Tuberculin testing in two Liverpool social clubs: the effects of a tuberculosis outbreak on background positivity

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Abstract

Background – Tuberculin testing remains the standard method for assessing infection due to tuberculosis in the UK. However, there are no data on the incidence of tuberculin positivity among the general adult population in the UK and consequently interpretation of Heaf test results is often difficult.

Methods – During the investigation of an outbreak of tuberculosis in a Liverpool social club 198 members were interviewed and Heaf tested and 171 members of a second social club in Liverpool were similarly screened as a control group. Comparisons between the results from the two populations provided both an estimate of baseline Heaf test positivity in indigenous white adults from a British inner city population, and a measure of the effect on this baseline of recent exposure to tuberculosis.

Results – In both club populations the proportion of positive Heaf tests increased with age. Independent of age, the tuberculosis exposed population had a higher proportion of positive Heaf grade results (40.9%) than those in the control group (26.9%). Multivariate analysis confirmed both the differences in Heaf results between clubs and between age groups but identified no other behavioural or medical factors which affected Heaf test results.

Conclusions – Heaf test positivity increases with age at least up to 54 years, and recent exposure to tuberculosis increases the proportion of positive Heaf tests in each age group. Interpretation of positive Heaf tests when assessing the effects of a tuberculosis outbreak should take account of background levels of Heaf positivity.

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Keywords: age effects, tuberculin positivity, tuberculosis outbreak.

England and Wales are no exception to the global increase in the incidence of tuberculosis. Despite a 9% annual decline in tuberculosis in England and Wales between 1980 and 1985, subsequent years (1987-93) have shown an annual rise of 3%.¹ The epidemiology associated with this increase is still a matter of some debate, with potential contributory factors including changes in patterns of im-

migration and socioeconomic circumstances such as overcrowding and unemployment.¹⁻⁴

Irrespective of any specific epidemiological mechanism, a changing incidence of tuberculosis in England and Wales must inevitably lead to changes in exposure for some or all of the general population. The standard method for assessing exposure to tuberculosis is by tuberculin testing. However, routine tuberculin testing is currently only carried out on either school children prior to BCG vaccination⁵ or on specific individuals as part of a contact tracing process.⁶ There are no recent studies of tuberculin testing of adult populations in the UK with no known exposure to, or specific risk factor associated with, tuberculosis infection. Consequently, the current proportions of tuberculin positivity among any given adult population in the UK can only be a matter of conjecture. Such information would be valuable when considering a diagnosis of tuberculosis since some indication of the expected proportion of tuberculin reactors in any given age group would provide a suitable context in which to interpret the tuberculin test result.

Both the absence and potential value of baseline tuberculin test data were recently highlighted during the investigation of an outbreak of tuberculosis in a social club in Liverpool in which club members were screened by interview, a brief self-completed questionnaire relating to lifestyles, Heaf testing, and chest radiography. Typically, the interpretation of Heaf test results was confounded by a lack of baseline data regarding Heaf grades in unexposed populations. Using the same methods, a similar investigation was therefore carried out in a second Liverpool social club where no cases of tuberculosis had been recorded. The results of these two investigations offer a unique opportunity, firstly, to analyse the incidence of tuberculin positivity in indigenous white adults from a British inner city population and, secondly, to determine how contact with a tuberculosis outbreak alters levels of positivity through recently acquired infections.

Methods

During a six month period from April to September 1992 six adults (five of whom were sputum smear positive) and a child from North Liverpool were diagnosed as having pulmonary tuberculosis. Initial interviews with these individuals revealed that all adults congregated frequently in the same social club. Furthermore, subsequent DNA analysis⁷ revealed

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Table 1 Characteristics of the tuberculosis exposed and control social club cohorts

	Cohort	
	Tuberculosis exposed club (n = 198)	Control club (n = 171)
Age median (range)	48 (15–83)	54 (15–82)**
Men (%)	76.8	71.3
White (%)	99.5	99.4
Ever had BCG (%)	69.8	63.8
Ever had tuberculosis (%)	1.0	2.7
Current smoker (%)	60.8	45.8*
Current drinker (%)	98.9	93.5*
Persistent cough (%)	15.5	22.4
Median years at club (range)	7.4 (0.5–17.5)	20.5 (0.3–49.5)**

* p<0.01; ** p<0.001.

