

Original articles

Tuberculosis and HIV: estimates of the overlap in England and Wales

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Abstract

Background A study was designed to determine the extent of the interaction between tuberculosis and human immunodeficiency virus infection in England and Wales.

Methods Data were obtained from the United Kingdom national AIDS surveillance and the Medical Research Council tuberculosis notification surveys in England and Wales (1983 and 1988). The proportion of patients reported with AIDS known to have had tuberculosis and the proportion of patients notified with tuberculosis known to have HIV infection were estimated.

Results Of the 4360 patients with AIDS reported by 30 June 1991, 200 (4.6%) were in patients reported to have had tuberculosis. Only one of the 3002 patients (0.03%) reported in the 1983 survey of tuberculosis notifications in England and Wales was known to be infected with HIV compared with nine of 2163 patients (0.42%) in the 1988 survey.

Conclusion Although the reported number of cases of HIV infection with tuberculosis in this country is increasing it remains small. Complete reporting of cases of AIDS and notification of cases of tuberculosis are essential to enable the two infections to be monitored as the HIV epidemic develops. Special studies, such as those reported here, will need to be undertaken regularly to assess the future extent of the interaction.

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Both tuberculosis (disease resulting from infection with *Mycobacterium tuberculosis* or *M. bovis*) and infection with the opportunist mycobacteria are well established complications of human immunodeficiency virus (HIV) infection and the acquired immunodeficiency syndrome (AIDS).¹ Tuberculosis, however, poses an infectious threat to others and, in almost all patients, can be successfully treated. A slowing in the decline in the number of reported cases of tuberculosis in the United States in recent years has been attributed to the epidemic of HIV infection,^{2,3} and increases in the incidence of tuberculosis due to the same cause are now being reported from parts of Africa.⁴

Most cases of tuberculosis in people infect-

ed with HIV are believed to occur as a result of reactivation of prior tuberculous infection,⁵ though the contribution of newly acquired infections may be important in countries or population groups where the prevalence of tuberculosis is high. Before extrapulmonary tuberculosis was included as an AIDS defining condition in 1987⁶ reports indicated that tuberculosis was generally diagnosed before or around the time of the diagnosis of AIDS, mostly within six months of the AIDS diagnosis.⁷ Tuberculosis in patients with AIDS is important not only because of the increased threat to the health of the patient with AIDS but also because nosocomial spread of tuberculosis to other patients and health care workers has been reported.^{8,9}

The number of cases of tuberculosis developing in people with HIV infection in Britain will depend largely on the proportion of the population with previous tuberculous infection. Although there are estimates of the prevalence of HIV infection in some selected groups in England and Wales, and estimates of prior tuberculous infection (as measured by tuberculin sensitivity) in unvaccinated school children aged 12-14 years, we do not have estimates for the prevalence of these infections in the population as a whole. The likely extent of the interaction between tuberculous and HIV infection can be assessed by studying the distribution of reported diagnoses of tuberculosis in patients with AIDS, and vice versa. This information would help clinicians to make informed decisions about the need for HIV testing in their patients, as well as providing prevalence estimates that can be compared with estimates from elsewhere and in future years. This paper reports three approaches to studying the interaction between these two infections, based on information collected for the surveillance of AIDS and on surveys of tuberculosis notifications.

Methods

Two primary sources of information were used in this study:

1 *United Kingdom (UK) national AIDS surveillance*

A confidential voluntary reporting system of cases of AIDS in the UK by clinicians to the Public Health Laboratory Service (PHLS) AIDS centre at the Communicable Disease Surveillance Centre, London, and to the Communicable Diseases (Scotland) Unit.¹⁰

