Are healthcare workers in England and Wales at increased risk of tuberculosis?

Sarah Meredith, John M Watson, Kenneth M Citron, Anne Cockcroft, Janet H Darbyshire

Abstract

***Objective*—To determine whether healthcare workers in England and Wales are at increased risk of tuberculosis and to examine the frequency of drug resistance in this population.**

***Design*—Comparison of notification rates by occupation obtained from national tuberculosis notification surveys in 1988 and 1993, with denominators from the 1991 census.**

***Subjects*—People with notified tuberculosis in professional and associate professional occupations from the two surveys.**

***Main outcome measures*—Rates of notified tuberculosis in health professionals (mainly doctors) and health associate professionals (mainly nurses) compared with rates in other professional and associate professional occupations, adjusted for ethnic group, sex, and age.**

***Results*—119 cases of tuberculosis were identified in healthcare workers, including 61 nurses and 42 doctors. The crude notification rate in healthcare workers was 11.8 per 100 000 per year (95% confidence interval 9.8 to 14.1) compared with 3.3 per 100 000 per year (2.9 to 3.6) in other professional and associate professional occupations; rate ratios were higher (range 1.7 to 3.2) in all ethnic groups. The relative risk adjusted for ethnic group, sex, and age was 2.4 (95% confidence interval 2.0 to 3.0), slightly higher for health professionals (2.7 (1.9 to 3.8)) than for associate professionals (2.0 (1.5 to 2.6)). No multiple drug resistant strains of tuberculosis were identified in healthcare workers.**

***Conclusions*—Better detection and notification of cases of tuberculosis in healthcare workers may account for some of the apparent increased risk, but these findings imply that tuberculosis remains a hazard for healthcare workers and highlight the importance of ensuring that occupational health monitoring and protection workers are not neglected.**

Department of Epidemiology and Medical Statistics, London Hospital Medical College, London E1 4NS
Sarah Meredith, *lecturer in public health*

Public Health Laboratory Service Communicable Disease Surveillance Centre, London NW9 5EQ
John M Watson, *consultant epidemiologist*

Royal Brompton Hospital, London SW3 6NP
Kenneth M Citron, *consulting physician*

Royal Free Hospital and School of Medicine, London NW3 2QG
Anne Cockcroft, *consultant in occupational health*

Medical Research Council HIV Clinical Trials Centre, University College London Medical School, London WC1E 6AU
Janet H Darbyshire, *head*

Correspondence to:
Dr Sarah Meredith, Department of Preventive Medicine, Vanderbilt University School of Medicine, Nashville, TN 37232-2637, USA.

sarah.meredith@mcmail.vanderbilt.edu

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Introduction

Tuberculosis in healthcare workers may result from occupational exposure, and infected workers may transmit the disease to susceptible patients. It was established early this century that healthcare workers were at increased risk of tuberculosis.[1-6] However, most studies since the introduction of effective chemotherapy, including three recent studies from the United Kingdom, have found that, with the exception of pathology and mortuary staff, healthcare workers were no more likely to develop tuberculosis than other members of the population.[7-12]

The recent increases in tuberculosis notifications[13] and the occurrence of multiple drug resistant strains and associated mortality in the United States[14] have revived concern about risks to healthcare workers, although relatively little drug resistance has been found in Britain.[15] We aimed to determine whether healthcare workers in England and Wales have a higher risk of tuberculosis than other socioeconomically comparable groups, taking into account the confounding effects of ethnic group, sex, and age,[16] and to examine the frequency of drug resistant disease.

Method

We identified cases of tuberculosis from two national surveys of tuberculosis notifications in England and Wales: *(a)* the Medical Research Council's survey of 1988[16] and *(b)* the 1993 collaborative survey by the Public Health Laboratory Service, British Thoracic Society, and Department of Health.[17] The surveys used similar methods, described elsewhere[16]; in brief, clinical and microbiological information was collected on all cases of tuberculosis notified during the first six months of each year and, in 1993, on those under 55 years old for the whole year. Clinical details were received for 99.4% of eligible cases in 1988[16] and 93.4% in 1993.

We coded occupations according to the standard occupational classification,[18] and identified all the cases in the "corporate management," "professional," "associate professional and technical," and "clerical" categories. Cases in this last group were included because of the difficulty in classifying accountants, who may be "professional" or "clerical" depending on qualifications. We compared rates in healthcare workers (professionals and associate professionals) with those in the other occupations selected. We analysed two broad occupational categories separately: professional occupations (including corporate managers) and associate professional occupations (including clerks).