Table 2 Relationship between Heaf grade and social club cohort

Cohort	Heaf grade					Total
	0	1	2	3	4	
Tuberculosis exposed club	23 (11.6)	22 (11.1)	72 (36.4)	40 (20.2)	41 (20.7)	198 (100)
Control club	43 (25.1)	23 (13.5)	59 (34.5)	27 (15.8)	19 (11.1)	171 (100)

Values in parentheses are percentages.

that these infections were from the same strain of *Mycobacterium tuberculosis* and therefore probably resulted from a single index case. On the basis of this evidence it was decided that all members of the social club, as well as any other regular attenders, should be screened for tuberculosis.

The club was therefore visited by the Consultant in Communicable Disease for Liverpool who gained permission from the club officers for tuberculin testing to be undertaken and for questionnaires to be completed at the club site. Club members were then written to individually to explain the purpose of the exercise and to ask them to attend the club for screening. Over the course of 10 weekends 306 members and affiliates attended. With the help of screening staff, club members completed a questionnaire requesting basic demographic data (sex, age, ethnicity, etc) along with more specific information on length of club membership, smoking and drinking habits, and medical history including previous tuberculosis disease and BCG vaccination. Heaf tests were carried out using 100 000 TU Purified Protein Derivative (PPD) smeared on the outer surface of the forearm and injected intradermally with a Heaf gun using a disposable magnetic multiprong head. The members were asked to attend the following weekend to have their Heaf test read. Those having a clinically significant positive Heaf test (grade 3 or 4)⁵ were referred for chest radiography which was repeated after six months to ensure that no disease had developed.

As a control for the above outbreak, a similar social club was approached in a different part of Liverpool in which no cases of tuberculosis had been reported recently. After permission from the club officers and ethical approval were obtained (Research Ethics Committee, Broadgreen Hospital NHS Trust), the same process of Heaf testing and questionnaire completion was employed resulting in 187 control club members being screened over seven week-

ends. To ensure comparability of results the same screening staff were used to administer and grade the Heaf tests in both clubs.

STATISTICAL ANALYSIS

Simple descriptive statistics were used to characterise the two club cohorts and initial comparisons between them made use of χ^2 and Mann-Whitney U tests. However, to establish the specific effects of tuberculosis exposure and various demographic variables (age, smoking, drinking, etc) on Heaf test results, logistic regression was employed.^{8,9} All analyses concerning Heaf test results critically compared individuals with grades below 3 with those having reactions graded 3 or above. All analyses were carried out on the statistical package SPSS except for stratified non-parametric analyses which employed the methods of Meddis.¹⁰

Results

Of the 493 individuals who completed part or all of the questionnaire, 74.8% also had a Heaf grade test (exposed club 198 of 306; control club 171 of 187). Analysis of the questionnaire data from those individuals who were Heaf tested and those who only completed the questionnaire showed no significant differences in the control population. In the exposed population, however, individuals who did not complete a Heaf grade test were more likely to be female (p<0.05) and less likely to have had a BCG vaccination (p<0.01).

The analyses presented in this paper are limited to those 369 individuals who completed both the questionnaire and Heaf test. For these, the median age of the control club population was significantly higher (z=3.365, p<0.001) than for members of the exposed club (table 1). Furthermore, there were significantly more current smokers (p<0.01) and current drinkers (p<0.01) among the members of the exposed club, but the members had significantly fewer years of club membership (p<0.001). There were no significant differences between clubs with respect to sex ratio, ethnicity, current persistent cough, and history of BCG vaccination or tuberculosis.

