

TRAVEL ASSOCIATED LEGIONNAIRES' DISEASE IN EUROPE: 2002

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Twenty countries reported 676 cases of travel associated legionnaires' disease to the EWGLINET surveillance scheme, and 94 clusters were detected.

80.5% of all cases were diagnosed by the urinary antigen test. On average there were 20.5 days between onset and report of cases, compared with 51.5 days in 1993.

Between the introduction of the EWGLI investigation guidelines (on 1st July 2002) and the end of 2002, 37 six-week investigation reports were accepted as satisfactory and on time by the coordinating centre. 274 sites were investigated in total in 2002. The travel patterns of the main reporters in EWGLINET influenced the months of peak activity, and helped to determine which countries bore the greatest investigation burden.

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Introduction

In 1987, a European surveillance scheme for travel-associated legionnaire's disease (now called EWGLINET) was established by the European Working Group for Legionella Infections (EWGLI). The aims of this scheme are to monitor levels of travel associated legionnaires' disease in Europe, detect clusters and outbreaks, and collaborate in the control and prevention of further cases. Its history and current activities are described in detail on its website (www.ewgli.org).

This paper provides results and commentary on cases reported to EWGLINET with onset in 2002.

Methods

A single case of travel associated legionnaires' disease is defined as a person who, in the ten days before onset of illness, stayed at or visited an accommodation site that had not been associated with any other cases of legionnaires' disease, or a person who stayed at an accommodation site linked to other cases of legionnaires' disease but after an interval of at least two years (1).

A cluster of travel associated legionnaires' disease is defined as two or more cases who stayed at or visited the same accommodation site

in the ten days before onset of illness and whose onset is within the same two-year period (1).

Cases of legionnaires' disease are detected and followed-up by national surveillance schemes, and those defined as travel-associated are reported to the EWGLINET coordinating centre at the Communicable Disease Surveillance Centre (CDSC) in London and are entered into the EWGLINET database. Epidemiological, microbiological and travel histories are reported. Upon receipt of a new case, the database is searched by the coordinating centre for any previous cases reported to have stayed at the same accommodation site within the last two years.

In July 2002, European guidelines were introduced to standardise the response that countries made to EWGLINET notifications (1). Different levels of intervention are expected from the public health authorities for sites associated with single or multiple cases. These include issuing a checklist for minimizing risk of legionella infection at sites associated with single cases, and conducting risk assessments, sampling for legionella and implementing control measures at sites associated with clusters. The guidelines have introduced a procedure whereby the country of infection is expected to carry out a risk assessment and initial control measures within two weeks, and sampling and full control measures within six weeks of receipt of the notification. Both of these stages are documented by the collaborator in the country of infection, by completion of standard forms ('Form A' and 'Form B') which are sent to the EWGLINET coordinating centre. If this documentation is not received in the specified time period, EWGLINET publishes details of the cluster on its public website (www.ewgli.org) since the coordinating centre cannot be confident that the accommodation has adequate control measures in place. The notification is removed once the relevant form(s) have been received confirming that measures to minimise the risk of *legionella* at the site have been carried out.