We calculated rates by occupation using denominators from the 1991 census. Population data by occupation, ethnic group, sex, and age were available only for broad occupational categories known as submajor groups.[18] Therefore, rates in doctors could not be estimated separately from all "health professionals," a category that also includes dentists, pharmacists, ophthalmic opticians, and veterinary surgeons, nor could nurses be distinguished from other health associate professionals (midwives, radiographers, physiotherapists, chiropodists, dispensing opticians, medical technicians, occupational and speech therapists, and environmental health officers). Data by submajor group, ethnic group, sex, and age were available for Great Britain and not separately for England and Wales.[19] To estimate the relevant figures for England and Wales we calculated the proportion of the population belonging to each ethnic group in Great Britain for each submajor group, sex, and age category. We then applied these proportions to the population of England and Wales stratified by submajor group, sex, and age group to give population estimates by ethnic group.

We estimated the numbers of cases in people aged 55 years or over in 1993 from the proportion of notifications in the whole year reported in the first six months (scaling factor 1.8857). Because the 1988 survey was only for six months, we divided population estimates by the relevant scaling factor (1.9348) to prevent inappropriately narrow confidence intervals which would result from multiplying the cases.[16]

We used STATA software[20] for Poisson regression analysis of the relative risk of notified tuberculosis in healthcare workers compared with workers in socioeco-

Table 1—*Notified tuberculosis in healthcare workers in both surveys, by occupation*

Occupation	1988	1993	Total
Health professionals:			
All	16	32	48
Doctor	13	29	42
Pharmacist	3	2	5
Dentist	0	1	1
Health associate professionals:			
All	25	46	71
Nurse or midwife	22	41	63
Medical radiographer	0	1	1
Chiropodist	0	1	1
Pharmacy dispenser	0	2	2
Occupational or speech therapist	2	1	3
Other health associate professional	1	0	1
All healthcare workers	41	78	119

nomically comparable occupations, adjusted for ethnic group, sex, and age. Ethnic groups were based on those for the 1991 census: white, Indian subcontinent (Indian, Pakistani, and Bangladeshi), Afro-Caribbean ("black other" combined with Caribbean and African), and "all other."

Results

In all, 119 healthcare workers and 364 people in the other relevant occupations were identified as having tuberculosis. The occupational distribution of healthcare workers was similar in 1988 and 1993 (table 1). Nurses and midwives made up 89% (63/71) of the health associate professionals, and doctors 88% (42/48) of the health professionals.

The health professionals were slightly younger, and a smaller proportion of them than of other professionals were male (table 2). Cases of tuberculosis in associate professionals were predominantly in women, and the proportion was greater in health associate than in other associate professional occupations. There were pronounced differences in the ethnic distribution by occupation. Similar proportions of those in Indian subcontinent ethnic groups were born outside the United Kingdom (90% (37/41) of healthcare workers and 88% (100/114) of the people in other occupations).

The site of disease was known in 423 cases (the information was not requested for cases notified in the second half of 1993). Most disease was reported to be respiratory: 76% (77/101) of healthcare workers and 69% (223/322) of people in other occupations had respiratory disease (73% (74) and 62% (199) respectively with respiratory disease only). Information on previous treatment for tuberculosis was available for 458 (95%) of the 483 cases; four (4%) of 110 healthcare workers and 26 (7%) of 348 people in other occupations were known to have been treated previously.

Culture results were known in 360 cases (75%) and were positive in 279 of these (64 (76%) of 84 healthcare workers and 215 (78%) of the 276 people in other occupations. Among those for whom site and bacteriology results were available, 36 (30/83) healthcare workers had smear positive pulmonary tuberculosis, including 20 nurses and seven doctors. Sensitivity results were available for 251 (90%) of the 279 positive cultures; of 58 positive cultures from healthcare workers there were three (5%) resistant strains (one resistant to streptomycin, one to isoniazid alone, and one to both drugs), compared with 14 (7%) resistant strains in other occupational groups, including one multiple drug resistant strain (resistant to isoniazid and rifampicin).

The crude notification rate in healthcare workers was 11.8 per 100 000 per year (95% confidence interval 9.8 to 14.1), compared with 3.3 per 100 000 per year (2.9 to 3.6) in other occupations. Although the size of the relative risk (3.6) was due in part to differences in ethnic group, rate ratios were raised in each ethnic group (table 3). The relative risk adjusted for ethnic group, sex, and age (table 4) was 2.4 (2.0 to 3.0) for all healthcare workers and slightly higher for health professionals (2.7 (1.9 to 3.8)) than for health associate professionals (2.0 (1.5 to 2.6)).

