Travel-associated Legionnaires' disease in Europe: 2006

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Twenty countries reported 921 cases of travel-associated Legionnaires' disease to EWGLINET (the European Surveillance Scheme for Travel-Associated Legionnaires' Disease) with onset during 2006; 875 confirmed and 46 presumptive. Thirty three cases died, giving a case fatality rate of 3.6%.

Of the 124 new clusters detected in 2006, 43 would not have been identified without the EWGLINET scheme. A total of 146 investigations were conducted at cluster sites according to the standards of the EWGLINET investigation guidelines; 111 of these investigations were associated with the new clusters while 35 investigations were associated with re-offending sites (where additional cases had onset after a report was received to say that investigations and control measures had been satisfactorily conducted). The names of four accommodation sites were published on the EWGLI website.

Overall, there has been an upwards trend in case numbers since the scheme was founded, which has implications for the work load of public health authorities across Europe and for the tour industry. Despite this increasing pressure on public health authorities, environmental investigations are being conducted in a timely manner.

Introduction

In 1986, the European Working Group for Legionella Infections (EWGLI) was formed to facilitate the exchange of information and to collaborate in the management of Legionnaires' disease across Europe. A year later EWGLI members established the European Surveillance Scheme for Travel-Associated Legionnaires' Disease (EWGLINET), which aims to identify clusters of Legionnaires' disease cases in Europe that may not be detected by national surveillance systems alone, and to initiate investigation and control measures at the sites implicated. These measures are standardised in the European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease, which were endorsed by the European Commission in 2003 [1]. The history and current activities of EWGLI are described further on its website (www.ewgli.org).

This paper provides results and commentary on cases of travel-associated Legionnaires' disease reported to EWGLINET with onset in 2006.

Methods

EWGLINET uses standard case definitions to ensure that the data reported to the scheme are consistent regardless of the country of report. These definitions are available on the EWGLI website [2]. National surveillance schemes collect basic epidemiological, microbiological and exposure information on cases of travel-associated Legionnaires' disease that occur in residents of their country. These are reported to EWGLINET's co-ordinating centre at the Health Protection Agency Centre for Infections in London, which maintains a database of all reported cases. The database is searched each time a new case report is received in order to determine whether it is a single case or part of a cluster.

A single case is defined as a person who stayed, in the two to ten days before onset of illness, at a public accommodation site that has not been associated with any other previous case 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. A cluster is defined as two or more cases who stayed at or visited the same accommodation site in the two to ten days before onset of illness and whose onset is within the same two year period [1].

The European Guidelines for Control and Prevention of Travel-Associated Legionnaires' Disease [1] were introduced in 2002 to standardise the investigations conducted across Europe in response to EWGLINET cluster alerts. The response required for single cases is minimal because the epidemiological evidence suggesting that the accommodation site is the source of infection is relatively low; as such, the responding collaborator is only required to send the accommodation site a checklist for minimising risk of legionella infections, so that the site can ensure that it is following the best practice.

However, if the site is associated with a cluster, the guidelines state that more detailed investigations must be conducted; these include a risk assessment, sampling and control measures. The collaborator in the country of infection must report the progress of these investigations to the co-ordinating centre after two weeks ('Form A') and six weeks ('Form B'). If these reports are incomplete or are not received on time, EWGLINET will publish details of the cluster site on its public website (www.ewgli.org), stating that the coordinating centre cannot be certain that risk of legionella infection is under control at the site. This notice is removed once the relevant form(s) have been received, confirming that measures to minimise risk are in place.

If a cluster is satisfactorily investigated under the guidelines and is subsequently associated with a further case, it is termed a 're-offending' site and a complete re-investigation is required.

Results

Cases and outcomes

Of the 35 collaborating countries in EWGLINET, 18 reported a total of 916 cases of travel-associated Legionnaires' disease with onset during 2006 (counting England and Wales, Scotland and Northern Ireland as one country). In addition, four cases were reported by the United States and one by Australia, two countries that do not form part of the official network. This brought the total number of cases reported to the EWGLINET scheme with onset in 2006 to 921, which is a major increase on 2005 when 755 cases were reported and continues the annual upward trend (Figure 1). The mean time between onset and report to EWGLINET was 36 days in 2006 in comparison with 29 days in 2005.

