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Predictors of tuberculin reactivity among prospective Vietnamese migrants: the effect of smoking

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SUMMARY

We investigated the prevalence and predictors of positive tuberculin skin test (TST) results among prospective Vietnamese migrants. We interviewed and medically screened 1395 Vietnamese people aged over 15 years who had applied to migrate to Australia. Approximately 44% of applicants had an induration of 10 mm or more, and 18·6% had an induration of 15 mm or more. A positive tuberculin skin test at 5 mm, 10 mm and 15 mm of induration cut-points was significantly associated with age (OR 1·01–1·02 per year) and duration of smoking (OR 1·03–1·12 per year). Smoking appears to be an important factor associated with increased susceptibility to mycobacterial infection. It is not yet clear whether the increased tuberculin reactivity associated with smoking reflects an increased risk of tuberculosis among these migrants.

INTRODUCTION

Australian surveillance data have indicated that persons migrating from countries that have a high prevalence of tuberculosis (TB) have high rates of TB post-migration [1], and that tuberculosis remains an important health problem among these migrants. Similar findings have been reported in the United States [2]. Vietnamese migrants have the highest risk for TB of any ethnic group in Australia, having a notification rate in 1997 of over 13 times the national rate [1]. We aimed to document the prevalence and predictors of positive tuberculin skin test (TST) results among prospective Vietnamese migrants to Australia.

Studies of risk factors for *M. tuberculosis* infection and disease are an important component of efforts to improve current methods of TB control [3]. The TST has been widely used to indicate the presence of mycobacterial infection, the likelihood of infection with *M. tuberculosis*, and the risk of TB [4, 5], although few studies have examined the predictors of tuberculin reactivity. Greater knowledge about the predictors of tuberculin reactivity has the potential to improve our understanding of the factors associated with the risk of *M. tuberculosis* infection, and potentially, the risk of TB. Although the TST has several well-known weaknesses [6], it remains the most widely used test to determine the risk of *M. tuberculosis* infection, and has been shown to have predictive value [7].

METHODS

We recruited prospective Vietnamese migrants from a pre-departure standardized medical screening pro-

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Table 1. *Significant independent predictors of completion of the tuberculin skin test*

Characteristic	Adjusted Odds Ratio (95% CI)*	*P*
Previous TB (yes)	0·25 (0·12–0·54)	< 0·001
Pregnancy (pregnant)	0·26 (0·10–0·68)	0·006
Gender (male)	0·52 (0·38–0·69)	< 0·001
Education (years)	1·09 (1·05–1·14)	< 0·001
BMI (kg/m²)	0·94 (0·90–0·98)	0·009
English proficiency (reference: poor/very poor)		
Fair	0·89 (0·64–1·24)	0·50
Excellent or good	0·34 (0·20–0·56)	< 0·001

* Adjusted for other significant predictors displayed.
Abbreviations: CI, confidence interval; TB, tuberculosis; BMI, body mass index.

gramme (operated by the International Organisation for Migration) for migrants or students applying for a visa to Australia. Prospective migrants were eligible to participate in the study if they were Vietnamese and intended to migrate to, or study in Australia for a period of more than 2 years. The purpose and format of the study were explained, and participants were assured that all information obtained would remain confidential and would not affect their chances of migration.

A total of 1669 prospective migrants aged between 16 and 87 years were recruited into the study between January 1997 and June 1999. Prospective migrants completed a structured interview and underwent a TST. The TST was carried out by trained staff using the Mantoux method, with an intracutaneous administration of 5 International Units (IU) of purified protein derivative (PPD). The TST was read at approximately 48 h, but no later than 72 h, following administration of the test. A ball-point pen was used to identify the dimensions of the induration prior to measurement with calipers. We chose to describe the predictors of a positive TST across three commonly used cut-points for positive reactions, namely equal to or greater than 5 mm, 10 mm and 15 mm of induration. This allowed an evaluation of the predictors for each level of reactivity, as well as the consistency of effects found across levels.