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Table 1 Age and sex distribution of patients with AIDS reported to the Communicable Disease Surveillance Centre by 30 June 1991 and number with tuberculosis (England and Wales, excluding visitors)

| Age (y) at diagnosis | Sex | | | | | | | | |
|----------------------------|-------|-------------------|-----|--------|-------------------|-------|------------|-------------------|-----|
| | Male | | | Female | | | Both sexes | | |
| | Total | With tuberculosis | | Total | With tuberculosis | | Total | With tuberculosis | |
| No | | % | No | | %* | No | | % | |
| 0-19 | 53 | 3 | 5.7 | 24 | 1 | (4.2) | 77 | 4 | 5.2 |
| 20-29 | 801 | 38 | 4.7 | 77 | 9 | 11.7 | 878 | 47 | 5.4 |
| 30-39 | 1728 | 66 | 3.8 | 69 | 5 | 7.2 | 1797 | 71 | 4.0 |
| 40-49 | 1070 | 50 | 4.7 | 28 | 1 | (3.6) | 1098 | 51 | 4.6 |
| 50+ | 440 | 24 | 5.5 | 11 | 0 | (0.0) | 451 | 24 | 5.3 |
| Unknown | 56 | 3 | 5.4 | 3 | 0 | (0.0) | 59 | 3 | 5.1 |
| Total | 4148 | 184 | 4.4 | 212 | 16 | 7.5 | 4360 | 200 | 4.6 |

*Parentheses indicate percentage based on under 50 cases.

2 Medical Research Council (MRC) tuberculosis notification surveys^{11 12}

Confidential surveys of all notified cases of tuberculosis in England and Wales in the first six months of 1983 and 1988, with information from the notifying physician on ethnic group, clinical characteristics, and bacteria identified. Only disease believed to be due to *M tuberculosis* or *M bovis* is notifiable.

The relation between HIV infection and tuberculosis was studied in three ways:

1 The clinical features (current or previous) of all cases of AIDS reported in England and Wales to the Communicable Disease Surveillance Centre by 30 June 1991 were reviewed. In some cases the initial report was supplemented by information derived from further reports returned by other clinicians. In addition, further information was available from the death certificate in about 40% of patients who had died.

2 Patients reported in the MRC tuberculosis notification surveys of 1983 and 1988 were compared with those reported to the Communicable Disease Surveillance Centre national AIDS reporting system to establish whether any patients were common to both lists. For reasons of confidentiality the AIDS reporting system does not require patients to be identified by name. In cases where the name is withheld a name code (Soundex)¹³ is used instead. The matching process was carried out by computer to select patients with the same Soundex code, sex, and year of birth. Potential matches were then compared by inspection of the original report forms, with name if given, ethnic group, exact date of birth, district of residence, and marital status as matching criteria.

3 Physicians notifying one or more unmarried white men aged 25-64 years with tuberculosis during the 1988 MRC tuberculosis survey were sent a questionnaire that asked (a) whether they had tested any of the patients they had notified during the survey for HIV infection and (b) if so the total number tested and the number positive. This group was selected because unmarried white men in this age group alone accounted for most of the cases of AIDS reported to the Communicable Disease Surveillance Centre by the end of June 1988.

Results

CASES OF AIDS REPORTED TO THE COMMUNICABLE DISEASE SURVEILLANCE CENTRE

By 30 June 1991 a total of 4360 patients with AIDS had been reported to the Communicable Disease Surveillance Centre from England and Wales, of whom 4148 (95%) were male and 3773 (87%) aged 20-49 years (table 1). Two hundred patients (4.6%) were reported to have had tuberculosis.

The number of cases of AIDS reported in England and Wales had risen each year from 46 during 1979-83 to 940 in 1990 (table 2), and the proportion with tuberculosis increased during this period: 17 (2.3%) with tuberculosis were reported in the three years 1984-6, but 146 (5.6%) in 1988-90. This apparent increase should be viewed with caution, however, in the light of the change in the definition of AIDS in 1987.⁶

Of the 4360 patients with AIDS, 3595 (82%) were reported to be of "white" origin and only 259 (6%) to be of "black" and 118 (3%) of "other" ethnic origins (table 3). Tuberculosis was reported in 137 (3.8%) of the "white" compared with 36 (13.9%) of the "black" and 11 (9.3%) of the "other" groups. No trend with age was apparent in the proportion of cases of AIDS with tuberculosis.