The countries that reported the most cases in 2006 were the United Kingdom (250 cases, from England and Wales, Scotland and Northern Ireland), France (174), the Netherlands (158) and Italy (130) (Table 1).

Cases in males outnumbered cases in females by a considerable margin and a ratio of 2.8:1 (677 males and 244 females), maintaining the gender profile seen in previous years (up from 2.5:1 in 2005). As in previous years, cases in 2006 were also skewed towards older age groups (with peaks in the 50-59-year age group for men and the 60-69-year group in women). The median age for male cases was 58 years (age range 18-91 years; two cases had unknown age) and for female cases 61 years (age range 18-93 years).

The peak month for onset of illness in 2006 was August compared with September in 2005, continuing the summer seasonal pattern of high incidence associated with this travel-associated scheme.

Among the 921 cases, 369 (40.1%) had an outcome provided and 33 deaths were notified (3.6%). This case fatality rate was similar to that in 2005 (29 deaths, 3.8%). The 33 deaths were reported for cases aged 34 to 84 years. Of these, 27 were male and six were female (4.5:1 compared with 4.8:1 in 2005), and the median age was 48. The majority of deaths (29) were associated with single cases (87.9%), and the remaining four (12.0%) with cluster cases. In 2005, 21 (72.4%) of the reported deaths were linked to single cases and eight (27.6%) to clusters.

Microbiology

The dataset of cases reported with onset in 2006 contains 875 confirmed and 46 presumptive cases; confirmed cases include those that are culture-positive, those diagnosed by urinary antigen and any *Legionella pneumophila* serogoup 1 cases diagnosed by serology four-fold rise, whilst presumptive cases include all other cases diagnosed by serology (fourfold rise non-*L. pneumophila* serogroup 1 cases and all single high titres) and those diagnosed by PCR. As in previous years the main method of diagnosis in 2006 was by urinary antigen detection at 89.2% (822 cases), the proportion increasing from 85.8% in 2005. The number of culture-proven cases rose from 37 in 2005 to 48 in 2006, but as a proportion of all cases remained similar in 2005 (4.9%) and 2006 (5.2%). Seven cases (0.8%) were diagnosed primarily by PCR (down from 2.3% in 2005). Serology as the main method of diagnosis has continued to decrease, falling to 44 cases (4.8%) in 2006 (compared with 7.0% in 2005); 11 cases (1.2%) were diagnosed by fourfold rise (2.5% in 2005) and 33 (3.6%) by single high titre (4.5% in 2005). Of the cases diagnosed by fourfold rise, five were *L. pneumophila* serogroup 1, whilst one was a *L. pneumophila* serogroup 6 and the others had unknown serogroup.

Travel

A total of 63 different countries were visited by the cases during their incubation periods in 2006 (Figure 2). Ninety four cases (10.2%) visited countries outside the EWGLINET scheme; 66 cases visited more than one European country, and ten visited more than one country outside Europe. Eleven cases were associated with cruise ships. The four countries associated with most cases of infection were Italy, France, Spain and United Kingdom. Together they accounted for 58.5% of the total data set in 2006 (538 cases); Italy was associated with 198 (21.7%) cases, France 159 (17.3%), Spain 126 (13.8%) and United Kingdom 55 (6.0%). In previous years, Turkey was the fourth country on the list but in 2006 it accounted for 45 cases (4.9%), less than United Kingdom.

Of the infections associated with travel in Italy, 58.1% occurred among Italian nationals travelling in their own country (115 cases). Likewise, 61.6% of cases visiting sites in France were French nationals (98 cases) travelling internally in their own country, as

FIGURE 1

Number of travel-associated Legionnaires' disease cases reported to EWGLINET since the scheme began in 1987 (n=6349)