We designed an interviewer-administered questionnaire to assess sociodemographic indicators including age, sex, the number of years of school and university education completed, living situation (number of people sharing a bedroom with the applicant) and English proficiency (excellent, good, fair, poor or very poor). Current smoking habits were assessed, including the duration of smoking in years and the average number of cigarettes smoked per day. Previous history of TB and exposure to TB from close contacts such as friends or relatives with TB (classified as yes/possibly versus no) were recorded and Body Mass Index (BMI) was calculated using the formula wt(kg)/ht(m²).

Two translators independently translated the questionnaire into Vietnamese, and a review panel evaluated the adequacy of the translations and the concepts used. Back-translation of the instrument was used to confirm the validity of the translation. The questionnaire was administered in Vietnamese by trained Vietnamese interviewers.

We used Microsoft Access 97 (Microsoft Corporation Inc, 1996) and SPSS version 9.0.1 (SPSS Inc, 1999) to process the data. Binomial logistic regression analysis was used to identify independent predictors of a positive TST result for each of the cut-points of interest. A main effects model was initially determined. Variables were entered into a forward stepwise model, with the probability criterion for entry set at 0·05 and exit at 0·10. Odds ratios adjusted for the other variables in each model are reported. Effect modification was explored, and the inclusion of interactions was determined by the significance of the change in log likelihood of the model.

RESULTS

Tuberculin skin test completion

Of the total sample of 1669 prospective migrants who completed the medical screening and interview, 274 (16·4%) did not complete the TST. Non-completion of the TST was most frequently associated with a

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Table 2. *Association between sociodemographic characteristics and tuberculin skin test result at three different definitions of a positive reaction*

	5 mm+ induration		10 mm+ induration		15 mm+ induration	
Characteristic	Odds Ratio (95% CI)	*P*	Odds Ratio (95% CI)	*P*	Odds Ratio (95% CI)	*P*
Age (years)	1·02 (1·01–1·04)	< 0·001	1·01 (1·00–1·02)	0·02	1·01 (1·00–1·03)	0·03
Gender (male)	2·07 (1·57–2·74)	< 0·001	1·45 (1·13–1·85)	0·003	1·19 (0·88–1·62)	0·26
Education (years)	1·03 (0·996–1·06)	0·09	1·01 (0·98–1·04)	0·44	0·99 (0·95–1·02)	0·41
English proficiency (reference: excellent or good)						
Fair	0·97 (0·63–1·50)	0·89	1·11 (0·74–1·69)	0·61	1·57 (0·88–2·79)	0·13
Poor or very poor	0·83 (0·54–1·28)	0·39	0·89 (0·59–1·35)	0·59	1·22 (0·68–2·20)	0·50
Living situation (reference: own bedroom)						
Share bedroom with one other person	0·81 (0·64–1·02)	0·08	0·84 (0·67–1·06)	0·15	1·09 (0·81–1·46)	0·59
Share bedroom with two or more others	1·10 (0·78–1·57)	0·58	1·04 (0·75–1·45)	0·81	1·13 (0·74–1·71)	0·58
Ever had close contact with someone with TB	0·88 (0·53–1·47)	0·63	0·91 (0·55–1·50)	0·71	0·89 (0·46–1·73)	0·73
Productive cough lasting > 2 weeks (yes)	2·75 (1·21–6·26)	0·02	1·50 (0·81–2·80)	0·20	0·90 (0·40–2·05)	0·80
Ever smoked (yes)	2·60 (1·79–3·77)	< 0·001	1·68 (1·24–2·27)	0·001	1·51 (1·05–2·16)	0·03
Duration of smoking (years)	1·12 (1·06–1·17)	< 0·001	1·05 (1·02–1·08)	< 0·001	1·03 (1·01–1·06)	0·006
Number of cigarettes smoked per day (reference: 0)						
1–5	1·97 (1·28–3·04)	0·002	1·55 (1·07–2·26)	0·02	1·61 (1·04–2·49)	0·03
6 or more	4·62 (2·28–9·34)	< 0·001	1·90 (1·19–3·04)	0·007	1·35 (0·77–2·36)	0·30
Time since quit smoking (reference: current smokers)						
Quit within previous 10 years	0·97 (0·42–2·25)	0·94	1·03 (0·55–1·93)	0·94	0·90 (0·44–1·85)	0·78
Quit more than 10 years ago	0·57 (0·14–2·31)	0·43	0·24 (0·06–0·93)	0·04	0·25 (0·03–2·04)	0·20