Table 2—*Demographic characteristics of notified cases of tuberculosis by occupational category. Values are numbers (percentages) of cases*

	Professional		Associate professional		
	Health (n = 48)	Other (n = 138)	Health (n = 71)	Other (n = 226)	All (n = 483)
Ethnic group:					
White	7 (15)	72 (52)	43 (61)	112 (50)	234 (48)
Indian subcontinent	33 (69)	49 (36)	8 (11)	65 (29)	155 (32)
Afro-Caribbean	3 (6)	8 (6)	13 (18)	33 (15)	57 (12)
Other	5 (10)	9 (7)	7 (10)	16 (7)	37 (8)
Sex:					
Female	15 (31)	33 (24)	60 (85)	115 (51)	223 (46)
Male	33 (69)	105 (76)	11 (15)	111 (49)	260 (54)
Mean age (years)	34.7	38.8	35.2	34.6	35.9

Table 3—*Incidence by occupational category and ethnic group*

	Cases (rate per 100 000 per year)		Rate ratio (95% confidence interval)
	Healthcare	Other	
Professional groups:			
All	50 (23.9)	143 (2.5)	9.6 (6.8 to 13.3)
White	8 (4.6)	76 (1.4)	3.4 (1.4 to 7.0)
Indian subcontinent	34 (148.2)	50 (68.9)	2.1 (1.3 to 4.0)
Afro-Caribbean	3 (119.0)	8 (17.3)	6.9 (1.2 to 28.6)
Other	5 (55.7)	9 (15.5)	3.6 (0.9 to 11.9)
Associate professionals:			
All	74 (8.9)	231 (4.0)	2.2 (1.7 to 2.9)
White	44 (5.7)	116 (2.1)	2.7 (1.9 to 3.8)
Indian subcontinent	8 (79.1)	65 (67.0)	1.2 (0.5 to 2.5)
Afro-Caribbean	14 (47.4)	34 (40.0)	1.2 (0.6 to 2.3)
Other	8 (45.4)	16 (28.8)	1.6 (0.6 to 3.9)
All occupations:			
All	124 (11.8)	374 (3.3)	3.6 (2.9 to 4.6)
White	52 (5.5)	192 (1.7)	3.2 (2.3 to 4.3)
Indian subcontinent	42 (127.1)	115 (67.8)	1.9 (1.3 to 2.7)
Afro-Caribbean	17 (53.0)	42 (32.0)	1.7 (0.9 to 3.0)
Other	13 (48.9)	25 (22.0)	2.2 (1.0 to 4.5)

Numbers of cases were estimated; notifications in people aged 55 years and over were collected for only the first half of 1993 and were scaled up to estimate the numbers for the year (see methods section).

Discussion

Despite relatively crude methods and potential inaccuracies, this study shows that healthcare workers in England and Wales are two to three times more likely to have notified tuberculosis than other people, after socioeconomic status, ethnic group, age, and sex have been taken into account. We found no evidence, however, of multiple drug resistance in healthcare workers notified in 1988 or 1993.

The relative risk is similar to that found in studies of doctors and nurses earlier this century[1-6] but is at odds with the results of more recent research.[10-12] The main explanation for this inconsistency may be that in this study the rates in healthcare workers were compared with those in people in occupations of similar socioeconomic status rather than with rates in the whole population, which includes poor and unemployed people, who are likely to be at higher risk of tuberculosis.

These findings do not necessarily mean that healthcare workers are at increased risk of disease, although they strongly suggest this. Pre-employment screening, awareness of symptoms, and encouragement by occupational health services for workers with symptoms to come forward may increase the probability and

Table 4—*Results of Poisson regression analysis, adjusted for ethnic group, sex, and age group. Values are rate ratios (95% confidence interval)*