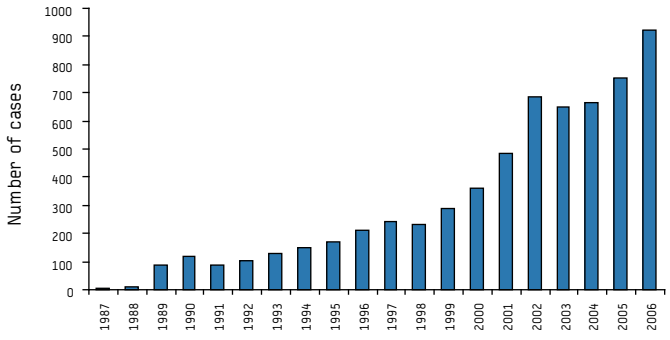

TABLE 1

Countries reporting more than 10 cases of travel-associated Legionnaires' disease to EWGLINET in 2005 and 2006

	Number of cases	
Country of report	2005	2006
United Kingdom	202	250
France	157	174
The Netherlands	134	158
Italy	96	130
Spain	30	73
Sweden	23	28
Denmark	40	26
Belgium	13	16
Austria	18	14
Norway	13	12

Note: In addition, ten other countries reported fewer than 10 cases, and are not listed here

were 47 of the cases linked to the United Kingdom (85.5%), and 35 (27.8%) of the cases linked to travel in Spain. Only one Turkish case was reported with travel within Turkey. The proportion of cases associated with clusters in Italy was 30.3% (60 cases). In France the proportion was 25.8% (41 cases), in Spain 42.1% (53 cases) and in the UK 5.5% (3 cases). In Turkey the proportion was 37.8% (17 cases) - a decrease from 53.2% in 2005 and 43.8% in 2004.

Clusters

One hundred and twenty four new clusters were identified in 2006, compared with 93 in 2005, 86 in 2004 and 89 in 2003. This does not include clusters which were identified in previous years and were associated with a subsequent case in 2006 ('cluster updates'); these clusters are included in the previous years' figures. The number of new clusters reported for 2006 represents a substantial increase of 33.3% compared with 2005. A total of 274 cases (29.8%) were part of clusters in 2006. Most of the clusters (107) comprised only two cases and 13 comprised three cases, so that 96.8% of all clusters fell into this group (Figure 3), compared with 93.5% in 2005. The largest cluster in 2006 involved five cases (down from eight cases in 2005). Forty three (34.7%) of the new clusters consisted of a single case that was reported by each of the two or more countries. These clusters would not have been detected without EWGLINET.

Clusters were detected in 27 countries, with Italy associated with the highest number (29), followed by Spain (24), France (23), Turkey (7), Greece (4) and Germany (4) (Table 2). Of the remaining clusters, 15 (12.1%) occurred in countries outside EWGLINET, a slight reduction on the 15.1% identified in 2005.

Ninety one of the clusters (73.4%) occurred during the summer period between May and October but clusters were detected during every month of 2006 (by date of onset of the second case in the cluster).

Figure 2

Countries visited by more than 10 cases of travel-associated Legionnaires' disease in 2006, by type of case, EWGLINET data

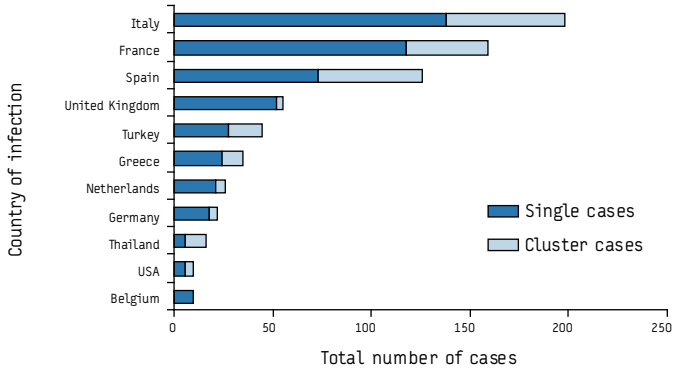

Figure 3

Number of cases of travel-associated Legionnaires' disease per cluster, by year, from 2003 to 2006, EWGLINET data

