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Legionnaires' disease in Europe 2000–2002

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SUMMARY

Each year, countries that participate in the European Surveillance Scheme for Travel Associated Legionnaires' Disease (EWGLINET) are requested to complete a set of standardized reporting forms that provide epidemiological and microbiological information on the total number of cases (non-travel as well as travel-related cases) detected in their country. Trends at the national and aggregated European level have been analysed for 2000–2002. For this period, 10 322 cases of Legionnaires' disease were reported and national infection rates ranged from 0 to 34·1 cases per million population. A total of 189 outbreaks were associated with nosocomial infection, community exposure or travel. The upward trend in diagnosis through the urinary antigen detection test has resulted in a higher ascertainment of cases in many countries. However, the decline in diagnosis by culture of the organism is likely to severely hamper outbreak investigations in the future if fewer clinical isolates are available for matching with environmental isolates. This important data-set has been used for studying the effectiveness of surveillance and legionella control and prevention programmes within Europe.

INTRODUCTION

Since the organism responsible for Legionnaires' disease was discovered in 1976, a large knowledge base has been established about the ecology of the *Legionella* species and its associated epidemiological and environmental factors. In 1986 the European Working Group for Legionella Infections (EWGLI) was established to bring together the scientific expertise in Europe on this newly discovered disease and in 1987 a European Surveillance Scheme for Travel Associated Legionnaires' Disease (EWGLINET) was introduced by the group. Travel-associated legionella infections remain a significant public-health problem in Europe, as do legionella infections associated with other settings such as hospitals, spa pools and the community. In recent years changes in diagnostic methods and improved surveillance in many countries have led to a dramatic rise in the number of cases detected in Europe as a whole. Large outbreaks have also contributed to this increase. Data on trends between 1996 and 1999 are already published [1–4]. This paper reviews the overall impact of Legionnaires' disease in Europe and trends between European countries based on data for all categories of cases for the years 2000–2002.

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METHODS

Each year, countries that participate in EWGLINET are asked to complete a set of standardized reporting forms that provide epidemiological and microbiological information on the total number of cases

detected in each reporting country (non-travel- as well as travel-related cases). The data are sent annually to the EWGLINET coordinating centre for analysis of European trends and trends between countries and are available from 1993 onwards. Seven forms are used to collect the data. One table provides data on total cases and deaths together with the population base for calculating the annual rate per million population within the respective country. Four tables request data on the annual total of cases by sex, category of exposure [hospital (nosocomial), community, travel], country of travel for travel-associated infections and details of outbreaks by type, duration, suspected source of infection and number of associated cases. Two tables provide information on methods of diagnosis and number of legionella isolates by species and serogroup. The number of countries completing the forms has increased from 19 in 1993 to 32 in 2002. This paper examines the data for the years 2000–2002 and was provided by 28, 29 and 32 countries respectively.

Investigation of travel-associated cases

Between 2000 and 2002, important changes in case definitions and reporting procedures were introduced by EWGLINET for cases of travel-associated Legionnaires' disease. In January 2001 the European-wide case definition for travel-associated clusters detected or reported to EWGLINET was changed from being two or more cases who stayed at or visited the same accommodation site within 6 months of each other to one where onset of infection was within 2 years of each other. This change simplified EWGLINET advice for following up accommodation sites associated with clusters or outbreaks. In 2002 European Guidelines for the Control and Prevention of Travel Associated Legionnaires' Disease [5] were introduced by EWGLINET that placed further emphasis on the need for a rapid public-health response to cluster alerts. This emphasis includes a requirement by the participating country of infection to report back to the EWGLINET coordinating centre, within a specified time period of 2 and 6 weeks from the cluster alert, on the immediate control measures taken and the final investigation results obtained at the accommodation site or other suspected site of infection. Both the change in case definition and the introduction of the European Guidelines have led to an increase in the number of travel-associated clusters detected and acted upon from 2001 onwards.