Table 3. *Adjusted associations with tuberculin skin test result at three different definitions of a positive reaction*

	5 mm + induration		10 mm + induration		15 mm + induration	
Characteristic	Odds Ratio (95% CI)	*P*	Odds Ratio (95% CI)	*P*	Odds Ratio (95% CI)	*P*
Age (years)*	1·17 (1·11–1·22)	< 0·001	1·13 (1·08–1·19)	< 0·001	1·12 (1·05–1·19)	0·001
Gender (male)†	2·10 (1·58–2·79)	< 0·001	1·45 (1·13–1·86)	0·004	1·17 (0·86–1·60)	0·31
Ever smoked (yes)†	2·31 (1·58–3·38)	< 0·001	1·53 (1·13–2·09)	0·007	1·37 (0·95–1·97)	0·09
Duration of smoking (years)†	1·09 (1·04–1·14)	0·001	1·04 (1·02–1·07)	0·001	1·03 (1·004–1·06)	0·02
Number of cigarettes smoked per day (reference: 0)						
1–5‡	1·58 (0·95–2·61)	0·08	1·20 (0·78–1·84)	0·41	1·21 (0·73–2·01)	0·47
6 + ‡	2·60 (1·08–6·26)	0·03	1·05 (0·55–1·98)	0·89	0·71 (0·32–1·56)	0·39
Time since quit smoking (reference: current smokers)						
Quit within previous 10 years‡	1·03 (0·44–2·43)	0·95	1·11 (0·58–2·13)	0·75	0·98 (0·47–2·04)	0·95
Quit more than 10 years ago‡	0·64 (0·14–2·85)	0·55	0·28 (0·07–1·13)	0·07	0·28 (0·03–2·36)	0·24
Productive cough lasting > 2 weeks (yes)§	2·42 (1·05–5·59)	0·04	1·35 (0·71–2·54)	0·36	0·80 (0·35–1·84)	0·60

* Adjusted for age squared; † adjusted for age and age squared; ‡ adjusted for age, age squared and duration of smoking; § adjusted for age, age squared, duration of smoking and cigarettes smoked per day.

refusal to undergo the test. Failure to deliver the test by the examining doctor also contributed to non-completion of the TST. Medical staff reported non-administration of the TST due to a recent diagnosis of TB, current or recent treatment for TB, or pregnancy. Based on the interview data, previous TB and current pregnancy were the two strongest predictors of completion of the TST (Table 1). Gender, English proficiency, the number of years of school and university education and BMI were also significant predictors of TST completion. Age, duration of smoking and living situation were not significant predictors of TST completion. Prospective migrants who did not complete the TST were excluded from the following analyses.

Sample description

The majority of the 1395 prospective migrants studied were young adults, and most were women (75·7%). The mean age of the sample was $29{\cdot}14 \pm 10{\cdot}52$ years, and age ranged from 16–81 years. Completion of less than 8 years of education was reported by 22·7% of prospective migrants, and 45·7% reported poor or very poor English proficiency. Approximately 8·9% of prospective migrants reported being current smokers, 5·2% previous smokers and 85·9% lifetime non-smokers. Applicants who had ever smoked were more commonly men (90·9%) than women (9·1%). There was no significant difference in the duration of smoking reported between men and women ($10{\cdot}09 \pm 10{\cdot}43$ years and $9{\cdot}45 \pm 8{\cdot}57$ years respectively; $P = 0{\cdot}79$), and the association between age and duration of smoking was similar for men and women ($r_s = 0{\cdot}69$, $P < 0{\cdot}001$ and $r_s = 0{\cdot}74$, $P < 0{\cdot}001$ respectively). The duration of smoking was also positively associated with the average number of cigarettes smoked per day ($r_s = 0{\cdot}44$, $P < 0{\cdot}001$).