Variable and comparison	Professional groups	Associate professionals	All
Ethic group compared with white group:			
Indian subcontinent	43.7 (31.4 to 60.8)	26.8 (20.3 to 35.4)	33.7 (27.5 to 41.4)
Afro-Caribbean	14.7 (7.8 to 27.6)	14.9 (10.7 to 20.6)	15.6 (11.7 to 20.9)
Other ethnic groups	11.9 (6.7 to 21.1)	11.4 (7.4 to 17.6)	11.6 (8.2 to 16.3)
Females compared with males	0.7 (0.5 to 1.0)	0.9 (0.7 to 1.1)	0.9 (0.7 to 1.0)
Age group compared with group aged 16-29 years:			
30-44 years	0.7 (0.5 to 1.0)	1.1 (0.8 to 1.4)	0.9 (0.7 to 1.1)
45-59 (males,45-64) years	0.6 (0.4 to 0.9)	0.9 (0.7 to 1.2)	0.7 (0.6 to 0.1)
≥60 (males,≥64) years	1.8 (0.9 to 4.0)	0.9 (0.4 to 2.2)	1.3 (0.7 to 2.3)
Healthcare workers compared with other workers	2.7 (1.9 to 3.8)	2.0 (1.5 to 2.6)	2.4 (2.0 to 3.0)

speed of diagnosis. Capewell and colleagues found that eight out of 23 cases of tuberculosis in healthcare workers in Lothian, Scotland, were detected by pre-employment screening.[10] Although the slightly smaller proportion of healthcare workers with both respiratory and non-respiratory disease is compatible with less advanced disease in this group, the proportion of positive cultures did not differ between occupational groups, which might be expected if healthcare workers were diagnosed earlier in their illness.

It is possible that when tuberculosis is diagnosed it is more likely to be notified for healthcare workers than for people working in other occupations. However, it is also possible, for reasons of professional confidentiality, that notification is less likely among healthcare workers. In a study of cases of diagnosed tuberculosis in east London, only 73% had been notified.[21] If notification of healthcare workers were complete, but only 73% of those in other occupations were notified, the rate ratio would be 1.37. Therefore, even a difference in practice of this degree would account for only a third of the increased risk.

Although detection and notification bias may have affected the results, rates for healthcare workers were almost certainly underestimated by dilution of the denominators with people with no more exposure to tuberculosis than in the comparison occupations. Only 61% of health professionals in Great Britain in the 1991 census were doctors[19]; if the proportion was the same for England and Wales, the notifications of the 42 doctors would represent a rate of 33 per 100 000 per year, 13 times the rate for other professional groups (unadjusted). The broad occupational categories selected for this study and defined according to the standard occupational classification,[18] are a very crude basis for the assessment of risk to healthcare workers. On the one hand, occupations with little or no exposure to tuberculosis were included, and, on the other, groups potentially at risk, such as laboratory and mortuary technicians, auxiliary nurses, and domestic staff on wards were excluded because appropriate denominators were not available.

The denominators were potentially inaccurate in three ways. Firstly, populations in England and Wales were estimated from data for Great Britain, and the underlying assumption that the ethnic mix in each occupational group in England and Wales is in proportion to that in Great Britain as a whole may not be valid. However, as 91% of the working population of Great Britain is resident in England and Wales[19] this is unlikely to have affected the results to any great extent. Secondly, the population surveyed in the 1991 census was not the population at risk in either 1988 or 1993, and, although it provided a reasonable midpoint estimate, there are concerns about its completeness.[22] Thirdly, the census is based on information from individuals whereas the survey data were from clinicians—occupation and ethnic group, in particular, may be described differently. However, although these three problems may have led to error in the calculation of rates, they would have biased relative risk estimates only if the patterns differed by occupation.

Information was not available on the source of infection in the healthcare workers. Further studies are needed to investigate the extent of occupationally acquired tuberculosis in healthcare staff and to evaluate possible detection bias, completeness of notification, and whether patients are at risk from those with the disease. On present evidence, tuberculosis remains a hazard for healthcare workers. Health service commissioners and occupational health services should ensure that the Joint Tuberculosis Committee's guidelines[23] for the control of tuberculosis are being followed and that patients and staff, including locums and students, are as well protected as possible.

Key messages

- Tuberculosis in healthcare workers may result from occupational exposure, and infected workers pose a potential infection risk to susceptible patients
- This study shows that rates of notified tuberculosis in healthcare workers in England and Wales were two to three times those in other socio-economically comparable occupational groups
- As many healthcare workers are unlikely to be exposed to tuberculosis infection, those who are may be at much greater risk than has been estimated
- No multiple drug resistant tuberculosis was found in healthcare workers
- It is important that health service commissioners and occupational health services are aware of the risks and ensure that the recommendations for the control of tuberculosis in health service staff and students are complied with

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Comparison of adverse events associated with use of mefloquine and combination of chloroquine and proguanil as antimalarial prophylaxis: postal and telephone survey of travellers