Results

Cases and Outcome

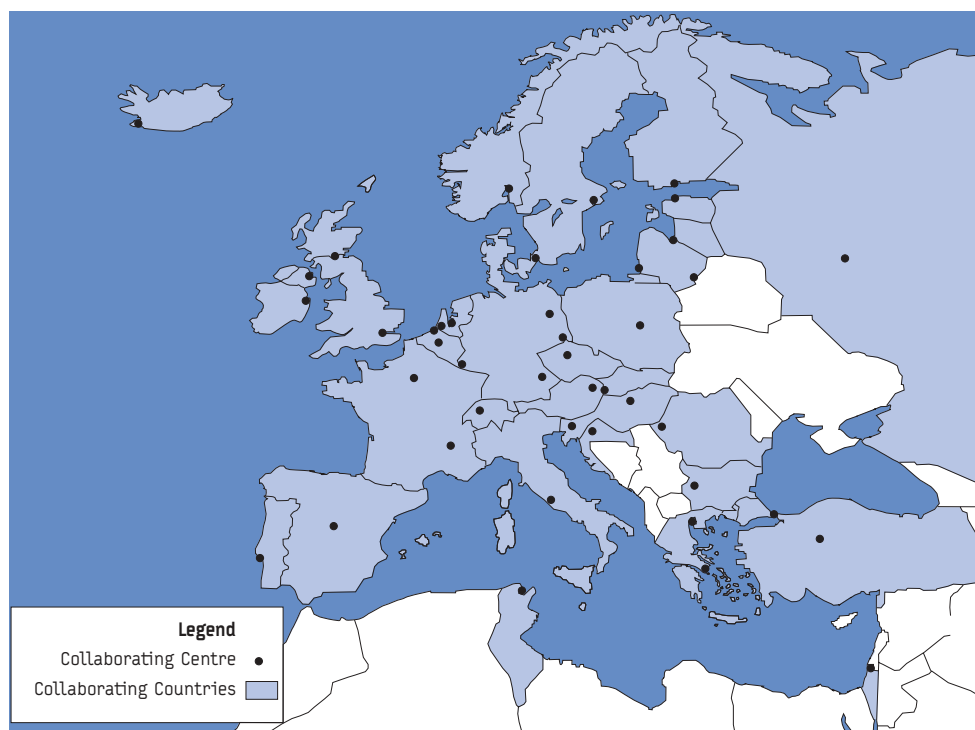
In 2002, 57 collaborators from 50 centres in 36 countries (FIGURE 1) participated in EWGLINET. Twenty of these countries reported a total of 676 cases of travel associated legionnaires' disease with onset in 2002.

Each year, cases reported to EWGLINET follow a distinctive age and sex profile. In 2002, male cases continued to outnumber female cases by nearly 2.5 to 1, and the peak age-group reported was 50-59 years for both sexes. The age range for males was 13-89 years and for females 22-89 years.

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FIGURE 1

EWGLI Collaborating Countries - 2002



As in previous years, the date of onset followed a seasonal pattern. The number of cases increased from January through the year, with peaks in July and September, before decreasing throughout the rest of the year.

The proportion of 'known' outcomes (death or recovery as opposed to 'unknown' outcomes – still ill or unknown) has been decreasing steadily since about 1995, due largely to an increase in the speed of reporting. The number of reported deaths has remained similar in 2002 at 43 compared with 41 in 2001, despite a large rise in the number of cases, lowering the case fatality rate from 8.5% to 6.4%. The absolute number of recoveries increased, but fell in percentage terms from 35.5% in 2001 to 29.7% in 2002. The 'still ill' category remained virtually unchanged, but the largest increase was in the 'unknown' category where absolute figures rose from 128 to 232, and the percentage increased from 26.6% to 34.3%.

Microbiology

Use of the urinary antigen test continued to rise, with 80.5% of all cases diagnosed by this method, compared with 78.6% in 2001. Use of other diagnostic tests remained relatively constant. Culture of the organism accounted for 7% of the diagnoses (the same as in 2001), serology 11.8%, and other methods 0.7% (FIGURE 2). The main category of organism detected was *Legionella pneumophila* serogroup 1 (68.3%). The remaining cases were reported as '*L. pneumophila* serogroup unknown' (12.7%), '*L. pneumophila* other serogroups' (2.1%), '*Legionella* species unknown' (4.6%), 'Other species' (0.9%), and 'Unknown' (11.4%).

Travel

Travel associated cases are usually diagnosed after they return to their country of residence. The main reporters of cases in 2002 were The Netherlands (151), England and Wales (126), France (119) and Italy (68) (FIGURE 2).

Cases visited a total of 51 countries. The highest numbers of cases were associated with travel to Italy (132), France (121), Spain (85) or Turkey (83). The proportion of cases linked to clusters was similar in three of the four main countries of infection at 25% in France and Spain and 24% in Italy. Although Turkey had fewer associated cases, 71% of them were part of clusters (see below) (FIGURE 3). Sixty one cases visited more than one European country, whilst only two visited more than one country outside Europe. A further 63 cases (9.3%) were associated with travel to countries outside the EWGLINET scheme, ten of which were in travellers to the USA.