Table 2 Number of cases of AIDS reported to the Communicable Disease Surveillance Centre by 30 June 1991 by year of diagnosis and numbers reported with tuberculosis (England and Wales, excluding visitors)

| Year of diagnosis of AIDS | Total cases of AIDS | Cases with tuberculosis | |
|---------------------------|---------------------|-------------------------|-----|
| | | No | % |
| 1979-83 | 46 | 0 | 0.0 |
| 1984 | 97 | 1 | 1.0 |
| 1985 | 215 | 7 | 3.3 |
| 1986 | 429 | 9 | 2.1 |
| 1987 | 594 | 19* | 3.2 |
| 1988 | 797 | 37 | 4.6 |
| 1989 | 877 | 54 | 6.2 |
| 1990 | 940 | 55 | 5.9 |
| 1991† | 307 | 15 | 4.9 |
| Unknown | 58 | 3 | 5.2 |
| Total | 4360 | 200 | 4.6 |

*Change in case definition of AIDS in 1987.⁶

†Half year only.

Table 3 Age and ethnic group distribution of cases of AIDS reported to CDSC by 30 June 1991 and number with tuberculosis (England and Wales, excluding visitors)

| Age (y) at diagnosis | Ethnic group | | | | | | | | | | | |
|----------------------------|--------------|-------------------|-------|-------|-------------------|--------|-------|-------------------|-------------|-------|-------------------|-------|
| | White | | | Black | | | Other | | Unspecified | | | |
| | Total | With tuberculosis | | Total | With tuberculosis | | Total | With tuberculosis | | Total | With tuberculosis | |
| | | No | % | | No | % | | No | % | | No | % |
| 0-19 | 38 | 3 | (7.9) | 17 | 1 | (5.9) | 7 | 0 | (0.0) | 15 | 0 | (0.0) |
| 20-29 | 689 | 28 | 4.1 | 87 | 14 | 16.1 | 24 | 2 | (8.3) | 78 | 3 | 3.8 |
| 30-39 | 1508 | 46 | 3.1 | 100 | 14 | 14.0 | 48 | 4 | (8.3) | 141 | 7 | 5.0 |
| 40-49 | 936 | 42 | 4.5 | 34 | 5 | (14.7) | 28 | 2 | (7.1) | 100 | 2 | 2.0 |
| 50+ | 385 | 17 | 4.4 | 16 | 1 | (6.3) | 10 | 3 | (30.0) | 40 | 3 | (7.5) |
| Unknown | 39 | 1 | (2.6) | 5 | 1 | (20.0) | 1 | 0 | (0.0) | 14 | 1 | (7.1) |
| Total | 3595 | 137 | 3.8 | 259 | 36 | 13.9 | 118 | 11 | 9.3 | 388 | 16 | 4.1 |

Parentheses indicate percentage based on under 50 cases.

The proportion of cases with tuberculosis was slightly higher in women (16/212, 7.5%) than in men (184/4148, 4.4%) (table 4) and may be due to the relatively large proportion of cases of AIDS occurring in women of "black" ethnic origin, in whom rates of tuberculosis are higher than in the white population.

The site of tuberculosis was specified in 178 of the 200 reported cases (89%), and 112 (63%) of these had pulmonary disease, including 23 with extrapulmonary disease as well. Information was not available on the results of bacteriological examination of sputum for the pulmonary cases. The remaining 66 cases (37%) had extrapulmonary disease alone. The site of extrapulmonary disease in all 89 cases (including the 17 with pulmonary disease as well) is given in table 5.

COMPARISON OF CASES FROM TUBERCULOSIS SURVEYS AND AIDS REPORTS

The comparison of 3002 patients in the 1983 MRC tuberculosis notification survey with the patients with AIDS reported to the Communicable Disease Surveillance Centre up to the end of September 1990 gave no exact matches and only one probable match (there was a minor discrepancy in the first name and the date of birth differed by one day). When the list from the 1988 MRC tuberculosis survey was used, however, there were four exact and two probable matches, both with only minor discrepancies. A further three patients from the 1988 survey, known

Table 4 Sex and ethnic group distribution of cases of AIDS, and number with tuberculosis, reported to CDSC by 30 June 1991 (England and Wales, excluding visitors)

| Ethnic group | Sex | | | | | |
|----------------|-------|-------------------|------|--------|-------------------|--------|
| | Male | | | Female | | |
| | Total | With tuberculosis | | Total | With tuberculosis | |
| No | | %* | No | | %* | |
| White | 3485 | 136 | 3.9 | 110 | 1 | 0.9 |
| Black | 180 | 24 | 13.3 | 79 | 12 | 15.2 |
| Asian | 56 | 6 | 10.7 | 3 | 0 | (0.0) |
| Other or mixed | 53 | 5 | 9.4 | 6 | 0 | (0.0) |
| Unspecified | 374 | 13 | 3.5 | 14 | 3 | (21.4) |
| Total | 4148 | 184 | 4.4 | 212 | 16 | 7.5 |

*Parentheses indicate percentage based on under 50 cases.

