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Variation in time and space of non-outbreak Legionnaires' disease in Scotland

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SUMMARY

The main aim of this study was to measure and explain geographic variations in the incidence of Legionnaires' disease in Scotland, particularly to help understand the source of non-outbreak infection.

Between 1978 and 1986 the overall mean annual incidence rate was 7·9 per million (range 3·1–20·2), and for non-outbreak, non-travel cases it was 5·6. There were geographical variations by health board, by city and within cities, e.g. the mean annual incidence rate per million for non-travel, non-outbreak disease was 1·2 in Tayside Health Board, 3·7 in Lanarkshire, 5·6 in Lothian and 14·4 in Greater Glasgow. In Greater Glasgow Health Board non-travel cases lived in and around the city centre and in some postcode sectors there, the mean annual incidence rate exceeded 100. Travel-related cases lived in peripheral areas.

These variations could not be explained by differences in access to and use of diagnostic services, surveillance, or host susceptibility (as reflected by socio-economic status and frequency of other respiratory disease). The explanation probably lay in environmental factors, though differences in agent virulence were not excluded.

The two main conclusions are, that non-outbreak cases were not truly sporadic, and that the space-time variations in incidence support the hypothesis that cooling towers were an important source of infection for non-travel, non-outbreak cases. If so such infection is potentially preventable.

INTRODUCTION

Variation in the frequency of Legionnaires' disease has been reported often, particularly in studies which examine the proportion of pneumonias classified as Legionnaires' disease [1]. McFarlane and colleagues reported that 15% of 127 community-acquired pneumonias in Nottingham were Legionnaires' disease [2], and later, Woodhead and colleagues reported the corresponding proportion to be 5% (of 42) [3]. However, in Bristol 1·4% of 210 community-acquired pneumonias

were Legionnaires' disease [4], but none of 80 pneumonia cases in a London hospital [5]. The British Thoracic Society study of 25 hospitals showed that 2% of pneumonia admissions were diagnosed as Legionnaires' disease [6].

Incidence data on Legionnaires' disease are sparse and are not readily comparable by nation or region. However, there is an apparent geographical variation between and within countries [1, 7]. Annual figures from several European countries indicate marked variation (unpublished figures presented at the European Working Group on Legionella Infections, 1988 and 1989). In Scotland, between 1978 and 1986, about 9 cases per million population were diagnosed compared to about 3 cases per million in both England and Wales, and the United States of America [8]. There has been marked state-by-state variation in the notification rate for all [9], and sporadic [10], Legionnaires' disease in the United States of America. On a smaller scale, the incidence of Legionnaires' disease varied in different parts of the city of Glasgow [11].

Geographical variation in Legionnaires' disease remains unexplained but, as Legionnaires' disease is environmentally acquired, it is tempting to ascribe the variations in disease frequency to environmental differences resulting in varying exposure to legionellae. However, there are several reasons, other than chance or differences in case-definition, why geographical variation occurs, e.g. differences in the organization of the health services; differences in the surveillance methods; differences in clinicians' approach to the diagnosis; differences in host susceptibility; differences in agent virulence.

However, if these explanations could not account for all the geographical variation, then environmental differences might suggest hypotheses about the sources of infection. Presently, the known major sources of infection are hot water systems in institutions and cooling towers [12] but the source often remains elusive in outbreaks [13] and is only exceptionally found in sporadic infection [14].

The objective of this study was to assess whether non-outbreak Legionnaires' disease in Scotland varied in space and time and, if so, to assess the relative importance of the explanations above.

SOURCES OF DATA AND METHODS

Case listing, patient details and classification of cases

The Department of Laboratory Medicine at Ruchill Hospital, Glasgow, has acted as the Scottish reference laboratory for legionella infection since 1977. Details of the laboratory methods have been reported [15, 16]. In brief, the tests done include the indirect fluorescent antibody test (IFAT) using firstly, polyvalent, heat-killed antigens (the range has been extended as new serogroups have been discovered), a positive reaction leading to examination with monovalent heat-killed antigens; culture using buffered charcoal yeast extract agar; the direct fluorescent antibody test; and urinary antigen detection. Samples are accepted from other laboratories both for primary testing and confirmation of results and most Scottish laboratories had used the acting reference laboratory over the study period.

Case-lists held at the Ruchill Hospital Laboratory were cross-checked with another compiled by the Communicable Disease (Scotland) Unit, which is

responsible for surveillance and where voluntary laboratory returns are collated, and a 'master-list' of possible cases prepared.

The background and clinical details were obtained from laboratory request forms and, for cases occurring after mid-1984, from replies to a questionnaire sent by RJF to consultants-in-charge of cases. Details recorded by RJF during telephone calls and letters to clinicians about cases were also used. Rarely, computerized, microfiched Scottish Morbidity Records provided the only source of clinical (diagnostic codes) and address information. For six patients the postcode was not obtained and the health board of residence was deduced from the health board from which the laboratory request came [17].

Hospital consultants and general practitioners were sent a computer printout giving the name, address, date of birth, hospital number and date-of-onset of illness, of patients in their charge. Their view on the validity of the diagnosis was sought. General practitioners were asked about the patient's occupation, and whether the patient had been hospitalized or travelled abroad prior to illness. When permission was obtained from general practitioners, patients were written to; this allowed a further check on the address, and both the travel and hospitalization history. Hospital notes were sometimes examined, with permission from consultants, by RSB.