Table 1. *Total reported cases and rate per million population 1993–2002*

Year	No. of cases	No. of countries contributing data	Population (millions)	Rate per million population
1993	242	19	300	4·14
1994	1161	20	346	3·35
1995	1255	24	339	3·70
1996	1563	24	350	4·46
1997	1360	24	351	3·87
1998	1442	28	333	4·33
1999	2136	28	398	5·38
2000	2156	28	400	5·38
2001	3470	29	455	7·60
2002	4696	32	467	10·1

RESULTS

In the 10-year period 1993–2002, a total of 20 481 cases of Legionnaires' disease were reported by an annual average of 25 European countries (range 19–32 countries) (Table 1). The aggregated annual totals rose from 1242 in 1993 to 4696 in 2002, an increase of 74% over the 10 years. Over 10 000 of these cases occurred in the 3 years 2000–2002; 2156 in 2000, 3470 in 2001 and 4696 in 2002. Part of this rise is accounted for by the contribution of data from more countries in recent years, although overall incidence rates per million population show a similar increase from 4·14 in 1993 to 10·1 in 2002 (Table 1). The sharp rise in the total European data-set was first noted in 1999 when 2136 cases were reported, almost 700 more than the previous year. The next big increase occurred in 2001 when 3470 cases from 29 countries were reported, and a further rise of more than 1200 cases compared with the year before, was reported in 2002. Four countries in 2000 reported no cases detected (Estonia, Latvia, Lithuania and the Slovak Republic) and three countries also made nil returns in 2001 (Estonia, Lithuania and Northern Ireland) and 2002 (Bulgaria, Lithuania and Malta).

Reports from six countries, England & Wales, France, Germany, Italy, The Netherlands and Spain account for the majority of the overall rising trend between 2000 and 2002 (Table 2). Spain reported more than 1000 cases in 2001 and again in 2002 along with France. Other countries from lower baselines also reported the doubling or trebling of cases over the 3-year period (e.g. Finland and Switzerland). The

Table 2. *Cases and rate per million population by selected countries 2000–2002*

Country	Population (millions)	All reported cases 2000	All reported cases 2001	All reported cases 2002
Denmark	5·4	97 (18·3)	115 (21·7)	104 (19·2)
England & Wales	52·9	183 (3·5)	175 (3·3)	382 (7·2)
France	60·2	597 (10·2)	800 13·3)	1018 (16·9)
Germany	82·4	60* (1·5)	328 (4·0)	288 (3·5)
Italy	57·8	173 (3·0)	302 (5·3)	605 (10·5)
The Netherlands	16·1	176 (11·2)	182 (11·4)	288 (17·9)
Spain	40·5	466 (11·8)	1026 (25·5)	1380 (34·1)
Total reported cases (all countries)	467	2156 (5·4)	3470 (7·6)	4696 (10·1)

* Data based on regional population in 2000.

total reported European deaths in the same period were 801; of which 234, 284 and 283 were reported annually – an overall declining case fatality rate of 11% in 2000, 8% in 2001 and 6% in 2002 compared with 13% in 1998. Of the aggregated cases for the period 2000–2002, 65% were male, 24% were female and 11% were of unknown sex.

Incidence rates per million population

Calculation of infection rates per million population were based on regional populations rather than national populations for six countries in 2000 and four each in 2001 and 2002 and these data may not be representative of the national incidence rate in their respective countries. A rate of <1 case per million population was reported from the Czech Republic, Latvia, Northern Ireland and Poland in 2000, Ireland, Poland and the Slovak Republic in 2001 and Estonia, Poland and the Slovak Republic in 2002. Highest rates per million population were reported from Malta (26·3) and Denmark (18·3) in 2000, Spain (25·5) and Denmark (21·7) in 2001 and again Spain (34·1) and Denmark (19·2) in 2002 (Table 2).

Category of cases

Countries contributing to the European data-set are requested to report their cases according to whether they are associated with community, nosocomial or travel-acquired infection. In some countries it was not possible to obtain cases by category since epidemiological follow-up information was not available to the reporter.