Clusters

Ninety four clusters were identified in 2002 compared with 72 in 2001. These were defined as accommodation sites associated with a case in 2002, where one or more cases within the previous two-years had also been associated with the same site. Most clusters involved only two cases (60 clusters), but they ranged in size from 2-10 cases.

FIGURE 2

Countries reporting more than 10 cases in 2002

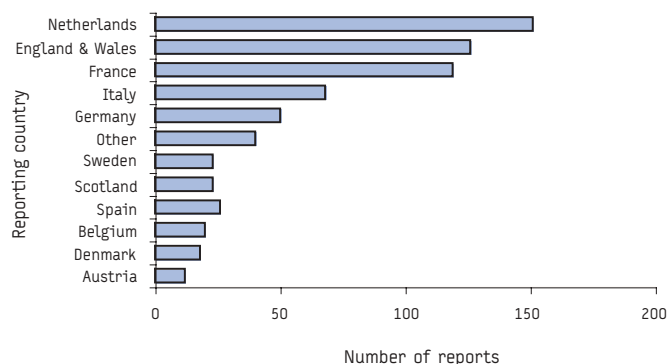
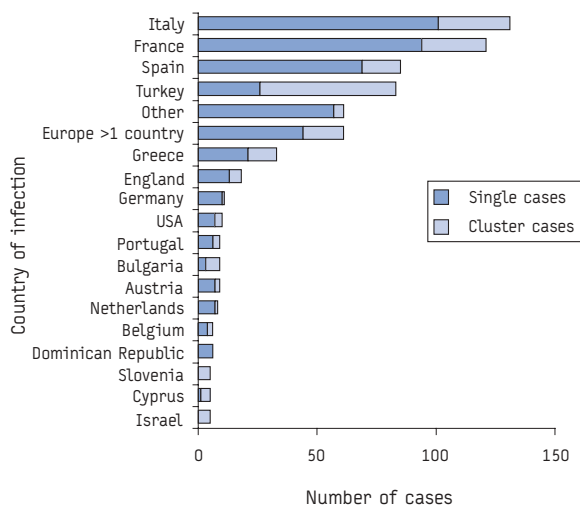


FIGURE 3

Countries visited by more than five travel cases in 2002, by type of case*



* Countries with more than 5 travel cases, all others summed in "OTHER"

26 of the 94 clusters consisted of a single case reported by each of two or more countries and would ordinarily not have been identified without the establishment of the international database.

The clusters were located in 19 countries. Turkey had the most (27), followed by Italy (17) and France (16). Eleven countries had just one cluster each in 2002, three of which occurred in countries outside EWGLINET (Dominican Republic, Russia and USA). Twelve clusters included cases that had stayed at two or more cluster sites before onset of illness compared with only four such incidents in 2001.

Most of the detected clusters with onset in 2002 occurred in summer, peaking in September. A second smaller peak was also observed around Easter time, however at least three clusters occurred every month in 2002. Over two thirds (68%) of the clusters included at least two cases with onset within six months of each other. Sixteen clusters (17%) had cases occurring between seven and 12 months of each other, and the remaining 14 clusters has cases occurring between 13 and 24 months of each other.

Investigations

Of the 94 clusters in 2002, 64 were notified between the introduction of the guidelines and the end of December 2002, and involved 70 accommodation sites. Sixty six of these sites fell within EWGLINET countries. Between July and December 2002, 37 'Form B' reports were accepted as being completed on time and stating that control measures were satisfactory, 17 sites (26%) had been published on the EWGLI website, and 12 were in the process of being investigated. Four of these published cluster sites (23.5%) have had extra cases subsequently, and five unpublished sites (10.2%) have also had subsequent cases.

For the whole of 2002, 128 cluster sites were investigated including 99 which were sampled, from which *legionella* was reported to have been detected in 35 (35%). 146 single case sites were also investigated, even though the guidelines do not require such sites to be investigated, and of these 106 were sampled, and 45 (42.5%) of the sampled sites detected *legionella* (TABLE 1).

TABLE 1

Results of environmental sampling for cluster sites and for all sites, where investigations were carried out in 2002.