Based on the above information and the case-definition below, each patient was assigned as a probable case (henceforth called case), possible case, or unlikely case. Further, patients were classified as nosocomial if there was any history of visiting a hospital during the incubation period; travel-associated if there was travel outside Scotland in the 2 weeks prior to their illness; and outbreak-related if they were part of the two outbreaks described in Scotland [18, 19]. The remaining cases, referred to as community-acquired, non-travel, non-outbreak cases were the group of principal interest.

Case definition for Legionnaires' disease

The cases were assigned to three groups as below:

(i) *Probable.* A case with a clinical history of an acute pneumonia or acute lower respiratory tract infection and one or more of the following:

(1) Culture of the organism.

(2) For *Legionella pneumophila* only:

(*a*) A fourfold rise in titre to $\geqslant 64$ (based on IFAT and monovalent heat-killed antigens), or a fourfold fall, but no other clinical diagnosis.

(*b*) A single or static titre of $\geqslant 256$ but no other clinical diagnosis.

(*c*) Positive direct fluorescent antibody test on respiratory secretions or tissue using specific reagents.

(*d*) Legionella antigen detected in urine.

For two cases exceptions were made for the sake of consistency: both had static titres of less than 256 but were categorized as cases during the 1984 Dennistoun outbreak [18].

(ii) *Possible.* This was defined as a patient with one of the following:

(1) An unclear clinical history but laboratory results compatible with infection.

(2) Pneumonia and a single or static titre of $\geqslant 256$ or fourfold rise in titre to $\geqslant 64$ for *Legionella* species other than *L. pneumophila*.

(3) A single or static titre of 64 or 128 to *L. pneumophila* with a history of acute pneumonia or lower respiratory tract infection with supporting epidemiological evidence, e.g. an outbreak.
(4) The criteria under (i) above but with evidence of another cause of pneumonia in addition to Legionnaires' disease.

(iii) *Unlikely or unclear.* A patient with one of the following:
(1) A clinical history of pneumonia, no other diagnosis and a titre of $\leqslant 32$.
(2) Unclear clinical history but a titre of 64 or 128.
(3) No illness, irrespective of laboratory results.

Geographical analysis

Addresses were converted (manually) to 7-unit postcodes using postcode directories. The postcodes were used to classify patients by postcode sector and health board of residence (this task was done by the Northern Health Boards Operational Research Unit using a computerized postcode directory).

The age-sex standardized incidence rates for Legionnaires' disease were calculated for postcode sectors in Scotland, using the 1981 census population as the standard with SMRATE and chloropleth maps were prepared using LINEMAP (Part of a package of computer programmes in the mapping package prepared by the Northern Health Boards, Operational Research Unit [21]).

The statistical significance level for a rate in a geographical unit was based on the Poisson distribution. Adjustment for multiple comparisons was by the formula whereby the adjusted P value is $1\text{-}(1\text{-}P)^m$ (The rationale for this formula is given in simplified form in reference 22).

Laboratory services study

This study will be reported in detail separately. Briefly, microbiology consultants in administrative charge in hospitals in Scotland were sent a short questionnaire (or telephoned). For those laboratories offering a diagnostic service for legionella infection information was collected on the tests done locally and the means by which positive and negative results were confirmed. Laboratories with no local service were asked to whom they sent specimens. All laboratories were asked about whether they would do legionella tests on a serum sample (or other specimen) from a patient with pneumonia only on request, routinely, or based on their judgement of the circumstances of the case.

Relating serology tests done to cases of Legionnaires' disease and pneumonia

Each serology request to the Ruchill Hospital Department of Laboratory Medicine between 1978 and 1986 was categorized by year, month and requesting laboratory. Where known, the numbers of serology tests done by other laboratories were added to the figures. The laboratories were then categorized by health board. The numbers of discharges and deaths for pneumonia (first diagnosis) by health board of residence were obtained from Scottish Hospital Inpatient Statistics [20]. The ratios of the number of serology tests done in each health board in relation to diagnoses of pneumonia and diagnoses of Legionnaires' disease, were calculated. These tests-to-pneumonia and tests-to-Legionnaires' disease ratios were used to assess whether the variation in disease incidence was simply due to variation in

testing for disease. In Greater Glasgow these ratios were calculated for each hospital.

Clinicians' approach to the diagnosis

A brief questionnaire was sent to 167 consultants known to have cared for patients with Legionnaires' disease which asked:

Which one of these three statements best describes your approach to the investigation of pneumonias:

(*a*) I request tests for Legionnaires' disease only if the diagnosis seems likely on clinical or epidemiological grounds.

(*b*) I request tests for Legionnaires' disease as part of the diagnostic 'work-up' of pneumonia on most or all occasions.

(*c*) I request tests for Legionnaires' disease once other common causes of pneumonia have been excluded.

Those who replied (*a*) or (*c*) were categorized as selective testers. Responses were analysed by health board (of workplace of consultants).

Host susceptibility: socioeconomic status and other respiratory disorders

Data from the 1981 census were used to compare the health board populations in terms of unemployment, the housing which was owner occupied, households with more than one person per room, population living in communal establishments, households with no car. For some variables, published data are aggregated for the four health boards in Strathclyde Region (Greater Glasgow, Lanarkshire, Argyll and Clyde, Ayrshire and Arran).