For the 3 years 2000–2002, 889 cases of Legionnaires' disease were reported as nosocomial, 3916 as community-acquired, and 2118 were associated with travel, either in the same country as the country of residence or abroad. The number of cases with unknown category of risk was reported as 3399 (Table 3). The overall proportion of cases linked to hospital infection halved during the 3 years from 12·8% in 2000 to 6·0% in 2002. France, Italy and Spain reported 73% of the total nosocomial cases during this period. Community-acquired cases comprised the largest group of cases in the European data-set but varied each year depending on the number of community outbreaks detected and reported. Four countries, England & Wales, France, Italy and Spain reported 80% of the total community cases for the 3 years under study. Of the 1424 cases associated with travel abroad, 93·5% were reported by only four countries – England & Wales, France, Germany and The Netherlands, and of the 687 cases associated with travel at home, 87% were reported by three countries, France, Italy and Spain. Fourteen countries in 2000, 13 in 2001 and 18 in 2002 reported not knowing the category of some cases. Six of these countries, Belgium, Estonia, Lithuania, Poland, Portugal and Russia reported more than 70% of their total legionella cases as of unknown category.

Outbreaks

Between 2000 and 2002, 189 outbreaks or clusters were detected by 13 individual countries and involved 1579 cases, 15·3% of the total data-set (Table 4). Thirty-four outbreaks were detected in 2000, 41 in 2001 and 114 in 2002. Most of the increase in 2002 is related to the change in the case definition for travel-associated clusters.

Table 3. *Cases and proportion by category of infection 2000–2002*

Category of infection	2000	2001	2002	Total
Nosocomial	275 (12·8%)	333 (9·6%)	280 (6·0%)	889 (8·6%)
Community	659 (30·5%)	1475 (42·5%)	1782 (38·0%)	3916 (37·9%)
Travel abroad	357 (16·6%)	482 (13·9%)	585 (12·4%)	1424 (13·8%)
Travel home	143 (6·6%)	185 (5·3%)	359 (7·6%)	687 (6·7%)
Travel unknown	—	5 (0·2%)	2 (0·1%)	7 (0·1%)
Not known	722 (33·5%)	988 (28·5%)	1688 (35·9%)	3399 (32·9%)
Total	2156 (100%)	3470 (100%)	4696 (100%)	10 322 (100%)

Table 4. *Number of outbreaks and associated cases by category of infection 2000–2002*

Category of outbreak	2000	2001	2002	Total
Nosocomial	8 (40)	14 (62)	14 (109)	36 (211)
Community	10 (193)	9 (525)	19 (341)	38 (1059)
Travel abroad	13 (31)	13 (35)	49 (125)	75 (191)
Travel home	3 (6)	4 (9)	31 (109)	38 (124)
Other (private home)	—	1 (2)	1 (2)	2 (4)
Total	34 (270)	41 (633)	114 (676)	189 (1579)

Nosocomial outbreaks

Thirty-six outbreaks involving 211 cases of Legionnaires' disease were linked to hospitals. They occurred in Austria, the Czech Republic, Denmark, France, Italy and Spain, the latter two countries accounting for 27 of these 36 outbreaks. Most involved small numbers of cases except for two in France in 2002 where 31 and 32 cases respectively were reported in the outbreaks. Twenty-nine nosocomial outbreaks were attributed to contaminated hot- or cold-water systems, two to cooling towers and five to an unknown source. The number of deaths associated with these nosocomial outbreaks could not be determined from the aggregated data-set.

Community outbreaks

Thirty-eight outbreaks were linked to community settings and were associated with 1059 cases. They occurred in Denmark, England, France, The Netherlands, Northern Ireland, Norway, Scotland, Spain and Sweden. Four large community outbreaks gave rise to over 700 cases of legionella infection. In 2000 one involved 70 cases in a Spanish industrial town where outbreaks had previously occurred; in 2001 the city of Murcia in Spain experienced the largest outbreak in the world so far with over 400 cases [6] and in 2002 another large outbreak of 108 cases was reported by Spain. A major community outbreak also occurred in England in 2002 and was associated with 137 cases [7]; it is the largest outbreak to date in the United Kingdom. Cooling towers were found to be the source of infection in 15 outbreaks, hot- or cold-water systems in three and whirlpool spas in three. Seventeen of the 38 outbreaks did not have a source identified.