A previous diagnosis of TB was reported by 17 (1·2%) prospective migrants. A cough, productive of sputum and lasting more than 2 weeks in the previous 6 months was reported by 41 (2·9%) prospective migrants. Only one prospective migrant reported ever having haemoptysis, and only three reported having sweats, chills or fevers at night that lasted a few nights in the previous 6 months. Thirteen prospective migrants reported close contact with a friend or relative who had been diagnosed with TB in the previous 6 months, and 30 reported ever having had close contact with someone with TB.

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Tuberculin skin test

The mean induration was 7·63 ± 6·31 mm, with a range 0–35 mm. Approximately 64·4% of prospective migrants had an induration equal to, or greater than 5 mm (95% CI 61·9–66·9), 43·8% had an induration equal to, or greater than 10 mm (95% CI 41·2–46·4), and 18·6% had an induration equal to, or greater than 15 mm (95% CI 16·6–20·6). The crude association between sociodemographic characteristics, smoking and TST result at the 5 mm, 10 mm and 15 mm cut-points is summarized in Table 2. The TST result was significantly associated with age, history of smoking, duration of smoking and the number of cigarettes smoked, across all three cut-points. The association between gender and TST result was only significant for the 5 mm and 10 mm cut-points. The significance of these associations decreased with the increasing level of tuberculin reactivity. The association between TST result and a productive cough that lasted for more than 2 weeks in the previous 6 months was only significant at the 5 mm cut-point. The TST result was not significantly related to BMI, reports of weighing less compared with 6 months previously, nor reports of a previous diagnosis of TB. Small numbers limited analysis of the association between TB symptoms and tuberculin reactivity.

In Table 3 significant predictors of the TST result following adjustment for age are presented. The adjustment for age included a term for age squared to account for the non-linear association between age and the risk of a positive TST result. The association between the average number of cigarettes smoked per day and the risk of a positive TST was only significant at the 5 mm cut-point after controlling for age and duration of smoking.

Predictors of TST result

Logistic regression models were used to determine the predictors of a positive TST result at 5 mm, 10 mm and 15 mm cut-points. Age, age squared and gender were entered into the first block of the model to adjust for these factors. The second block used forward stepwise methods to enter remaining significant predictors into the model. The indicators of smoking used in the model were duration of smoking and the number of cigarettes smoked per day. Other study variables that had a crude association with TST result where $P \leqslant 0{\cdot}25$ were included in the model for forward selection. Significant independent predictors of the TST result are summarized in Table 4. All models were tested for interaction terms and no significant effect modification was found involving any combinations of smoking indicators, age or gender. The association between tuberculin reactivity, age and smoking status is displayed in Figure 1.

DISCUSSION

The high prevalence of positive TST results among prospective migrants in this cohort is consistent with the high rate of active TB observed among Vietnamese migrants in Australia. The proportion of prospective Vietnamese migrants who had an induration of equal to, or greater than 10 mm was similar to that found among foreign-born persons applying for adjustment of immigration status in Denver, USA (42%) [8].

Although only a small proportion of prospective migrants did not agree to have a TST, our findings suggest multiple reasons were associated with non-completion of the test. The two strongest predictors of non-completion of the TST, namely a previous diagnosis of TB and pregnancy, suggest issues associated with the value and perceived risks of the TST are important considerations in administration of the test. Failure to complete the TST may also have been associated with perceptions of consequences for migration, despite prospective migrants having been assured that the TST results and other information collected would not influence the outcome of their application for migration. Fears about the negative influence of reports of smoking on the outcome of migration applications are likely to result in a greater amount of misclassification of smoking status than has been reported elsewhere for Vietnamese migrants [9]. The classification of a number of smokers as nonsmokers would have led to an under-estimation of the effect of smoking on tuberculin reactivity, suggesting that our estimates of the effect due to smoking may be conservative. A further limitation of this study was the use of 10 IU of PPD for a short period, due to a supplier error. Although the individuals affected in the cohort could not be identified, sequential examination of the data showed no obvious systematic effect. It is unlikely that the administration of 10 IU was distributed unequally according to smoking status. A recent study of the impact of the dose of tuberculin on reactivity found an average difference of only 1·5 mm between 5 TU and 10 TU doses of tuberculin [10].