Mortality rates by health board, were compared for pneumonia (ICD code = 480–486), cancer of the trachea, bronchus and lung (ICD = 162) and bronchitis (ICD = 490–491). Morbidity rates were derived from Scottish Hospitals Inpatients Statistics [20] and both published and *ad hoc* analyses were used. The diseases used were: all respiratory diseases (ISD code = 31–32); pneumonia (ISD code = 321); malignant neoplasm of trachea, bronchus and lung (ISD code = 101); and bronchitis, chronic and specified, and emphysema (ISD code = 329).

RESULTS

Quality of information

Assessments of the validity of the diagnosis of Legionnaires' disease were made by consultants, general practitioners and RSB based on their independently held data. Agreement on the diagnosis exceeded 80% of all patients, and 90% for the probable case group.

Of the 167 patients written to, 77% (129) replied. Ninety-five per cent of the addresses were correct; the errors were minor, usually concerning the street number or street. The history of travel abroad was correct in 97% of cases; one person had been wrongly coded as a travel case and three as non-travel cases. Five patients reported exposure to hospital within the incubation period, there being no previous record of this. Records of these 129 patients were corrected as appropriate. These findings show that the errors in the base data set were few.

Table 1. *Laboratory basis for the diagnosis for 378 cases*

Highest titre recorded	Culture positive	DFA positive	Antigen positive	Serology only	Cases
	1. Fourfold rise in titre group ($N = 233$)				
64	1	.	1	16	18
128	5	1	1	43	50
256	6	.	.	65	71
512	4	.	.	72	76
1024	.	.	.	11	11
⩾ 2048	.	.	.	7	7
	2. Fourfold fall in titre group ($N = 16$)				
64	.	.	.	2	2
256	.	.	.	5	5
512	.	.	.	6	6
1024	.	.	.	2	2
⩾ 2048	.	.	.	1	1
	3. Static titre group ($N = 129$)*				
8	9	8	.	.	13†
16	2	1	.	.	2‡
32	1	1	.	.	2
64	1	.	.	2§	3
128	1	2	.	.	3
256	2	1	.	49	51‡
512	.	.	.	47	47
⩾ 1024	.	.	.	8	8
Column total	32	14	2	336	378

* Row totals may differ from the sum of the numbers in each row as some patients were both culture and DFA positive.

† Four patients were both culture and DFA positive.

‡ One patient was both culture and DFA positive.

§ These two patients were defined as cases in the 1984 outbreak in Dennistoun.

Epidemiology

Of 456 potential cases, 378 were classified as 'probable' (henceforth called cases), 54 'possible' and 24 as 'unlikely or unclear'. All but one case had either acute pneumonia (the majority) or lower respiratory tract infection; the exception had a ''flu-like illness' and was an outbreak case. Table 1 summarizes the laboratory evidence; about two-thirds of cases had a fourfold rise in titre. It is notable that the static titre group had a disproportionate number of DFA positive and culture positive cases. This preponderance is explained by the fact that patients who die shortly after admission can only be serologically tested once, and these patients are more likely to provide tissue, either post-mortem or during life, for culture and DFA test. Further, where a tissue based diagnosis has been made, a second serum may be considered unnecessary. Lastly, where a serological rise has been demonstrated the need for tissue is obviated. The two patients with a static titre of 64 were part of the 1984 outbreak. *Legionella pneumophila* serogroup one accounted for 92% of cases.

The ages of the patients ranged from 14 to 86 years (mean 59) and the male to female ratio was 2:1.

Table 2. *Number of cases and incidence rate by year and travel history and for non-outbreak cases*

Year	No travel history: All cases	No travel history: Non-outbreak	Travel history	All cases
1973*	0	0	4	4
1974*	1	1	1	2
1975*	0	0	0	0
1976*	0	0	2	2
1977*	0	0	4	4
1978	12 (2·3)	12 (2·3)	6 (1·2)	18 (3·5)
1979	20 (3·9)	20 (3·9)	14 (2·7)	34 (6·6)
1980	15 (2·9)	15 (2·9	13 (2·5)	28 (5·4)
1981	11 (2·1)	11 (2·1)	5 (1·0)	16 (3·1)
1982	21 (4·1)	21 (4·1)	11 (2·1)	32 (6·2)
1983	35 (6·8)	35 (6·8)	12 (2·3)	47 (9·1)
1984	85 (16·5)	52 (10·1)	19 (3·7)	104 (20·2)
1985	59 (11·5)	46 (8·9)	7 (1·4)	66 (12·8)
1986†	8 (1·6)	8 (1·6)	13 (2·5)	21 (4·1)
Total‡	267 (5·8)	221 (4·8)	111 (2·2)	378 (7·9)

* Due to the small numbers, rates were not calculated for the years to 1977.
† Using 1985 population figures.
‡ Rates for totals are based on the average of 1978–1986 using the 1981 census data as denominator.

