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Non-tuberculous pulmonary infections in Scotland: a cluster in Lothian?

Friederike G E Böllert, Brian Watt, Andrew P Greening, Graham K Crompton

Abstract

***Background* – A retrospective study was carried out to confirm the clinical impression that, in Lothian, non-tuberculous mycobacterial infections are as common as pulmonary tuberculosis.**

***Methods* – All pulmonary isolates of *Mycobacterium tuberculosis/bovis* and non-tuberculous mycobacteria in Scotland from April 1990 to March 1993, and the notes of all patients with *M malmoense* isolates in Lothian, were reviewed. Information on mycobacterial culture procedures in Scottish laboratories was obtained as part of an audit project.**

***Results* – Of all pulmonary isolates of mycobacteria in Lothian 53% (108/205) were non-tuberculous strains compared with 18% (140/800) for Scotland outside Lothian. Although comparable in population size and laboratory techniques, Lothian (108) had almost twice as many isolates of non-tuberculous mycobacteria as Glasgow (56), but the proportions of *M malmoense* and *M avium intracellulare* complex were similar in both areas. Of 41 patients with *M malmoense* isolates in Lothian 30 (75%) had clinically significant lung disease; only one was HIV positive.**

***Conclusions* – Non-tuberculous mycobacteria pose an increasing clinical problem in Scotland as a cause of pulmonary disease. There is a cluster of cases with *M malmoense* infection in Lothian which cannot be attributed to the high local prevalence of HIV.**

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Keywords: non-tuberculous mycobacteria, *Mycobacterium malmoense*, Lothian.

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A review of all pulmonary mycobacterial isolates in Scotland over three years revealed that almost half of all Scottish isolates of *Mycobacterium malmoense* were from patients in Lothian. *M malmoense* was first described as a pulmonary pathogen in 1977[1] but has since been reported in increasing frequency in Europe.[2–7] The organism has only rarely been isolated in the USA and from immunocompromised patients.[8–10] This study attempted to determine whether the clustering of patients with *M malmoense* in Lothian was genuine or due to the use of different laboratory methods.