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Table 4. *Significant independent predictors of tuberculin skin test result at three different definitions of a positive reaction*

Model	Adjusted Odds Ratio (95% CI)†	*P*
5 mm+ ($\chi^2 = 87{\cdot}33$, $P < 0{\cdot}001$)*		
Age	1·17 (1·11–1·23)	< 0·001
Age²	0·998 (0·998–0·999)	< 0·001
Gender (male)	1·79 (1·31–2·44)	< 0·001
Duration of smoking (years)	1·05 (1·003–1·10)	0·036
Productive cough > 2 weeks	2·34 (1·01–5·40)	0·047
10 mm+ ($\chi^2 = 44{\cdot}10$, $P < 0{\cdot}001$)*		
Age	1·13 (1·08–1·19)	< 0·001
Age²	0·998 (0·998–0·999)	0·002
Gender (male)	1·26 (0·95–1·65)	0·11
Duration of smoking (years)	1·04 (1·01–1·06)	0·02
15 mm+ ($\chi^2 = 21{\cdot}63$, $P < 0{\cdot}001$)*		
Age	1·13 (1·06–1·20)	< 0·001
Age²	0·999 (0·998–0·999)	0·001
Gender (male)	1·01 (0·71–1·43)	0·97
Duration of smoking (years)	1·03 (1·01–1·06)	0·03

* Model χ^2.

† Adjusted for other significant predictors in the model.

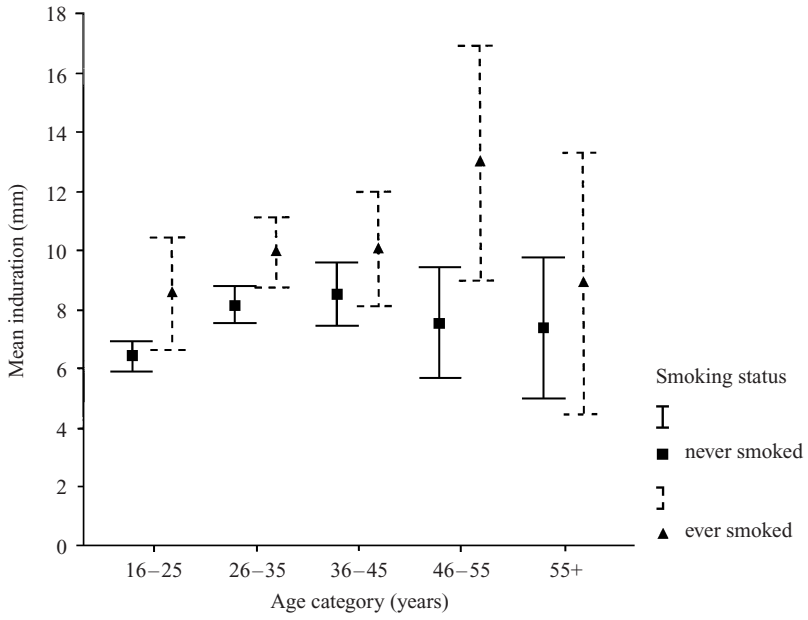

Fig. 1. Mean induration in millimetres by age category and smoking status. Error bars show 95% confidence intervals.

In a high-prevalence environment, the risk of exposure to *M. tuberculosis* is likely to be in part time-dependent, indicators of infection are less likely to be strongly related to indicators of exposure, and there is a lower likelihood of a mismatch between periods of increased individual susceptibility and exposure. Duration of smoking and age were significant independent predictors of TST result across all three cut-points. Nisar and coworkers [11] also found an association between smoking and tuberculin reactivity in institutionalized elderly adults, although their study was not designed to investigate the socioeconomic confounders of this association. An association between tuberculin reactivity and smoking was also identified in another report [12], where it was observed that this association varied by gender, but it was not

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determined whether gender remained a significant independent predictor of tuberculin reactivity after controlling for smoking. Exploration of the influence of gender on the association between smoking and tuberculin reactivity in a more recent study of prison inmates who had a negative TST on admission [13] was precluded by the predominantly male sample.