Other outbreaks

Two outbreaks were reported to be linked to private homes – one in Spain in 2001 and the other in England in 2002. Each was associated with two cases. The hot-water system was responsible in the English outbreak but no source was reported from Spain.

Travel-associated outbreaks

A total of 113 travel-associated clusters were reported between 2000 and 2002 and gave rise to 315 cases, 15% of the total reported travel cases. Seventy-five clusters were linked to travel outside the country of residence in Europe and 38 to the same country as the country of residence. Most clusters were linked to hotels and comprised less than three cases each but an outbreak at a hotel in Belgium used by coach parties in 2002 gave rise to 10 cases, mostly among British nationals. One outbreak in 2002 was linked to a whirlpool spa in Sweden and involved 23 cases among their own nationals. Where the source of infection was identified, hot- or cold-water systems were responsible in 30 outbreaks, and whirlpool spas in four. Reporting countries did not provide the source of infection for the remaining 79 outbreaks.

Table 5. *Cases and proportion by main method of diagnosis 2000–2002*

Main method of diagnosis	*L. pneumophila* sg1	*L. pneumophila* (other serogroup), or serogroup not determined*	Other *Legionella* species† or species not known	All legionella cases
Isolation	857 (10·8%)	243* (13·9%)	54† (8·0%)	1154 (11·2%)
Antigen detection				
Urinary	6252 (79·2%)	507 (29·0%)	179 (26·6%)	6938 (67·2%)
Serology				
Seroconversion	281 (3·6%)	465 (26·6%)	135 (20·1%)	881 (8·5%)
Serology				
Single high titre	434 (5·5%)	321 (18·4%)	138 (20·5%)	893 (8·7%)
Antigen detection				
Respiratory	18 (0·2%)	24 (1·4%)	13 (1·9%)	55 (0·5%)
PCR	8 (0·1%)	58 (3·3%)	8 (1·2%)	74 (0·7%)
Other	25 (0·3%)	76 (4·3%)	14 (2·1%)	115 (1·1%)
Not known	25 (0·3%)	55 (3·1%)	132 (19·6%)	212 (2·1%)
Total (each case counted only once)	7900 (100%)	1749 (100%)	673 (100%)	10 322 (100%)

* Sg2, 9; sg3, 35; sg4, 5; sg5, 10; sg6, 22; sg7, 1; sg8, 2; sg10/14, 7; sg unknown, 152.
† *L. anisa*, 2; *L. bozemanii*, 4; *L. dumoffii*, 2; *L. gormanii*, 1; *L. longbeachea*, 3; *L. micdadei*, 9; *Legionella* sp. unknown, 33.

Travel-related sporadic legionella infections

Altogether 23 countries reported a total of 1803 sporadic travel-associated cases. Approximately one third of these (563) were linked to travel in the same country as the country of residence and 1233 to travel abroad. Seven were unknown.

Travel within Europe accounted for 1891 (89%) of the total travel cases, the remainder were associated with the Americas, the Caribbean, the Far East, Africa and the Middle East. For the 3 years 2000–2002, the highest number of cases was associated with travel in Spain (500), followed by Italy (353), France (319), and Turkey (218). However, in Spain, Italy and France, 51, 48 and 54% respectively of the cases occurred as a result of travel by Spanish, Italian and French nationals within their own country. In contrast, all of the cases associated with Turkey occurred in residents of other European countries. Ninety cases travelled in more than one European country before onset of illness. A more comprehensive analysis of the travel-associated cases of Legionnaires' disease is published separately [8].