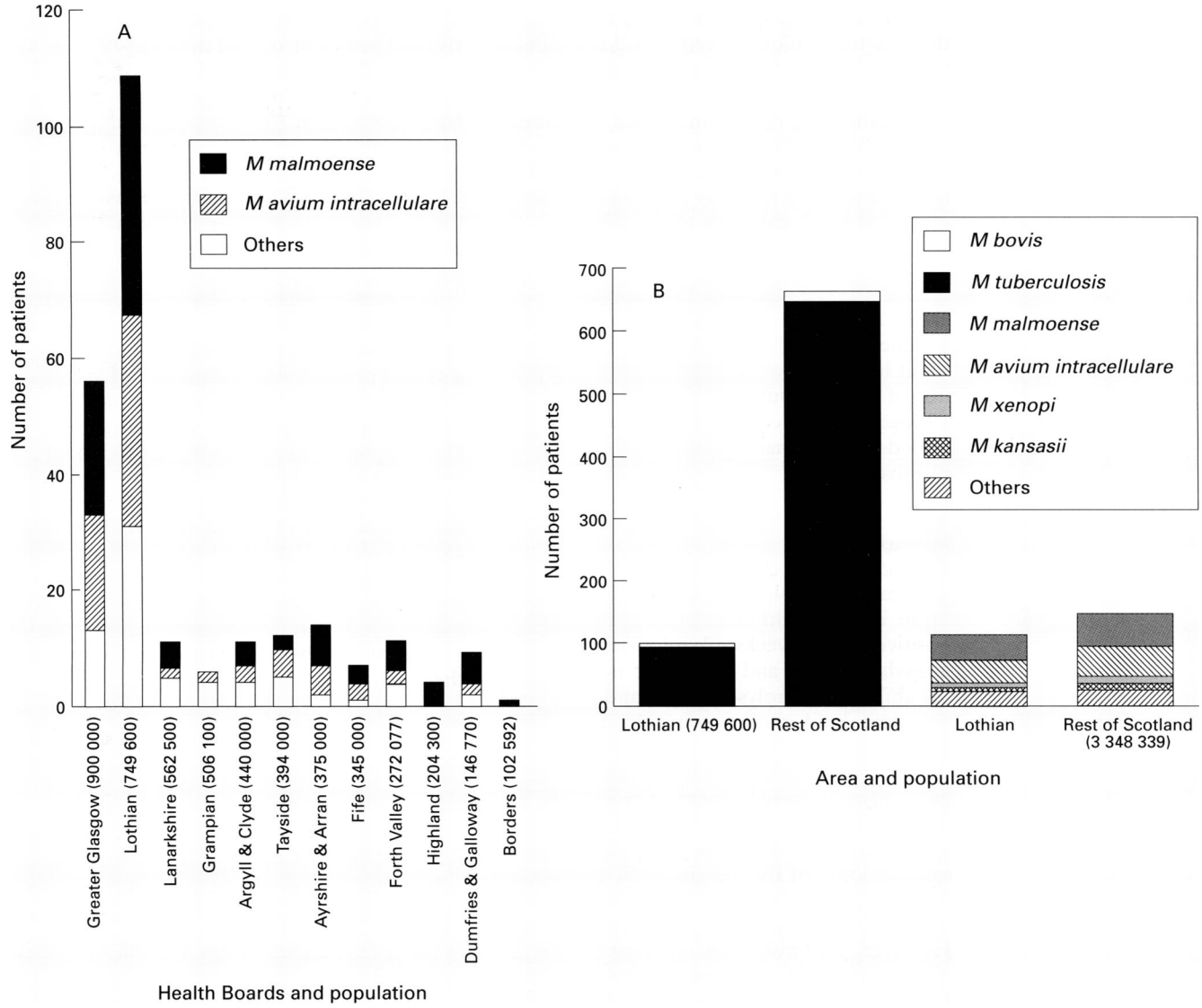
Methods

The names of all patients in Scotland with positive pulmonary isolates (sputum, bronchial washings, lung tissue, pleural fluid, and biopsies) of *M tuberculosis*, *M bovis*, and non-tuberculous mycobacteria during the period April 1990 to March 1993 were obtained from the Scottish Mycobacteria Reference Laboratory in Edinburgh. Age, sex, postcode, HIV status, and details of antimycobacterial treatment for these patients were collected from general practitioners and consultant colleagues. Information on mycobacterial culture procedures in Scottish bacteriology laboratories was available through an audit project of the Reference Laboratory. In order to assess possible clustering of cases within Lothian we related the number of patients with *M malmoense* strains to their postcode districts and the population figure of that area based on the 1991 census.

Results

All data concerning positive mycobacterial cultures represent pulmonary samples of patients which were received by the laboratories during the period April 1990 to March 1993.

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(A) Number of patients with pulmonary isolates of non-tuberculous mycobacteria from April 1990 to March 1993 (listed according to Health Boards in descending order of population size). (B) Number of patients with pulmonary isolates of M tuberculosis/M bovis and non-tuberculous mycobacteria in Lothian and the rest of Scotland from April 1990 to March 1993.

SCOTLAND OUTSIDE LOTHIAN (M TUBERCULOSIS/BOVIS COMPARED WITH NON-TUBERCULOUS MYCOBACTERIA)

There were 800 mycobacterial isolates comprising 644 *M tuberculosis*, 16 *M bovis*, and 140 (18%) non-tuberculous mycobacteria (*M malmoense* 54, *M avium intracellulare* 46, *M xenopi* 11, *M kansasii* 12, and rapid growing mycobacteria 17) in Scotland outside Lothian. The number of patients from whom non-tuberculous mycobacteria were isolated for each health board and the numbers of patients with isolates of *M tuberculosis*, *M bovis*, and non-tuberculous mycobacteria for Lothian and the rest of Scotland are shown in the figure.

LOTHIAN (M TUBERCULOSIS/BOVIS COMPARED WITH NON-TUBERCULOUS MYCOBACTERIA)

There were 205 mycobacterial isolates of which 93 were *M tuberculosis*, four were *M bovis*, and 108 (53%) were non-tuberculous mycobacteria (*M malmoense* 41, *M avium intracellulare* 36, *M xenopi* 9, *M kansasii* 4, and rapid growing mycobacteria 18) in Lothian.