All sites	n
<i>Legionella</i> detected	80
<i>Legionella</i> not detected	125
Unknown	69
Total	274
Cluster sites	n
<i>Legionella</i> detected	35
<i>Legionella</i> not detected	64
Unknown	29
Total	128

Environmental investigations will be examined in greater detail in a further paper.

Discussion

2002 saw the highest number of travel associated cases of legionnaires' disease reported to EWGLINET since the scheme began in 1987. This rise in case reports is almost certainly linked to wider use of the urinary detection test and improved surveillance in many European countries. The fall in the case fatality rate is also part of this general trend whereby less seriously ill cases are being detected

and reported more regularly, and the risk of death is being considerably reduced through more rapid diagnosis and application of appropriate antibiotic therapy, made possible by the widespread introduction of the urinary antigen detection test. Whilst rapid diagnosis has benefited cases, it has also negatively impacted on epidemiological information in relation to the outcome of cases reported as "still ill" or with unknown outcome, and also on microbiological information because the lack of clinical isolates prevents analysis of strain matches between patient and environmental specimens. In order to demonstrate that a particular infection comes from a particular site, the clinical sample must be matched with an environmental sample, and culture is the only method by which this can be done.

Eleven per cent of the cases reported to EWGLINET in 2002 did not have data provided on the category of organism detected. This is not in accordance with the reporting procedures since all cases reported to EWGLINET must state the main method of diagnosis, and each microbiological diagnosis should at the very least determine the organism (*legionella*) and species (*pneumophila*). The urinary antigen detection method is highly specific to *L. pneumophila* serogroup 1, and serological diagnostic methods are capable of determining the species and serogroup of *Legionella*. Since over 90% of the reported cases in 2002 were diagnosed by these methods, the microbiological information should be available for a large majority of the "unknown" cases. Any lack of information exchange between laboratories and national collaborating centres should be addressed to ensure that microbiological details are provided for all cases. This is increasingly important as more and more accommodation sites are subject to environmental investigations.

The main change to occur to the EWGLINET scheme in 2002 was the introduction, on 1st July that year, of the European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease¹. These have now been successfully implemented in the investigation of a large number of sites, including a cluster involving ten cases who stayed at a hotel in Belgium.

There is some preference among holiday-makers for travel to particular destinations, and this can influence which countries of infection are most often reported to the scheme. This can have interesting effects when the preference is country-specific. For instance, Turkey has a market share of 24% of the total Dutch flight travel package market. In the summer of 2002, approximately 600,000 Dutch package travellers visited Turkey from a population base of 16 million. When this is combined with the high frequency of Dutch reporting to the EWGLINET scheme, it is hardly surprising that so many of the Dutch *legionella* cases are associated with travel to Turkey.

Because of the bias amongst holiday-makers for travel to particular destinations, it is useful to look at the number of EWGLINET cases associated with travel to a particular country, relative to the total number of visitors. The Office of National Statistics Travel and Tourism Survey (2) can provide this information for UK travellers (TABLE 2). Whilst ten UK tourists fell ill after visiting Turkey, giving a rate of 9.95 cases per million UK travellers, the thirty-five UK tourists who fell ill after visiting Spain give a rate of only 2.78 travellers because there is so much more UK travel to Spain, than to Turkey.

France and Italy have begun to report more cases associated with internal travel within their own country; this has greatly increased their number of case reports to the coordinating centre (76 out of 121 cases travelling in France in 2002 were French, whilst 60 out of 132 cases were Italians travelling in Italy). This has an effect on the main countries of infection reported to the scheme, as described

TABLE 2

Rates for cases of Legionnaires' Disease per million travellers from the UK to some of the most popular countries in 2002

Country of travel	Number of UK cases	Number of UK travellers	UK cases/million travellers from the UK
Turkey	10	1 004 670	9,95
Italy	20	2 648 518	7,55
Spain	35	12 606 068	2,78
Greece	7	2 999 994	2,33
France	18	11 706 943	1,54

Office for National Statistics: Overseas Travel and Tourism 2002.

above. However, it also highlights the fact that many countries do not notify EWGLINET of travel-associated cases in their own country by their own residents, and EWGLINET may therefore be missing an unknown number of clusters.