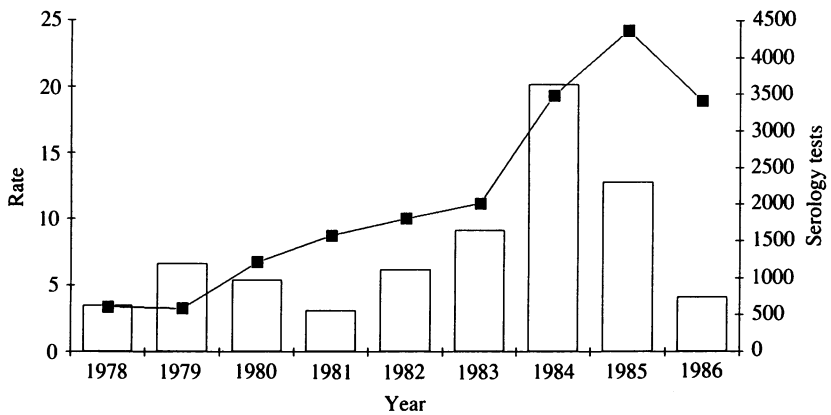

Fig. 1. Relationships of annual incidence rate (□) and the number of serology tests (■).

One hundred and eleven (29%) cases had travelled outside Scotland within the 2 weeks prior to illness, another 33 were linked with the 1984 outbreak, 13 with the 1985 outbreak and 16 were possible nosocomial cases.

Table 2 shows the number of cases and incidence rate per million, by year of illness and travel history. The mean annual incidence rate between 1978 (when a systematic laboratory service was first provided) and 1986 was 7·9 but fluctuated,

Table 3. *The numbers and cumulative incidence rates (adjusted for age and sex) of travel- and non-travel-associated cases by health board, 1978–86*

	Travel-associated cases		Non-travel-associated cases		All cases	
Health board	Number	Rate/ million	Number	Rate/ million	Number	Rate/ million
Argyll and Clyde	6	13·7	6	14·1	12	27·8
Ayr and Arran	8	21·1	8	21·0	16	42·1
Borders	1	9·1	3	24·5	4	33·6
Dumfries and Galloway	3	15·4	2	9·9	5	25·3
Fife	5	15·1	4	12·0	9	27·1
Forth Valley	5	18·8	4	15·1	9	33·9
Grampian	2	4·5	4	8·5	6	13·0
Greater Glasgow	36	34·4	167	160·6	203	195·0
Highland	4	22·0	1	5·6	5	27·6
Lanarkshire	9	16·5	23	40·4	32	56·9
Lothian	11	15·4	36	49·9	47	65·3
Orkney	0	0·0	1	49·0	1	49·0
Shetland	0	0·0	0	0·0	0	0·0
Tayside	10	25·8	4	10·5	14	36·3
Western Isles	0	0·0	1	34·4	1	34·4
Total	100	19·4	264	51·3	364	70·7

e.g. for non-outbreak cases there was a six-fold variation, and for travel-related cases a 2·2-fold variation. Figure 1 shows the annual variations in incidence were largely unrelated to the number of serology tests done. Table 3 shows the incidence, by travel history, of Legionnaires' disease by Scottish Health Board; there was marked variation. The relative risk of infection in Greater Glasgow Health Board, particularly for non-travel disease, was much higher than elsewhere as shown in Table 4. There was modest variation in travel-related disease. These variations were unlikely to result from chance, e.g. the probability of having 119 or more cases of community-acquired, non-travel, non-outbreak cases in Greater Glasgow Health Board, given the distribution for Scotland, was $< 0{\cdot}00005$ (Poisson Distribution, adjusted for multiple comparisons).

There were abrupt changes in the annual incidence of disease within several health boards, e.g. in Lothian Health Board there were no cases in 1981, 11 in 1982, 16 in 1983 and 2 in 1984 (variation in time will be discussed in detail in a future paper).

The incidence rate was calculated for all Scotland's postcode sectors (about 900) and 16 postcode sectors were identified as having a significantly high number of non-travel cases ($P < 0{\cdot}01$); two were in Lothian Health Board, the others in Greater Glasgow. In four postcode sectors the number of non-travel cases remained significantly high ($P < 0{\cdot}0001$) after adjustment for multiple comparisons; the rates (cases) were 101 (10), 115 (6), 176 (14) and 273 (17) per million per year compared to the Greater Glasgow average of 17·8. When only community-acquired, non-outbreak, non-travel cases were considered, six postcode sectors had a significantly high number of cases and two were statistically significant after

Table 4. *Relative risk of infection in Greater Glasgow compared to the rest of Scotland and selected health boards*

Comparison groups	Relative risk
Travel-associated infection	
Greater Glasgow compared to	
Rest of Scotland	2·2
Lothian	2·2
Lanarkshire	2·1
Tayside	1·3
Argyll and Clyde	2·5
Non-travel infection	
Greater Glasgow compared to	
Rest of Scotland	6·9
Lothian	3·2
Lanarkshire	4·0
Tayside	15·3
Argyll and Clyde	11·4
Non-travel, non-outbreak infection	
Greater Glasgow compared to	
Rest of Scotland	5·6
Lothian	2·6
Lanarkshire	3·9
Tayside	12·3
Argyll and Clyde	9·2
Non-travel, non-outbreak, community-acquired infection	
Greater Glasgow compared to	
Rest of Scotland	5·6
Lothian	2·4
Lanarkshire	3·6
Tayside	10·9
Argyll and Clyde	9·8

adjustment for multiple comparison; the rates (cases) were 93 (9) and 117 (6) per million per year compared to the Greater Glasgow average of 12·7. The postcodes with a high incidence either lie north of the River Clyde and in central areas of the city, or lie elsewhere near to the river; as shown in Fig. 2(*a*, *b*), which with maps outlines the postcode sector boundaries and shows both the place of residence of cases and the standardized incidence rates.