The population in the club exposed to tuberculosis had a significantly different distribution of Heaf grade results ($\chi^2=16.072$, p<0.005), due primarily to a greater proportion of individuals with Heaf grades 3 or 4, from the tuberculosis exposed club (table 2). This difference is not a function of the discrepancy in age structure between the two cohorts. In all age categories members of the tuberculosis exposed club had higher proportions of individuals with a Heaf grade of 3 or above (figure). Analysis of the difference in proportion of Heaf grades 3 or above between the two clubs, stratified by age groups,¹⁰ still showed a highly significant difference (z=3.080, p<0.005). The overall relationship between age and Heaf grade is best summarised as a rise in proportion of positive Heaf tests up to the age of 55–64 at which level positive results plateau (z=5.841). However, in order to remove any

Relationship between Heaf grade and age in members of the social club exposed to tuberculosis (●) and those from the club with no known tuberculosis exposure (■). Vertical lines give the standard error of the mean. Data values below the x axis represent sample sizes in each age category.

further confounding effects of sex, smoking, drinking, period of club membership, history of BCG, or previous tuberculosis infection, these variables were analysed along with age category and club of origin using logistic regression models.⁸⁹ Only the club of origin ($p < 0.005$) and age category ($p < 0.0001$) of the subject were found to be significant predictors of a Heaf grade 3 or 4. All other factors showed no significant relationship with a positive Heaf test result.

Discussion

The multifactorial determinants of an individual's response to a Heaf test limit the use of such tests as a diagnostic tool. However, some understanding of both the proportion of individuals with a positive Heaf test in the general population and the effects that tuberculosis exposure has on such proportions add to their clinical value. During an outbreak of tuberculosis amongst patrons of a Minneapolis bar (USA), screening of 97 patrons identified 41 with a positive tuberculin skin test.¹¹ Although all 41 infections were attributed to recent contact with a single index case, there were no data on background level of Heaf positivity in patrons of Minneapolis bars with no known exposure to tuberculosis. Without this information the actual number of positive tests attributable to the recent outbreak cannot be accurately assessed. We have shown that, although recent exposure to tuberculosis significantly increases the proportions of grade 3 and 4 Heaf results, a substantial number of individuals (26.9% in our control club) may have positive Heaf grades despite no known recent exposure to tuberculosis.

In our club cohorts the only significant predictors of Heaf positivity were recent exposure to tuberculosis and increase in age (figure). In apparent contrast, we have shown previously that Heaf grade positivity declined progressively with the age of residents in Liverpool homes for the elderly.¹² However, the disparities between this study and that in elderly res-

idential homes can probably be explained by differences in the age distribution of each cohort: only 19 of the 369 club members (5.1%) were 75 years or older compared with over 2165 of the 2661 tested in the homes for the elderly (81%). Data from other studies have shown that Heaf positivity in developed countries tends to peak in the 60–70 age range and declines progressively thereafter.^{13,14} The age related decline in positive Heaf tests in our elderly population and the converse increase in this social club study are therefore probably both part of the same continuum. This same age continuum determines the potential duration of smoking and subsequent effects on the local immune system.¹⁵ Thus, although a significant effect of smoking on Heaf positivity was identified in the study of homes for the elderly¹² (odds ratios compared with non-smokers of 1.2 for ex-smokers and 1.59 for current smokers), our social club study failed to reach significance (odds ratios 1.190 for ex-smokers, 1.272 for current smokers).

Our two clubs differed in the proportion of individuals who completed the Heaf testing process. However, those individuals who did not complete the Heaf tests differed from those who did only in sex ratio and levels of BCG vaccination. Since neither of these factors was shown to affect the Heaf grade result significantly, it is unlikely that any differences between clubs were the result of such selection bias. Consequently, the increase in positive Heaf test results from 26.9% in members of the non-exposed club to 40.9% in those exposed to tuberculosis (14%; equivalent to 28 additional positive club members) was probably the result of recent infections and therefore these individuals may be at an increased risk of developing tuberculosis. In order to detect any newly developing disease, chest radiographs of all members of the club exposed to tuberculosis with Heaf grades of 3 or 4 ($n = 81$) have been undertaken as an appropriate precaution under guidelines in operation at the time.¹⁶ Although this screening has not detected any further cases of tuberculosis, evidence from a study in Puerto Rico shows that, at least in children, an appreciable portion (1.7%) of those with tuberculin reactivity will develop tuberculosis in subsequent years.¹⁷ No long term data are currently available on the risk of tuberculosis developing in healthy tuberculin positive adults. However, estimates of the size of the tuberculosis infected population may at least provide some guide to the population at risk over the next two or three decades.

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