An association between age and tuberculin reactivity supports the likelihood of *M. tuberculosis* infection rather than BCG vaccination as an explanation for a positive TST [14]. We found no evidence to indicate that the effect of smoking on tuberculin reactivity is modified by age. Age has been found to be a significant predictor of *M. tuberculosis* infection in a number of studies [14–20]. Presumably this relationship is in part a function of the greater chance of being exposed to *M. tuberculosis* over time [18]. There is also support for our finding of a non-linear association between age and tuberculin reactivity, as the likelihood of a positive TST has been found to increase with age, but also to decline in late adulthood [11, 21]. Decreased tuberculin reactivity in late adulthood is thought to be associated with altered functioning of the immune system associated with ageing. In a recent review [22] it was suggested that in addition to well-recognised alterations in adaptive immunity in later life, ageing-associated changes of the innate immune system are also likely to exert critical influences on the adaptive immune response to infectious disease.

Our finding that smoking was associated with higher levels of tuberculin reactivity (and presumably a greater probability of *M. tuberculosis* infection) may also be linked to changes in functioning of the immune system. The suggestion that exposure to cigarette smoke may impair resistance to mycobacterial infection [11] is consistent with other studies suggesting that smoking is a risk factor for the development of active TB [23–25]. Current smokers are more likely to develop respiratory infection and illness following viral infection than nonsmokers due to the effects of smoke on immune processes that limit viral replication as well as nonspecific mucosal processes that provide the first barrier against infection [26]. A recent study of a nonspecific indicator of mucosal immunity [27] has confirmed that mucosal immunity declines with age and is significantly lower in current smokers and females. Other research supports lower natural killer cytotoxic activity in current smokers as compared with ex-smokers [28], and suppression of T-cell dependent humoral and cellular immune responses and suppression of T cell function in the respiratory tract [29].

The literature on smoking and cell-mediated immunity suggests that smoking is likely to lower reactivity to tuberculin. As we found smoking to be associated with a higher level of tuberculin reactivity, this effect would be best explained by an increased susceptibility to infection associated with smoking. Our finding that the effect of smoking on tuberculin reactivity is greatest at 5 mm provides some support for the suggestion that smoking undermines the presence of larger reactions to tuberculin. The use of a large cut-point for the definition of a positive TST among smokers may lead to an under-detection of the increased risk of infection among this subgroup.

Alternatively, Nisar and coworkers [11] suggest that the association between smoking and tuberculin reactivity may be a social class phenomenon. As exposure to *M. tuberculosis* is the primary factor associated with infection, it is likely that some demographic and socioeconomic variables are directly related to this association [20]. Based on the absence of significant associations of tuberculin reactivity with English proficiency, education and living situation, we found that a social class effect was unlikely to explain an association between smoking and tuberculin reactivity. We accept that the indicators of social class we used were limited, but, our conclusion concurs with that of Evans *et al.* [27] who found that smoking largely accounted for the association between social class and immune status.

Nisar and coworkers [11] generated a single predictive model for ordinal TST reactivity data, which assumed that the predictors of tuberculin reactivity would not vary with the definition of a positive TST used. Our findings provided some support for this assumption among core predictors of tuberculin reactivity. In the multivariate analysis, gender and the presence of a productive cough for more than 2 weeks in the previous 6 months were the only predictors to become non-significant at higher levels of reactivity.