The pattern described above was seen in 1978, 1979, 1983, 1984 and 1985, and applied to both men and women, and to cases above and below 65 years (maps available from authors). By contrast, as shown in Fig. 3(*a*, *b*), travel-related Legionnaires' disease was commoner in peripheral areas of Greater Glasgow.

Laboratory services

Data were obtained from all 36 laboratories contacted and all used the Ruchill hospital laboratory either to confirm positive results or to do tests on their behalf. Two laboratories routinely did serology for legionella infection on all patients with pneumonia. They were in health boards with a low incidence of disease.

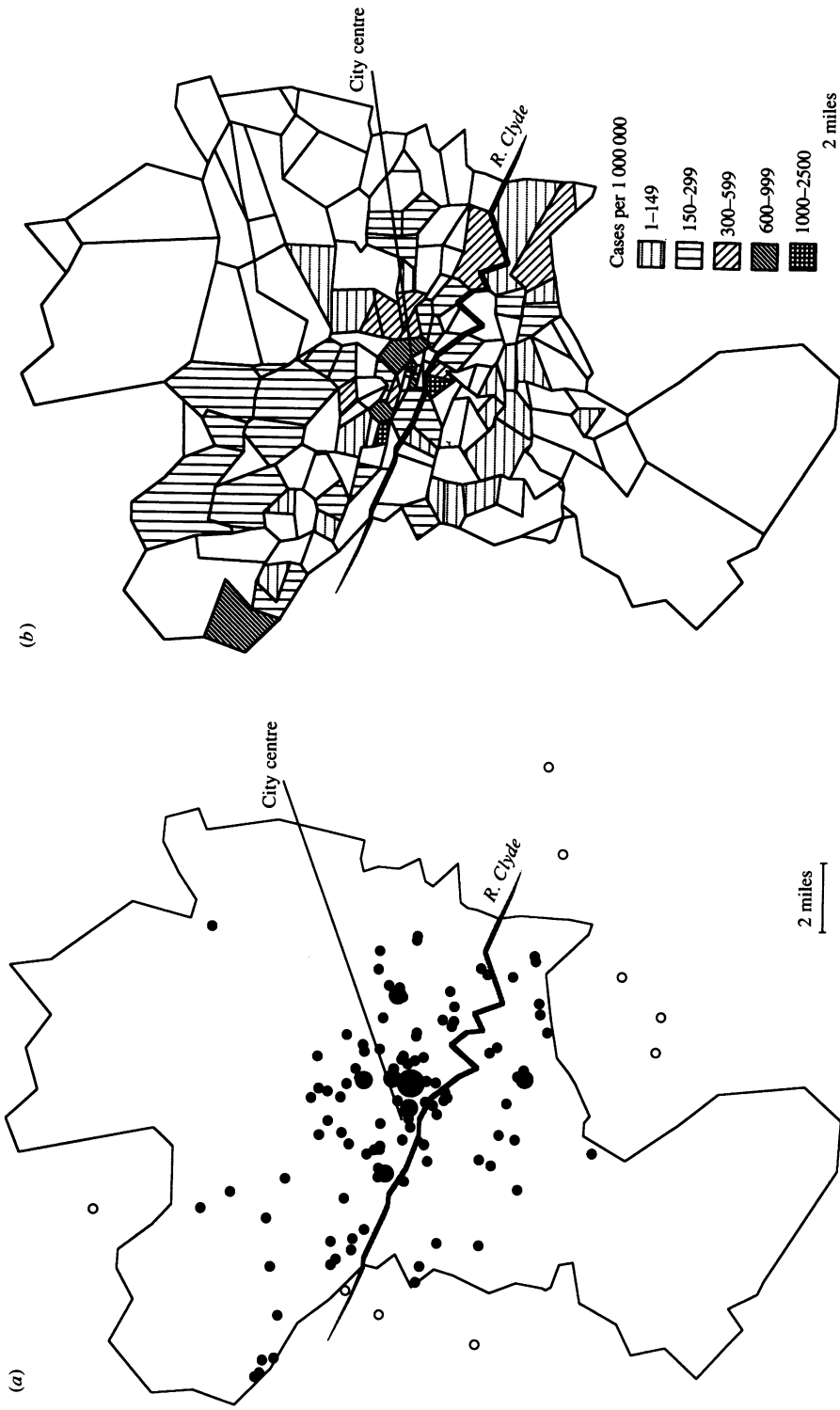

Fig. 2. (*a*) Community-acquired, non-travel, non-outbreak Legionnaires' disease in GGHB and surroundings 1978–86.
(*b*) Community-acquired, non-travel, non-outbreak cases in GGHB, rates per million 1978–86 by postcode sectors.

