the Netherlands.

In depth investigation focused on the 28 cases infected during work in the Netherlands. Among them sixteen 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. Five cases however 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 tuberculosis with a unique fingerprint after she injured herself at a needle in a laboratory.

Characteristics of HCWs (n=23) and their index patients

The median age of the HCWs was 28 years (range 21-65) and most of them were female (18/23). The following professions were involved: fourteen nurses, four doctors, two ward assistants, two bronchoscopy assistants and one assistant of an out-patient department. Twenty-one were infected in the hospital and two outside the hospital. The hospital workers were deployed at the following departments: 9 at a pulmonology ward, 5 at an internal medicine (including AIDS) department, 2 at a bronchoscopy unit, 2 at an out-patient departments and 3 at other wards. Ten

cases had pulmonary tuberculosis (among them two cases smear-positive), twelve pleural tuberculosis and one tuberculosis of the skin. None of the cases reported a previous history of TB. There were no HCWs with human immunodeficiency virus (HIV) co-infection. However, as they 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 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, sixteen 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 tuberculosis, except for two cases: one with disseminated tuberculosis with chest X-ray 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 age of the index patients was 45 years (range 25-87 years), with 44% of the index patients (8/18) older than 60 years. 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 non-hospitalised 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 non-hospitalised 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 more than a year. One of these HCWs even developed pleural TB four months before the index patient was diagnosed.

The interval between infection and disease of TB cases among HCWs are 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 ten index cases, mostly elderly patients with co-morbidity, 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 (LTBI) (table 3)

Eight HCWs were diagnosed with TB in a contact investigation or pre-employment screening. Three HCWs developed TB despite treatment for LTBI with six months isoniazid (one of them was diagnosed later in a pre-employment screening). In three HCWs LTBI was missed due to a false negative TST.

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 his 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 our 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 (66%) out of 101 HCWs with TB, the route of infection could be determined. Among them, 42% (28/67) was infected during work in the Netherlands, 28% (19/67) was community acquired and 30% (20/67) was 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 about twice higher than the incidence rate for Dutch citizens during the study period (average 4.4 per 100,000), but still lower than rates for all citizens in the Netherlands (average 9.8 per 100,000 with immigrants accounting for more than 50% of all cases) [10]. We also calculated the relative risk for health care work in the Netherlands by classifying cases in categories. The relative risk of 2.47 compares to 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 4), probably does not influence the distribution of cases among the three categories and the relative risk 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 our study developed early manifestations of TB, such as primary pulmonary tuberculosis, pleural tuberculosis or tuberculosis 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 – we also found a relative 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 our 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 even at greater risk if TB is not suspected and diagnosis 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 our study, diagnostic delay was the main cause of patient-to-HCW transmission in 50% of the cases, often in an elderly Dutch patient with co-morbidity. 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, have the potential to reduce diagnostic delay and nosocomial transmission [23]. In some cases in our 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 health care workers [18, 23, 28]. Although the study design did not allow for a standardised assessment of ventilation during the study period, the relevance of air-flow is also well known [21]. In our study four cases 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 been described in case reports and reviews by several other authors [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 health care institutions and early diagnosis of latent TB infection or active TB in HCWs is needed in high-risk settings. In our study 70% of cases (16/23) had been examined one or more times 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 tuberculin skin test and failure of (unsupervised) preventive treatment. However, our 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.

We conclude that DNA fingerprint surveillance can be used to confirm expected and reveal unexpected cases of nosocomial transmission, thus providing the necessary evidence for policymakers and professionals to take appropriate action. High suspicion of TB by the clinician, adequate infection control measures by the hospital authorities and early identification of latent TB infection in HCWs by occupational specialists form the essential components of a comprehensive package to prevent tuberculosis in health care workers.

Acknowledgments

The authors thank the public health nurses and physicians of the Departments 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, Kwok D, Manoach S, Floris M, Martinez D, Sathianathan K, Brown E, Berger JJ, 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. A clinician's guide to tuberculosis. Philadelphia: Lippincott Williams & Wilkins, 1999.
10. Index Tuberculosis 1999, The Netherlands. The Hague: Royal Netherlands Tuberculosis Association, 2001.
11. van Embden JD, Cave MD, Crawford JT, Dale JW, Eisenach KD, Gicquel B, Hermans P, Martin C, McAdam R, Shinnick TM, 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, Hoofdrapport en Bijlagen, 2002.
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. Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. *MMWR Recomm Rep* 2000; 49(RR-6): 1-51.
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, Srivastava PU, Bernardo J, Catalano MT, Mendelson MH, Nicholas P, Pagano W, Sulis C, Onorato IM, Chamberland ME.