Table 5 Site of extrapulmonary tuberculosis in the 89 cases* of AIDS reported to the Communicable Disease Surveillance Centre by 30 June 1991 with extrapulmonary disease (England and Wales, excluding visitors)

| Extrapulmonary site | No of cases |
|-------------------------------|-------------|
| Lymph nodes (excluding hilar) | 42 |
| Disseminated | 16 |
| Gastrointestinal tract | 22 |
| Central nervous system | 11 |
| Pleura | 5 |
| Pericardium | 4 |
| Genitourinary tract | 5 |
| Other | 24 |

*Some patients had more than one site of extrapulmonary disease.

to have AIDS on the basis of information provided by the notifying physician, were not identified by the original matching procedure. They were, however, subsequently identified among the cases of AIDS that had been reported to the Communicable Disease Surveillance Centre; they had not been found by the matching procedure as a result of discrepancies in the spelling or form of their surname. At least nine patients therefore had AIDS out of a total of 2163 notified as having tuberculosis in the first six months of 1988 (0.42%) in a follow up period of 27-33 months, compared with one in 3002 (0.03%) in patients from the 1983 survey.

SURVEY OF PHYSICIANS

In the survey of physicians 293 had notified one or more cases of tuberculosis in unmarried white men aged 25-64 years in the 1988 MRC survey. The questionnaire was returned by 254 of the physicians (87%), and 58 of these (23%) stated that they had performed an HIV test on one or more patients notified as having tuberculosis during 1988. Eighty-four of these patients were reported to have been tested for HIV infection, and 18 of those (21%) were positive. As 5164 people of any age were notified with tuberculosis in 1988 in England and Wales¹⁴ the 18 patients reported by the physicians in the survey to be HIV positive give a minimum estimate of 0.43% (18/5164) of all patients with tuberculosis who were HIV positive.

Discussion

It was to be expected that the proportion of

notified cases of tuberculosis found to be in patients with AIDS, on the basis of the register matching exercise, would increase (0.03% in 1983, 0.42% in 1988) because the number of cases of AIDS reported each year in the UK had risen and because extrapulmonary tuberculosis became an AIDS defining condition in 1987. The contribution of the cases of AIDS to the total number of cases of tuberculosis remains very small, however. A further survey of notifications of tuberculosis in England and Wales is being conducted in 1993, and the register matching exercise will be repeated.

The prevalence of HIV infection among patients notified as having tuberculosis in 1988 on the basis of the survey of notifying physicians was at least 0.43%. This is likely to be an underestimate as only physicians notifying cases of tuberculosis in unmarried white men in the 25–64 year age group were surveyed, and therefore physicians seeing other patients at risk of HIV infection may have been omitted. In addition, only a small proportion of physicians carried out any HIV tests. Nevertheless, the prevalence of HIV infection among patients with tuberculosis as estimated by this method was similar to the prevalence of diagnosed cases of AIDS among notified cases of tuberculosis ascertained in the register matching exercise using the 1988 MRC survey (0.42%).

The change in the definition of AIDS in 1987 has made it more difficult to assess whether the diagnosis of tuberculosis precedes or follows the occurrence of other AIDS defining conditions and whether the timing has changed. This, together with the relatively small numbers and the fact that the information on the occurrence of tuberculosis in patients reported to have AIDS may be incomplete in many cases, means that it would not be prudent to attribute significance to this apparent increase in the proportion of patients with AIDS who have had tuberculosis. The overall figure of 4.6% is in broad agreement with the 6% reported by Helbert *et al.*¹⁵ in a series of over 200 patients followed up at a central London hospital.