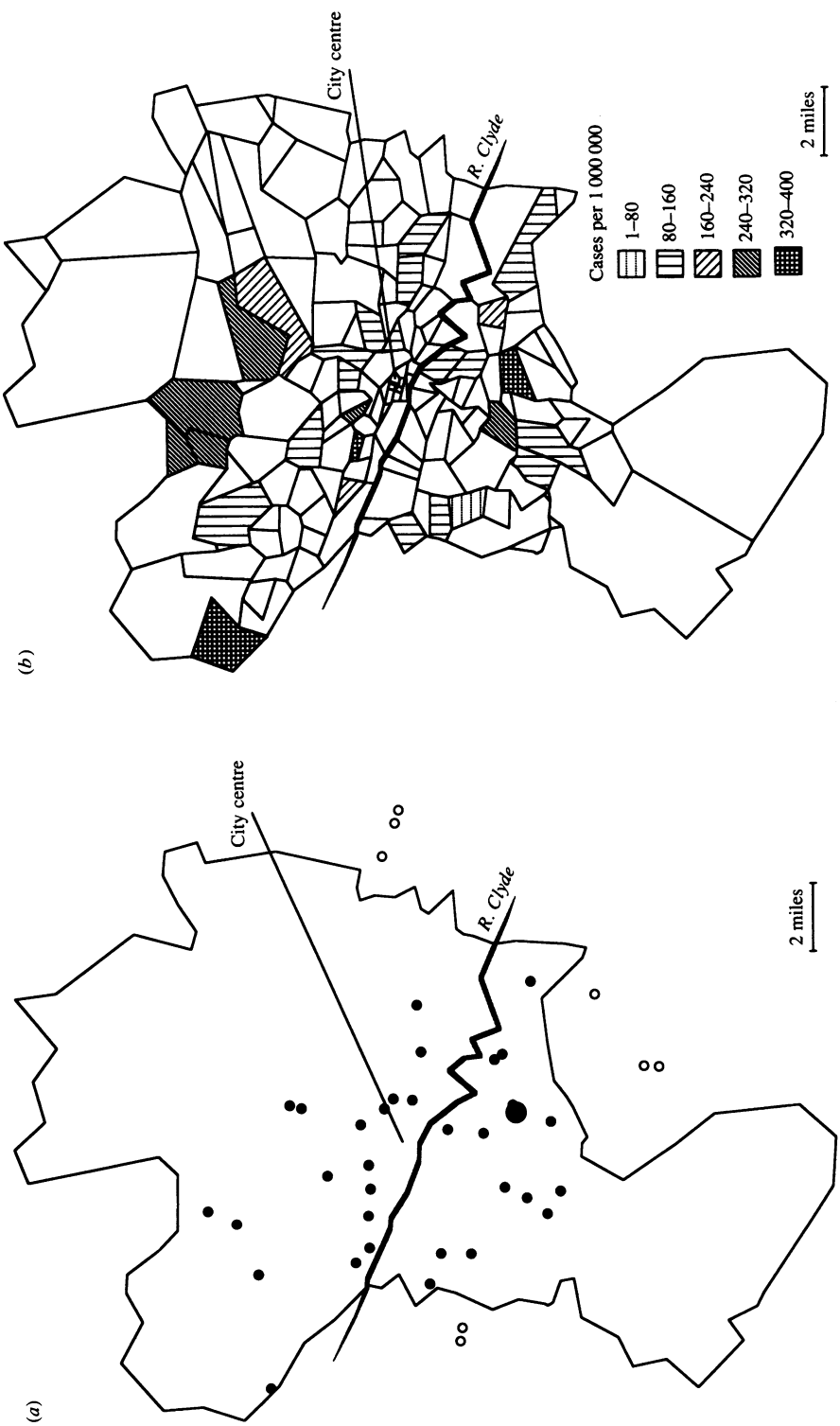

Fig. 3. (*a*) Travel-related Legionnaires' disease in GGHB and surroundings 1978–86. (*b*) Travel-related Legionnaires' disease in GGHB 1978–86, rates per million by postcode sector.

Table 4. *Relationship of serology tests to Legionnaires' disease and pneumonia by health board, 1978–86*

Health board	Serology tests	Legionnaires' disease cases	Pneumonias (1st diagnosis)	Ratio of tests to Legionnaires' disease	Ratio of tests to pneumonia
Argyll and Clyde	867	12	5221	72	0·17
Ayrshire	442*	16	4638	28	0·10
Borders	565	4	1083	141	0·52
Dumfries and Galloway	189	5	1511	38	0·13
Fife	658	9	2785	73	0·24
Forth Valley	471	9	3072	52	0·15
Greater Glasgow	8450†	203	15051	42	0·56
Grampian	406‡	6	5535	68*	0·07
Highland	480	5	1820	96	0·26
Lanarkshire	1716	32	5504	54	0·31
Lothian	3675†	47	8888	78	0·41
Orkney ‖	—	1	260	—	—
Shetland ‖	—	0	163	—	—
Tayside	966§	14	7005	69	0·14
Western Isles ‖	—	1	233	—	—
Totals or averages	18885	364	62769	52	0·30

* Local serology (RMAT); figures include local tests.
† Local serology results not included (two laboratories).
‡ Underestimate: serology from one hospital not included.
§ Based on Ruchill Hospital data 1978–84 and local laboratory data for 1985 and 1986.
‖ Tests diverted to Ruchill via other laboratories.