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. Wenger PN, Otten J, Breeden A, Orfas D, Beck-Sague CM, Jarvis WR. Control of nosocomial transmission of multidrug-resistant Mycobacterium tuberculosis among healthcare workers and HIV-infected patients. *Lancet* 1995; 345: 235-240.
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, Pesic I, Videnovic J, Zugic V, Rakovic J, Stojkovic M. 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.
28. 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.

Legends

Tables

Table 1: Classification of health care workers (HCWs) with tuberculosis (TB) in categories according to information from interviews, the Netherlands Tuberculosis Register and DNA fingerprints, 1995-1999.

Table 2: Underlying factors for patient-to-HCW transmission of *Mycobacterium tuberculosis*.

Table 3: Enrolment of health care workers (HCWs) with tuberculosis (TB) in active case finding activities

Figure

Figure: Interval between contact and diagnosis of 19 tuberculosis cases among health care workers

Tables

Table 1: Classification of Health Care Workers (HCWs) with Tuberculosis (TB) in categories according to information from interviews, the Netherlands TB Register and DNA fingerprints, 1995-1999

	Category 1: 'HCW, infected during health care work in the Netherlands'	Category 2: 'HCW, infected in the community'	Category 3: 'HCW, infected abroad'	Category 4|: 'HCW, place of infection unknown'	Total
Number of cases	28 (28%)	19 (19%)	20 (20%)	34 (34%)	101
Born in the Netherlands	28 (100%)	15 (79%)	11 (55%)	27 (79%)	81 (80%)
Median age (range)	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%)

Table 2: Underlying factors for patient-to-HCW transmission of *Mycobacterium tuberculosis*.

	Number of HCWs with TB
Failure to identify and isolate index case	
- for some days after admission	4
- for three weeks	4*
- during (out-patient) 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 were used, but not all the times	2
Total "Inadequate infection control practices"	**5**
High-risk procedures (bronchoscopies)	**2**
No underlying factors identified	**2**
Incomplete information of the index patient**	**2**

HCW = health care worker

* One index patient, an 80-year old patient with Chronic Obstructive Pulmonary Disease, was diagnosed with smear-positive pulmonary tuberculosis two months after a previous hospital admission of three weeks and caused three secondary cases among HCWs, two cases among other elderly hospitalised patients (one of them died) and in one visitor. The four bacteriologically confirmed cases had identical DNA fingerprints as the index case.

** One HCW developed pleural tuberculosis (TB) 15 months after being diagnosed and treated for a latent tuberculosis infection (LTBI) after exposure in a hospital. The other HCW had pleural TB with a unique fingerprint. She was treated for LTBI nine years before 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.

Table 3: Enrolment of health care workers (HCWs) with tuberculosis (TB) in active case finding activities

In a contact investigation (10). *Result:* - 6 times TB diagnosed - 2 times LTBI missed (TST "false negative")* - 2 HCWs developed TB despite treatment with six months isoniazid for a latent TB infection.
In a pre-employment screening (2). *Result:* - 2 times TB diagnosed.**
In periodical screening (4). *Result:* - 1 time LTBI missed (TST "false negative")* - 2 HCWs were infected and developed TB within the screening interval - 1 BCG-vaccinated HCW was screened by periodical chest X-rays. No TB found
Not enrolled in a contact investigation or periodical screening (7)