Previous studies have both supported [18] as well as failed to find gender differences in tuberculin reactivity [14, 16], although these studies did not examine smoking habits concurrently. The assessment of gender differences in tuberculin reactivity without an assessment of smoking may produce misleading estimates in populations where smoking rates differ between men and women. Data presented on the gender-specific prevalence of tuberculous infection by smoking status from a study of Cubans in Florida [12]

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suggested that the reported significant difference in the age-adjusted prevalence of tuberculous infection between men and women can be largely explained by smoking. However, smoking alone is unlikely to account fully for the discrepant findings reported in the literature. In common with previous work [11, 13], our study suggests that gender has an independent effect on tuberculin reactivity, although unlike previous studies we only found evidence of this at the lowest level of reactivity examined.

Authors of a recent report [30] stated that it is unclear why TB is more prevalent among men, and suggested that the current consensus is that a combination of biological and social factors is responsible. We believe that there is a reasonable amount of evidence to support the identification of smoking as an important factor underlying this relationship. Yu and coworkers [25] found that smoking largely explained the effect of age and gender on the risk of TB, although it was not known at the time if smoking increased the chance of *M. tuberculosis* infection or contributed to the development of disease after infection [12, 25]. A more recent study found that smoking was associated with an increased risk of TB following infection [24] although these authors could not determine if smoking also increased the risk of exposure, or infection following exposure, or both. Our findings indicate that smoking is associated with a higher risk of mycobacterial infection following exposure in view of the high prevalence environment studied, and the lack of association of tuberculin reactivity with socioeconomic indicators. Our findings also indicate that smoking explains a large proportion of the observed gender differences in tuberculin reactivity.

Some studies that have detected a significant association between smoking and tuberculin reactivity have used indicators incorporating the duration of smoking [11, 13], rather than just current smoking status. Given evidence that following cessation of smoking the increased susceptibility to infection reverses [29, 31], the effect of smoking may be best modelled by indicators of the period of increased susceptibility, and ideally, dose. These indicators are more closely related to the proposed mechanism of the effect of smoking on tuberculin reactivity, being an increased susceptibility to mycobacterial infection during periods of smoking, should exposure occur. Categorization of smoking status due to current habits may not provide as good an indicator of this risk.

Our findings indicate that smoking is a risk factor for the development of mycobacterial, and most likely, *M. tuberculosis*, infection. Documented changes in immune system functioning with smoking provide a likely biological basis for this association. Confounding due to a close association between gender and smoking and the variable association between smoking and sociodemographic variables in different populations may provide some explanation for differences in findings among previous studies.

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REFERENCES

1. Gilroy N, National TB Advisory Group for the Communicable Diseases Network Australia and New Zealand. Tuberculosis notifications in Australia, 1997. Commun Dis Intell 1999; **23**: 337–48.
2. Centers for Disease Control and Prevention. Reported tuberculosis in the United States, 1999. 2000, National Center for HIV, STD and TB Prevention, Division of Tuberculosis Elimination.
3. Comstock GW. Tuberculosis: Is the past once again prologue? Am J Publ Hlth 1994; **84**: 1729–31.
4. American Thoracic Society. Diagnostic standards and classification of tuberculosis. Am Rev Respir Dis 1990; **142**: 725–35.
5. American Thoracic Society. Diagnostic standards and classification of tuberculosis in adults and children. Am J Respir Crit Care Med 2000; **161**: 1376–95.
6. Andersen P, Munk ME, Pollock JM, Doherty TM. Specific immune-based diagnosis of tuberculosis. Lancet 2000; **356**: 1099–104.
7. Watkins RE, Brennan R, Plant AJ. Tuberculin reactivity and the risk of tuberculosis: a review. Int J Tuberc Lung Dis 2000; **4**: 895–903.
8. Blum RN, Polish LB, Tapy JM, Catlin BJ, Cohn DL. Results of screening for tuberculosis in foreign-born persons applying for adjustment of immigration status. Chest 1993; **103**: 1670–4.
9. Wewers ME, Dhatt RK, Moeschberger ML, Guthrie RM, Kuun P, Chen MS. Misclassification of smoking status among Southeast Asian adult immigrants. Am J Respir Crit Care Med 1995; **152**: 1917–21.
10. Stuart RL, Bennett N, Forbes A, Grayson ML. A paired comparison of tuberculin skin test results in health care workers using 5TU and 10TU tuberculin. Thorax 2000; **55**: 693–5.