Serology studies

Table 5 shows that there was variation, by health board, in the tendency to undertake tests for possible Legionnaires' disease (tests-to-pneumonia ratio), and variation in the likelihood of making a diagnosis (tests-to-Legionnaires' disease). As indicated by the tests-to-pneumonia ratio, the tendency to test for possible Legionnaires' disease when managing pneumonia was greatest in Greater Glasgow, Borders, Lothian and Lanarkshire Health Boards. However, the yield of cases per test, as indicated by the tests-to-Legionnaires' disease ratio was high in Greater Glasgow but very low in the Borders, low in Lothian and intermediate in Lanarkshire Health Board.

Up to 1984 the tests-to-pneumonia ratios in Greater Glasgow (0·38) and Lothian Health Board (0·35) were similar, but, in 1985 and 1986, the years following the two Glasgow outbreaks, the ratio was 1·20 in Greater Glasgow and 0·62 in Lothian.

The tests-to-pneumonia and tests-to-Legionnaires' disease ratios showed much hospital-to-hospital variation in Greater Glasgow. The hospitals with the highest test-to-pneumonia ratios were in North Glasgow, and on average North Glasgow hospitals had twice as many tests per pneumonia case (0·8) compared with South Glasgow hospitals (0·4). However, the diagnostic yield per test, as indicated by the tests-to-Legionnaires' disease ratios, was also higher in North Glasgow (1 case per 37 tests) than in South Glasgow hospitals (1 case per 51 tests). Examination of

these ratios for each hospital by year showed that there were important trends in time, compatible with the view that when cases were diagnosed, serological testing increased rapidly but, in the face of a low number of cases, testing rates increased slowly.

Consultants' approach to diagnosis

Sixty-three per cent (106) of questionnaires were returned. Two thirds of consultants were selective testers, i.e. used approach (*a*) or (*c*). Thirteen of the 23 who were not selective testers worked in Greater Glasgow Health Board (25% of GGHB respondents), 4 in Lothian (17% of LHB respondents) and 6 in other health boards (20% of respondents).

Host susceptibility

Differences in socioeconomic indicators of deprivation existed but were moderate in relation to the variation in Legionnaires' disease as shown below:

(i) For unemployment amongst men (16–64 years) the range was 6·8% (Grampian) to 16·5% (Strathclyde Region, including Greater Glasgow);
(ii) Unemployment amongst women (16–64 years) ranged from 3·5% (Grampian) to 7·4% (Greater Glasgow);
(iii) Owner-occupied housing ranged from 30·3% (Forth Valley) to 42·4% (Lothian). The figure for Greater Glasgow was 32·0%.
(iv) Households with more than one person per room ranged from 26·8% (Dunfermline and Galloway) to 38·7% in Strathclyde Region.
(v) Population living in communal establishments ranged from 1·3% (Strathclyde Region) to 2·5% (Highland).
(vi) Population with no car in the household ranged from 35·9% (Dumfries and Galloway) to 54·6% (Strathclyde Region).

Similar analysis of the five health districts of Greater Glasgow (two of which are south of the River Clyde) showed no consistent, substantial and relevant differences in socioeconomic status.

For other respiratory diseases Greater Glasgow ranked high but the excess was relatively small. The standardized mortality ratios (SMRs) in Greater Glasgow for pneumonia, cancer of the trachea, bronchus and lung and bronchitis were 126, 139 and 116 respectively.

For hospital admission rates for respiratory disease a similar picture emerged: the range of rates in mainland health boards was relatively narrow and the Greater Glasgow rates ranked high as follows:

(i) For all respiratory diseases, rates per million ranged from 6899 (Dumfries and Galloway) to 12319 (Lothian) with the Greater Glasgow figure being 11392;
(ii) For malignant neoplasm of trachea, bronchus and lung the range was 1433 (Highland) to 2574 (Greater Glasgow);
(iii) For pneumonia the range was 855 (Fife) to 1772 (Tayside) with the Greater Glasgow figure being 1569;
(iv) For bronchitis the range was 385 (Forth Valley) to 1180 (Lothian), with the Greater Glasgow figure being 967;

(v) When rates of pneumonia discharges and deaths were tabulated by sex and a number of age-groups, the greatest margin was 64% (Greater Glasgow men 45–74 years compared to Lothian men 45–74).

Similar analyses were done for the five health districts in Greater Glasgow but no consistent and substantial differences were found for non-legionella respiratory disease to explain the excess of cases north of the River Clyde.

DISCUSSION

The mean annual incidence of Legionnaires' disease in Scotland (7·9 per million) was about 2·5 times that reported in England and Wales and the USA over the period 1978–88 [8], and varied in space and time. The geographical variation could theoretically be explained by differences in the organization of hospital and diagnostic services; surveillance methods; the approach of clinicians to the diagnosis; differences in host susceptibility; environmental differences; and agent virulence.

Organization of hospital and laboratory services

Legionnaires' disease is usually a diagnosis made in hospital and variability in access to hospital could, theoretically, result in variation in disease incidence. However, the admission rates for travel-related Legionnaires' disease, all pneumonias, and other respiratory diseases showed modest variation by health board. As we would expect this effect to be non-specific, this explanation cannot hold.

Laboratory services for the diagnosis of Legionnaires' disease were available throughout the study period at the Ruchill Hospital laboratory, and were developed in a number of other laboratories subsequently. Laboratories in Scotland sent specimens to the reference laboratory, either for primary tests or confirmation. Hence the findings are not an artefact arising from varying laboratory organization and practices.