The EWGLI guidelines have now been successfully introduced in all EU member states, with support from the Ministry of Health in each country. Norway, Turkey and a large number of the accession countries have also agreed to use them. In the majority of countries, the guidelines are functioning well, and clusters of cases of legionnaires' disease are being investigated and dealt with promptly. Turkey has adapted less successfully to the introduction of the guidelines and, as a result, has had more sites published on the EWGLI website to date than any other country. Assistance has been offered by EWGLINET to help countries such as Turkey reach the standard achieved by the majority. However, the fact that overall, nine of the cluster sites in Europe in 2002 have yielded additional cases subsequent to satisfactory control and prevention measures being reported is of concern. The countries involved should investigate the reason for these breakdowns, otherwise the long term credibility of the procedures adopted in the guidelines may be called into question.

Investigations that include sampling are now expected for all cluster sites, and they have shown a number of accommodation sites to be positive for *legionella*. Whilst these sites cannot conclusively be proven as the source of infection in the absence of clinical isolates for comparison, the presence of *legionella* is highly suggestive of the sites being the source. However, the proportion of positive *legionella* detections from water samples varies widely between countries, suggesting that some laboratories may be more successful than others in identification of the organism rather than an absence of the organism itself in the tested samples.

Closure of accommodation sites is at the discretion of local public health authorities, but the introduction of the guidelines has standardised the responses expected of the implicated sites. Tour operators and individual members of the public may withdraw from sites associated with large or extended outbreaks of legionnaires' disease, or when the accommodation name is posted on the EWGLI website. Sites that contract with the large tour operators face significant consequences if their name appears on the website, and they are therefore normally amenable to implementing the control measures expected of them. The cost of the measures is probably far lower than the loss of business should the tour operators withdraw.

The one major outbreak in Belgium in 2002 demonstrated how well the EWGLINET system can work to detect and respond to clusters.

The cluster was centred around hotel 'X' in Belgium and consisted of ten cases, six English, three French and one Scottish. Each case visited at least two of seven independent hotels, except for one case who visited only hotel X, which was additionally the only hotel visited by all of the other cases. The hotel was closed whilst investigations were carried out. An indistinguishable strain of *L. pneumophila* serogroup 1 was isolated from a patient sample from one of the outbreak cases and from water samples from the hotel X's water system. It is very important to establish this confirmatory link between cases and the source of infection, particularly when cases may have stayed at several hotels before onset of illness and when some of these hotels may also be linked to other clusters. The fact that this scenario is occurring more frequently than in previous years highlights one of the problems of an ever increasing database of accommodation sites. Many sites will feature in clusters simply by chance because of their use by tour operators and tourists alike.

Because of the trend for an increasing number of cases being reported to EWGLINET each year, it is important to consider what may happen to the scheme in future years. If the average increase in the number of cases each year from 1993-2002 is taken (121.3% each year), and then assumed for the years 2003 – 2008, EWGLINET could be dealing with over 2000 cases in 2008. Obviously there are many variables which can affect this. The projection assumes continuous growth of the scheme at the current rate, a continued increase in the uptake of urinary antigen testing, additional countries joining the scheme and contributing new cases, and an increase in surveillance by existing countries. The projection also assumes a reduction in the level of under diagnosis, a reduction in the level of under reporting, and it assumes that the impact of the guidelines is delayed until the true level of incidence is obtained.

If the number of cases does continue increasing in line with this projection, this has large implications for workload, both for the co-ordinating country and for the collaborators in the countries of report and infection, the latter of whom must ensure that each cluster is investigated thoroughly. The increase in multi-site clusters additionally threatens to increase the workload for all involved. However, the increase in cases reported to EWGLINET should be seen as a positive development, and not just as a problem to be overcome. It demonstrates that case detection by national surveillance schemes for legionnaires' disease is improving, which allows for more rapid and complete ascertainment of clusters, and this in turn gives an opportunity for countries to respond to outbreaks in a more timely and efficient manner.

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* http://www.ewgli.org/contact/contact_listof_collaborators.asp

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