TB = tuberculosis

TST = tuberculin skin test

BCG = bacille Calmette-Guérin

LTBI = latent tuberculosis infection

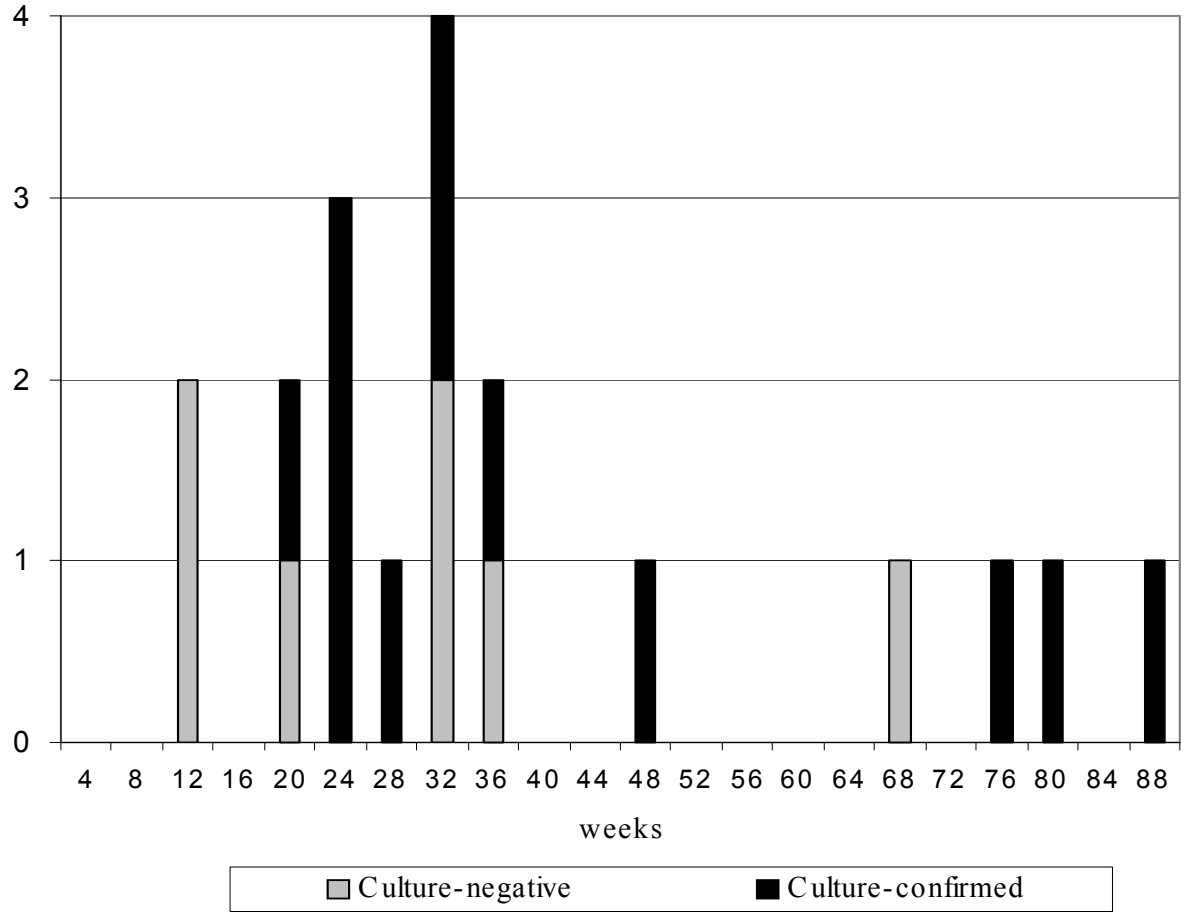
* Two HCWs had a negative tuberculin skin test (TST) in a contact investigation and one in a periodical screening but later developed pleural TB with the same strain as the presumed index cases. Retrospectively TSTs were false negative 7, 8 and 10 weeks after contact with the index

patient, while they were 10 mm, 19 mm and ‘strongly positive’ at the time of diagnosis, 31, 32 and 24 weeks after infection.

** One of them was diagnosed with LTBI before in a contact investigation at work. The HCW completed six months isoniazid preventive treatment, but had chest X-ray abnormalities four years later at pre-employment screening. TB was confirmed by a positive culture of material obtained by video-assisted thoracoscopy and the RFLP-pattern matched with the index patient.

Figure

Figure: Interval between contact and diagnosis of 19 tuberculosis cases among health care workers



- Pulmonary tuberculosis (TB) was diagnosed after 10, 12, 18, 23, 29, 31, 32, 75, 78 weeks and 4 years (last case not shown in the figure). 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 years (last case not shown in the figure). In seven of these cases TB was confirmed by a positive culture.
- Two cases (pleural TB and tuberculosis 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).