Methods of diagnosis

In total, 1154 cases (11·2%) were diagnosed by culture of the organism, 6938 (67·2%) by urinary antigen detection and 881 (8·5%) by a fourfold rise in antibody detection levels (Table 5). Single high antibody titres were reported for 893 cases (8·7%). The remaining cases were diagnosed by respiratory antigen detection, PCR or the method was unknown. In 2000 culture of the organism accounted for 336 (15·6%) of all cases compared to 383 (11%) in 2001 and 435 (9·3%) in 2002. In contrast, cases diagnosed by urinary antigen detection increased from 1228 (57%) in 2000 to 2278 (65·6%) in 2001 and 3432 (73·1%) in 2002. The proportion of cases detected serologically, either by seroconversion or by single high titre fell in the 3-year period from 23 to 12·4%.

L. pneumophila sg1 infection accounted for 7900 (76·5%) of the total cases, 11% of which were diagnosed by culture and 79% by urinary antigen detection. *L. pneumophila* (other serogroup), or serogroup not determined accounted for 1749 (17%) of the reports in 2000–2002. A total of 243 (14%) of these cases were diagnosed by culture, and 29% by urinary antigen detection. Reports totalling 673 (6·5%) were of other *Legionella* species or species unknown, the proportion falling from 7% in 2000 and 2001 to 5·8% in 2002.

Of the 1154 isolates reported, 857 (74%) were due to *L. pneumophila* sg1 infection, 152 (13%) were *L. pneumophila* (serogroup unknown) and 91 (8%) were

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serogroups 2–14. Twenty-one isolates were diagnosed as other species of *Legionella*. These were reported as *L. micdadei*, *L. bozemanii*, *L. longbeachae*, *L. dumoffii*, *L. anisa* and *L. gormanii*. For 33 isolates the *Legionella* species was not given (Table 5).

DISCUSSION

A major increase in reported cases of Legionnaires' disease occurred in many European countries between 2000 and 2002. Greater use of the urinary antigen detection test and new enhanced surveillance programmes in some countries mainly account for the overall rise in ascertainment of legionella infections although some of the increase was also due to the occurrence of large community outbreaks. The pooling of surveillance data at the European level has provided opportunities to evaluate surveillance at national levels and the sharing of knowledge and resources for contributing to control and prevention programmes in individual European countries.

Although ascertainment levels are increasing, detection, reporting and surveillance of legionella infection remains poor in many countries. The true incidence of community-acquired pneumonia due to legionella infection has been estimated as ranging from 2 to 16% in industrialized countries [9]. In England a 2% incidence would extrapolate to almost 4000 cases a year based on hospital admissions for specified and unspecified community-acquired pneumonia (all ages) for 2000–2001 [10], whereas in France an in-depth study in 1998 estimated that around 1200 annual cases should be expected [11]. No country in Europe has yet reached equilibrium between incidence, detection and reporting of cases of Legionnaires' disease although Denmark is possibly the closest as it consistently reports rates of approximately 20 cases per million population per year. Denmark's achievement may be due to the fact that it is a small country that carries out high levels of testing for legionella in patients with pneumonia, and one that also has a centralized legionella reference laboratory for diagnosing and reporting cases. A rate of 20 cases per million would produce the expected 1200 annual cases in France, compared with 1060 cases in England and 1640 cases in Germany. As far as England is concerned, its total of 382 cases in 2002 was artificially inflated by a rare (for England) but large outbreak. In all other recent years, up to 50% of the 200 or so annually reported cases acquire their infection abroad. Hence England's annual low number of indigenous cases suggests an ascertainment level of around 10% of estimated incidence. They are not contributing to the overall rise in case reports, nor to reducing the difference between incidence and detection of legionella cases. In contrast, France may have almost reached equilibrium levels within its surveillance system, with over 1000 cases reported in 2002. Thus convergence of incidence rates and detection rates overall remains limited.