In the light of the higher prevalence of previous tuberculous infection in people of "non-white" ethnic origin^{11,12} the higher proportion of patients with AIDS in these ethnic groups who had developed tuberculosis is not surprising; but 3.8% of those cases of "white" ethnic origin, which contributed 83% of all cases of AIDS in England and Wales, developed tuberculosis. No substantial differences were seen in the proportion of individuals developing tuberculosis in each of the age groups. This was surprising in view of the low prevalence of prior tuberculous infection in the 20–29 year group; the prevalence of prior infection in 13 year olds in the early 1970s, who would correspond to this cohort, was less than 2%,¹⁶ which raises the possibility of newly acquired infection.

The lungs were the most commonly reported site of tuberculosis in patients with AIDS: pulmonary disease was reported in

63% of cases. Tuberculous infection at this site might, however, be ascertained more often than tuberculous infection elsewhere as a result of the frequent investigation of pulmonary symptoms in patients with AIDS. Although data were not available on whether these patients were sputum smear positive, cases of pulmonary tuberculosis associated with HIV infection are likely to be as infectious as those without HIV infection.¹⁷

At present there is no evidence that the increases in notifications of tuberculosis in England and Wales in 1988 and 1989 are the result of the HIV epidemic.¹⁸ In view of the proportion of patients with AIDS in the UK who develop tuberculosis, however, and the predicted increase in the total number of cases of AIDS in the UK,¹⁹ continued monitoring of the interaction between the two infections is essential. Further follow up studies of cohorts of patients with HIV infection in Britain should be carried out.

The accuracy with which national trends can be monitored depends on the completeness of information. The confidential reporting system at the Communicable Disease Surveillance Centre, which is a valuable surveillance tool, is voluntary; clinicians are urged to report all cases of AIDS and to notify all cases of tuberculosis. Notification of tuberculosis is essential for appropriate contact tracing as well as for monitoring national trends. There is a statutory obligation to notify patients with tuberculosis whether or not they have HIV infection, and special issues of confidentiality in HIV infection should not interfere with this process.

Finally, as tuberculosis may be one of the earliest manifestations of HIV infection the Joint Tuberculosis Committee of the British Thoracic Society recommends that HIV testing should be considered in all cases of tuberculosis and undertaken, after appropriate counselling, in those with risk factors for HIV infection.²⁰

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Adventitia

Trials in the treatment of tuberculosis

The early 1950s was a testing time for young physicians trying to learn the techniques of antituberculous therapy. Our difficulties included the reluctance of injected air to go where it was needed, the bizarre side effects of the new chemotherapy, and thoracic surgeons. Of these three therapeutic alternatives, only the second is needed today and life is that much easier.

There were several kinds of air splintage of the lung and each of these could cause trouble for the inexperienced. To refill an extrapleural pneumothorax, for example, a subclavicular approach was sometimes needed. In one of my earlier efforts a jet of fluid from the water manometer, striking the ample bosom of the outpatient sister, gave her time to evade the subsequent stream of subclavian arterial blood. The induction of an intrapleural pneumothorax could also—in my hands at least—have alarming consequences. The unexpected passage of a litre of air from the thorax through hitherto undescribed anatomical channels into the scrotum enabled me to furnish the *BMJ* with an illustrated case report and a new physical sign. The outcome of pneumoperitoneum induction was equally unpredictable. An apologetic and tearful lady confessed to me on the evening of this procedure that she had done her utmost

to retain the air but eventually had to let it go.

The new drug isoniazid and its isopropyl derivative iproniazid (Marsilid) had just arrived on the scene and we had the opportunity to carry out the first clinical comparison of these two drugs. Iproniazid is a monoamine oxidase inhibitor and so we were able to observe the now well known hypertensive reactions to certain foods and to anticipate from the euphoria and weight gain it induced and from the depression which followed its withdrawal its subsequent use in psychiatry. Weight gain in the iproniazid group was in fact twice that in the isoniazid group and indeed was so dramatic that it masked the development of a full term pregnancy in a patient confined during the previous year to strict bed rest in a sanatorium run by the Sisters of St Vincent de Paul. The psychological effects of iproniazid, especially after withdrawal, were not all favourable. One psychotic patient, harbouring the perhaps not unreasonable conviction that I had poisoned him, attacked me in the clinic inducing multiple skull fractures and an antral haemorrhage. I have always regarded this incident as the taking off point of my career for it was then, for the first time, that my distinguished chiefs at The London Hospital discovered my name.

COLIN M OGILVIE