11. Nisar M, Williams CSD, Ashby D, Davies PDO. Tuberculin testing in residential homes for the elderly. Thorax 1993; **48**: 1257–60.
12. Centers for Disease Control and Prevention. Prevalence of tuberculous infection among U.S. residents of Cuban descent – Dade County, Florida, 1982–84. MMWR 1992; **41**: 74–5, 81.
13. Anderson RH, Sy FS, Thompson S, Addy C. Cigarette smoking and tuberculin skin test conversion among incarcerated adults. Am J Prev Med 1997; **13**: 175–81.
14. Lifson AR, Halcon LL, Johnston AM, et al. Tuberculin skin testing among economically disadvantaged youth in a federally funded job training program. Am J Epidemiol 1999; **149**: 671–9.
15. Kermode M, Crofts N, Speed B, Miller P, Streeton J. Tuberculosis infection and homelessness in Melbourne, Australia, 1995–1996. Int J Tuberc Lung Dis 1999; **3**: 901–7.
16. Rusen ID, Yuan L, Millson ME. Prevalence of *Mycobacterium tuberculosis* infection among injection drug users in Toronto. Can Med Assoc J 1999; **160**: 799–802.
17. Janis EM, Allen DW, Glesby MJ, et al. Tuberculin skin test reactivity, anergy, and HIV infection in hospitalized patients. Am J Med 1996; **100**: 186–92.
18. Martin Sanchez V, Alvarez-Guisasola F, Cayla JA, Alvarez JL. Predictive factors of *Mycobacterium tuberculosis* infection and pulmonary tuberculosis in prisoners. Int J Epidemiol 1995; **24**: 630–6.
19. Coolahan LM, Levy MH. The prevalence of tuberculosis infection in New South Wales police recruits. Med J Aust 1993; **159**: 369–72.
20. Reichman LB, O'Day R. Tuberculous infection in a large urban population. Am Rev Respir Dis 1978; **117**: 705–12.
21. Johnston RN, Ritchie RT, Murray IHF. Declining tuberculin sensitivity with advancing age. BMJ 1963; **2**: 720–4.
22. Pawelec G, Solana R, Remarque E, Mariani E. Impact of aging on innate immunity. J Leukoc Biol 1998; **64**: 703–12.
23. Alcaide J, Altet MN, Plans P, et al. Cigarette smoking as a risk factor for tuberculosis in young adults: a case-control study. Tubercle Lung Dis 1996; **77**: 112–6.
24. Altet MN, Alcaide J, Plans P, et al. Passive smoking and risk of pulmonary tuberculosis in children immediately following infection. A case-control study. Tubercle Lung Dis 1996; **77**: 537–44.
25. Yu G, Hsieh C, Peng J. Risk factors associated with the prevalence of pulmonary tuberculosis among sanitary workers in Shanghai. Tubercle 1988; **69**: 105–12.
26. Cohen S, Tyrrell DAJ, Russell MAH, Jarvis MJ, Smith AP. Smoking, alcohol consumption, and susceptibility to the common cold. Am J Publ Hlth 1993; **83**: 1277–83.
27. Evans P, Der G, Ford G, Hucklebridge F, Hunt K, Lambert S. Social class, sex, and age differences in mucosal immunity in a large community sample. Brain Behav Immun 2000; **14**: 41–8.
28. Meliska CJ, Stunkard ME, Gilbert DG, Jensen RA, Martinko JM. Immune function in cigarette smokers who quit smoking for 31 days. J Allergy Clin Immunol 1995; **95**: 901–10.
29. Holt PG. Immune and inflammatory function in cigarette smokers. Thorax 1987; **42**: 241–9.
30. Diwan VK, Thorson A. Sex, gender, and tuberculosis. (Tuberculosis progress report). Lancet 1999; **353**: 1000–1.
31. Tollerud DJ, Clarke JW, Brown LM, et al. The effects of cigarette smoking on T cell subsets. Am Rev Respir Dis 1989; **139**: 1446–51.