LOTHIAN (M MALMOENSE)

There was an even distribution of the 41 Lothian cases with *M malmoense* isolates (24 men, 17 women, median age 58 years) during the three year period (16, 10, and 15 cases).

Thirty one patients had at least two positive cultures and in 20 the first culture positive sample was also film positive. Eleven patients were tested for HIV; 10 had a negative result and one patient had AIDS.[8] Nine patients had their HIV status assessed as part of a research study and none had any risk factors for the virus.

Thirty of the 41 patients (75%) received treatment with varying combinations of antimycobacterial drugs for a median period of 14 months by the end of March 1993. All of these patients fulfilled the diagnostic criteria of non-tuberculous mycobacterial disease as listed by the American Thoracic Society.[11] In all but one patient regimens included at least rifampicin plus ethambutol. Treatment is ongoing in 16 patients and was started in one patient after March 1993.

Ten of the patients treated died and in four (duration of treatment: 3, 13, 21, and 27

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months) necroscopic examination revealed that the non-tuberculous infection had contributed to death. Three of these patients had additional infection with *Aspergillus fumigatus*.[12]

Identification of the incidence of patients (per 1000 population) with *M malmoense* isolates in selected postcode districts in Lothian revealed that the majority of them lived in the semirural south-east part of the area.

MYCOBACTERIAL CULTURE TECHNIQUES

Of 20 laboratories which culture mycobacteria routinely 17 (85%) incubated their specimens for at least eight weeks, five followed the practice of the Edinburgh Unit and incubated for 12 weeks, and five extended their incubation periods up to a maximum of 16 weeks for film positive samples.

Discussion

M malmoense is characterised by (1) the requirement of prolonged incubation periods of up to 12 weeks although most cultures will be positive at eight weeks; (2) microaerophilia; (3) growth at 25°C and 37°C but not at 45°C; (4) ability to hydrolyse Tween; and (5) a characteristic lipid pattern on thin layer chromatography.[1]

Colonies of the organism on solid media may be small and missed by inexperienced staff. The difference in mycobacterial procedures and lack of experience in detecting the organism might explain some of the geographical variation of *M malmoense* isolates within Scotland, notably in areas where there were no positive cultures. However, this would not account for the increased number of *M malmoense* isolates in Lothian compared with Glasgow, as the laboratory techniques were comparable.

Although our data for Scotland refer to pulmonary isolates of *M malmoense* which, in some cases, might represent casual contamination or colonisation rather than disease, the available literature[6 13] suggests that about 80% of isolates of *M malmoense* are clinically significant. This would result in 43 of the 54 cases (80%) in Scotland outside Lothian and a total figure of 73 cases (43 cases in Scotland outside Lothian plus 30 cases in Lothian) for the whole of Scotland from 1990 to 1993, which is more than a threefold rise in incidence compared with that quoted by France *et al.*[5]

Some clustering of cases was detected within the south-east of Lothian. The gross incidence does not take into account factors such as age distribution and environmental influences, but there was no obvious correlation with deprivation scores or overall mortality.

The natural reservoir for *M malmoense* is unknown, although the organism has been isolated from fresh water in Finland (personal communication, Katila) and from stools of healthy individuals.[14] All households in Lothian postcode areas receive their water as a mixture from a number of reservoirs which renders water contamination as a cause of clustering unlikely.

In summary, this study has revealed that non-tuberculous mycobacteria pose an increasing clinical problem in Scotland, and that there is a cluster of cases with pulmonary *M malmoense* infections in Lothian which cannot be attributed to the high local prevalence of HIV. Our findings might relate in part to laboratory practice and experience in the Reference Laboratory, though this does not hold true for the comparison of Glasgow and Edinburgh. Epidemiological studies into the possible environmental habitat of *M malmoense*, documentation and follow up of all patients with *M malmoense* isolates, and molecular typing of isolates should help to clarify our findings further.

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