P J Barrett, P D Emmins, P D Clarke, D J Bradley

See pp 528, 530, 533

Abstract

***Objective*—To compare the frequency of adverse events, particularly neuropsychiatric effects, from mefloquine and from chloroquine plus proguanil as used for malaria chemoprophylaxis.**

***Design*—Retrospective questionnaire to travellers taking either regimen between November 1993 and February 1995; telephone interview with those reporting pronounced side effects.**

***Setting*—Travellers from Britain who consulted an advisory helpline.**

***Subjects*—1214 adults taking mefloquine and 1181 taking chloroquine plus proguanil.**

***Main outcome measures*—Reported presence of and degree of disability from 12 neuropsychiatric and other symptoms, as assessed by the subjects and by referees and on the basis of behaviour change.**

***Results*—There were equal rates of any side effects (40%) and of stopping or changing medication. Overall, neuropsychiatric adverse events were significantly more common in travellers taking mefloquine. In all, 333 neuropsychiatric adverse events were reported by 1214 travellers taking mefloquine, compared with 189 such events in 1181 travellers taking proguanil plus chloroquine (P<0.001). In all, 0.7% of travellers taking mefloquine had disabling neuropsychiatric adverse effects, compared with 0.09% of those taking proguanil plus chloroquine (P = 0.021). Two travellers taking mefloquine (1 in 607) were admitted to hospital as a result of the adverse event, compared with 1 in 1181 travellers taking proguanil plus chloroquine.**

***Conclusion*—There is a significant excess of adverse neuropsychiatric events of intermediate degrees of severity associated with the use of mefloquine compared with proguanil plus chloroquine. This finding may also explain the discrepant findings between earlier studies and clinical experience.**

Medical Advisory Services for Travellers Abroad, London WC1E 7HT
P J Barrett, *senior medical adviser*
P D Emmins, *technical director*
P D Clarke, *medical director*

London School of Hygiene and Tropical Medicine, London WC1E 7HT
D J Bradley, *professor of tropical hygiene*

Correspondence to:

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Introduction

Malaria prophylaxis for British travellers to endemic areas includes avoiding infective mosquito bites, using chemoprophylaxis; travellers should also promptly seek treatment in the case of febrile illness.[1] Chemoprophylaxis poses the most problems because of existing drug resistance by the potentially fatal *Plasmodium falciparum*; travellers, however, are healthy people, so adverse events from antimalarial drugs are fairly unacceptable.

Between July 1993 and March 1995 the recommended chemoprophylaxis for travellers visiting areas where malaria resistant to chloroquine is widespread has been either a combination of proguanil 200 mg daily and 300 mg of chloroquine base weekly or mefloquine 250 mg weekly. During that time mefloquine was recommended for east and central Africa, mefloquine or proguanil plus chloroquine for west Africa, and proguanil plus chloroquine for the Indian subcontinent. Mefloquine has been increasingly used since it was licensed in Britain in 1990, though it is used less widely than in the United States and in some other European countries. The main concerns about mefloquine relate to reports of adverse neurological and psychiatric events. These include anxiety, depression, sleep disturbances, nightmares, hallucinations, and, in a few people, overt psychotic attacks or convulsions. The frequency of such events is unclear. Steffen *et al* reported that "serious" events occurred in around 1 in 10 000 people taking the drug[2] (with "serious" defined according to the restrictive definition of the Council for International Organisations of Medical Sciences as fatal, life threatening, leading to or prolonging a stay in hospital, or resulting in severe disability[3]), but anecdotal reports from doctors in Britain have suggested that this might be an underestimate. Because of this uncertainty about the extent of adverse side effects, we compared the adverse events associated with the use of mefloquine as antimalarial prophylaxis with those associated with the use of proguanil plus chloroquine. We specifically examined the results relating to temporarily disabling neuropsychiatric adverse events.

Subjects and methods

We retrospectively identified all travellers who had been advised between November 1993 and February 1995 via the travellers' telephone health line run by the Medical Advisory Services for Travellers Abroad to use either mefloquine or a choice of mefloquine or proguanil plus chloroquine as antimalarial prophylaxis for visiting a malarious area. We sent each traveller a postal questionnaire requesting information about any adverse events relating to antimalarial drugs taken. The questionnaire was timed to arrive after the traveller's return to Britain.

We sent all non-respondents a duplicate questionnaire four weeks later. Non-respondents to this were sent a final letter and repeat questionnaire a further four weeks later.

Respondents were included for analysis only if they had undertaken the journey that they had specified when contacting the health line and had indicated that they had taken either mefloquine or proguanil plus chloroquine.