This review has highlighted big differences in countries reporting cases acquired as a result of travel abroad. Rates between northern and southern countries will inevitably vary because of travel patterns that reflect northern Europeans' choice of holidays in southern European countries. Nevertheless, within the northern countries themselves, the proportion of cases attributed to travel abroad ranged from 13% in Belgium, 20% in Germany, 23% in Denmark, 41% in England & Wales, 57% in The Netherlands and 59% in Scotland. Lack of information and under-reporting are probably responsible for the low rates in Belgium and Germany, but an element of over-detection and bias in reporting of these cases relative to other types of cases could be happening in some other countries. Clinicians may well be more inclined to think of legionella during the summer when seeing patients with pneumonia who have just returned from holiday.

There are major implications for workloads in European countries as more and more cases of Legionnaires' disease are diagnosed each year. Countries have to be willing to prioritize resources to this particular infection and to undertake epidemiological and environmental investigations when cases are detected. However, public-health action and surveillance are weakened when cases with unknown exposure category are reported in the annual datasets. This is especially so at the international level for travel-associated cases. Nationally reported cases contribute to the detection of clusters involving cases from more than one country of residence and generate up to 30% more travel-associated clusters each year than are detected by individual countries alone [8]. These clusters require international action to identify sources of infection and the appropriate response at the national and international level. The recently EU-endorsed European Guidelines [5] have been written to harmonize procedures within Europe for following up cases of travel-associated legionella infections. Since their introduction in July 2002, all clusters in

countries using the guidelines have been investigated and information on the results fed back to the EWGLINET coordinating centre.

The fall in the annual proportion of deaths may or may not be real in this aggregated data-set since many countries were unable to supply information on the number of deaths that were associated with their reported cases. However, a very low fatality rate for cases in large community outbreaks has been observed in recent years [12]. This has been attributed to the fact that clinicians have a greater awareness of legionella infection during an outbreak, particularly when there is associated local or national media interest. If the legionella urinary antigen diagnostic method is used during the outbreak, rapid confirmation of infection contributes to the appropriate clinical management of the cases and a reduction in associated deaths. Also, because the diagnostic test is easy to administer, a greater pool of patients may be tested, highlighting a wider spectrum of illness than was previously recognized in earlier outbreaks. In contrast, it is mainly the more severely ill patients that are detected and reported as sporadic cases and their associated higher mortality rates are often a consequence of delayed diagnosis and initiation of appropriate antibiotic treatment. The overall picture of lower mortality rates should therefore be stratified into two separate profiles – one for outbreak cases where outcome is usually reported, and one for sporadic cases with known outcome. The latter group continue to show mortality rates ranging from 10 to 40%. However, as more and more countries adopt the urinary antigen detection test as their prime diagnostic method, cases are being diagnosed earlier in the acute phase of illness, which should lead to falling mortality rates. Nevertheless, more information on the eventual outcome of legionella cases should be a prime goal of national surveillance programmes in order to assess the full public-health impact of Legionnaires' disease in European residents.

Surveillance of Legionnaires' disease has been shown to be of variable quality in Europe. The number of member states within the European Union will increase from 15 to 25 when 10 of the 13 applicant countries are admitted in 2004. Within the accession countries, one of the public-health targets of the European Union is to support further development, where relevant, of their national surveillance programmes for communicable disease, in order that the new member states can also benefit from an early warning of threats to health through pooling of national data, and a recognition of threats to health that require international coordinated action. Twelve of the 13 applicant countries (Cyprus is the exception) already belong to EWGLINET and all countries, except Hungary, have completed the annual returns for cases of Legionnaires' disease in their residents since the year they joined the scheme. The number of cases that each of the applicant countries has reported since joining EWGLINET has mostly ranged from 0 to 10, with only the Slovak Republic reporting more than 10 cases per year. While the individual countries' desire to share data within an international network is acknowledged, the heterogeneity of their national public-health surveillance systems and the different priorities possibly accorded to different diseases within the various countries is currently affecting their ability, perhaps technically as well as logistically, to identify cases and produce data. Becoming part of the European Union and subject to Decision 2119/98/EC and being within the Community Network for the epidemiological surveillance and control of communicable diseases in the community [13] should enable these countries to contribute on a more equitable basis in the future.

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