Surveillance

The Communicable Diseases (Scotland) Unit collated voluntary laboratory returns throughout the study period, and the Ruchill Hospital Laboratory maintained registers of possible cases. Differences in the quality of surveillance cannot reasonably explain these findings.

Clinicians' approach to the diagnosis

The use of a diagnostic test relates to awareness of the disease and ease of access to the diagnostic service. Physicians in the Glasgow area would have been alerted by the publicity associated with the 'Benidorm' outbreak [23] and the two outbreaks in the City of Glasgow [18 19], and were closest to the reference diagnostic facility. Yet, despite intensive testing following the outbreaks, the tendency to do legionella serology in Greater Glasgow (56 tests per 100 pneumonia discharges/deaths) was little higher than in some other health boards, e.g. Lothian (41 tests per 100 pneumonias), and less than twice that in Scotland (30 tests per 100 pneumonias). Moreover, despite more tests being done, the likelihood of a positive result was higher in Greater Glasgow (one case per 42 tests) than in most

health boards, e.g. Lothian (one case per 78 tests), and Scotland as a whole (one case per 52 tests). Therefore, the high incidence of disease in Greater Glasgow was not a consequence of, but the reason for, a higher rate of testing. Indeed, up to 1984, when the first major outbreak occurred, the ratio of tests-to-pneumonia in Greater Glasgow (0·38), was comparable to that in Lothian (0·35); higher rates of testing followed the outbreaks [18, 19]. Similarly, the variation in the disease within Greater Glasgow Health Board could not be explained by the differences in the numbers of serology tests done in different hospitals.

Host susceptibility

Some of the geographical variation undoubtedly relates to host factors other than age and sex (for which adjustment has been made), e.g. smoking and alcohol consumption, occupation, immunosuppression. However, there is no population data to assess such effects.

A high population susceptibility would probably be non-specific and hence expected to be associated with an excess of other respiratory disorders, e.g. lung cancer, chronic bronchitis and emphysema (one common factor being smoking) and, perhaps all pneumonia. Variation between health boards for these disorders was comparatively small. Further, mortality and morbidity data for 87 neighbourhoods in Greater Glasgow Health Board show that the variation in rates for most respiratory disorders [24, 25] was small in comparison to Legionnaires' disease, e.g. the highest rate for lung cancer and bronchitis were 3·3 and 2·3 times, respectively, the health board average, but in several postcode sectors the incidence of Legionnaires' disease was about 10 times the health board average. (The variations shown by the routine data quoted above [24, 25] have not been validated and may be artefact.)

Agent virulence

Variation in Legionnaires' disease incidence could reflect geographical differences in the virulence of legionellae. Unfortunately, there is no empirical research on this matter and insufficient is known about the factors which determine virulence to predict, on first principles, whether this might be an important explanation.

Comparison of travel and non-travel infection

The modest variation in the incidence of travel-associated disease, provides further evidence against the hypothesis that the variation in community-acquired Legionnaires' disease merely reflects patterns of care, diagnostic capacity or ability, or host susceptibility. The incidence of travel-related Legionnaires' disease in GGHB was about twice the Scottish average; the differential might be explained as above or as a result of the Glasgow population travelling to higher-risk destinations than the rest of the population, or both.

By a process of exclusion there is support for the hypothesis that the geographical variation reflects environmental differences. We have unpublished observations in Glasgow which support the hypothesis (paper in preparation).

Presently, the major sources of outbreak-related infection are well understood,

i.e. cooling towers and complex hot-water systems [12], but the sources of non-outbreak infection are unclear [11, 12, 14, 26]. It is likely, though unproven, that aerosols from cooling towers and hot water systems also cause non-outbreak disease but their relative importance is unknown. The only conclusive published report on the subject traced the source of two cases of infection to home hot water supplies [14]. Addiss and colleagues [26] reported that the source of infection of two apparently sporadic cases of Legionnaires' disease who were diagnosed at about the same time, and who lived close to each other, was probably a cooling tower. The strains of *Legionella pneumophila* serogroup I isolated from the patients and from a cooling tower (which had no drift eliminator) 300 m from their homes were indistinguishable on monoclonal antibody and electrophoretic enzyme analysis. The patients lived downwind to this tower. Organisms from other environmental sites were distinguishable from the clinical strain. Current knowledge is insufficient to develop guidelines for preventing non-outbreak infection which, numerically, exceeds outbreak-related disease.

If community-acquired, non-travel, non-outbreak infection was acquired largely from hot-water sources such as showers, taps, baths, etc., we would expect that the risk would be fairly uniformly distributed across geographical boundaries, and relatively stable over time. By contrast, the risk of infection from cooling towers is variable, being related to maintenance procedures and the water quality and temperature changes which occur with the use of cooling towers. The observation that community-acquired, non-outbreak Legionnaires' disease varied in time and space supports the hypothesis that cooling towers were a source of such infection. If so, the implication for the prevention of such infection on a community basis is clear: better maintenance of cooling towers. By contrast, if the major source were hot water systems, particularly in the home environment, the prospect for control would be poor for they are numerous. The fact that non-outbreak cases showed clustering in space and time indicates they were not truly sporadic and points to a common source of infection. As such, the present conservative approach to the investigation of apparently sporadic cases needs to be questioned. The epidemiological investigation of these sporadic cases should be based on the premise that there may be a common link.

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