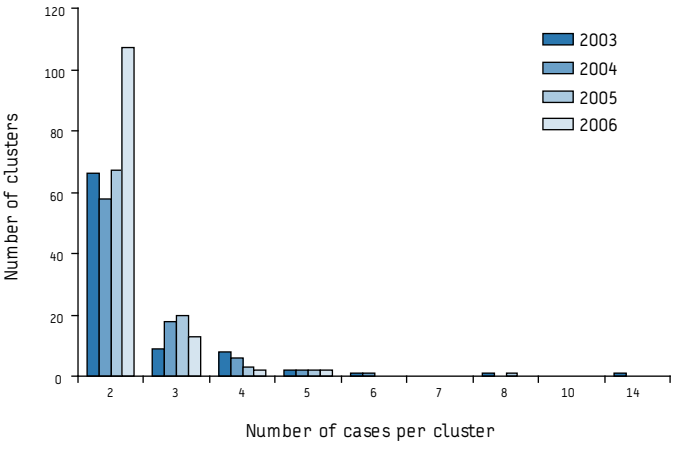

Table 2

Countries associated with clusters of travel-associated Legionnaires' disease in 2006, EWGLINET data

Country of infection	Number of clusters
Europe	
Italy	29
Spain	25
France	22
Greece	4
Germany	4
United Kingdom (England)	3
Sweden	2
The Netherlands	2
Poland Czech Republic	1
Poland	1
Malta	1
Luxembourg	1
Latvia	1
Germany/Italy	1
Jersey	1
Denmark	1
Croatia	1
Bulgaria	1
Austria	1
Non-Europe	
Turkey	7
Mexico	3
India	3
USA	2
Thailand	2
USA/Caribbean	1
USA/Mexico/Caribbean	1
Malaysia	1
Indonesia	1
Cuba	1

Investigations and publication

One hundred and thirty four accommodation sites were associated with the 124 new clusters in 2006. Twenty three of these sites were located in countries not signed up to follow the European guidelines, leaving 111 cluster sites that required EWGLINET investigations (an increase of 24.7% compared with the 89 sites that required investigations in 2005). Eighty two sites were associated with cluster updates issued in 2006, 33 of which included clusters where additional cases were detected after investigations had been completed and control measures were reported as satisfactory (re-offending sites); under the terms of the guidelines, these sites required further investigation. Two of the sites in 2006 fell into this 're-offending' category twice each. Thus, EWGLINET requested that a total of 146 investigations be conducted in 2006.

Ninety seven (66.4%) of the 146 Form B reports related to these investigations stated that *Legionella* spp. at concentrations equal to or greater than 1000 cfu/litre [1] were isolated from water samples taken at the accommodation sites. This compares with 57.4% of positive samples in 2005. Of the remaining 49 sites investigated, 46 (31.5%) reported that legionella was not detected in samples at the required levels, and three 'Form B' reports (2.1%) reported 'unknown' results due to site closures.

Whilst 35 investigations were conducted at re-offending sites, 33 distinct sites were involved with two sites re-offending twice (compared with 26 distinct sites in 2005, six of which re-offended twice). Fourteen of these sites were situated in Italy, six in France, five in Turkey, three in Greece and one each in Bulgaria, Malta, Poland, Spain and the United Kingdom. Twenty one of the 35 reinvestigations (57.1%) returned positive samples (compared with sixteen out of 32 reinvestigations in 2005 (50.0%)). One of the re-offending sites was part of a complex cluster (where the cases implicate more than one accommodation site as a potential source).

Only two accommodation sites (including one re-offending site) were published on the EWGLI website during 2006 for failure to return Form A or Form B reports on time, or for failure to implement appropriate control measures within the required period. Two further re-offending sites from 2006 were published in 2007. These sites were located in Bulgaria, France, Poland and Turkey. This represents a significant reduction from the nine site names published during 2005, four in 2004 and 27 published in 2003.

There is no requirement to investigate sites associated with a single case report within the EWGLINET guidelines. However, some countries do carry out these investigations and in 2006 reports were received for 82 such sites (114 sites in 2005), 48 (58.5%) of which were reported positive for *Legionella* spp. (at concentrations equal to or greater than 1000 cfu/litre [1].

Discussion

In 2006, the number of cases of travel-associated Legionnaires' disease reported to EWGLINET was higher than in any previous year, continuing the overall increasing trend in case numbers seen since the scheme began. Legionnaires' disease case numbers are increasing across Europe [3] (not only travel-associated cases), and several factors are driving this upward trend. Improved surveillance in national centres is an important factor contributing to the rise in cases; diagnosis, detection and reporting are being strengthened across Europe. However, some countries still only detect a handful of cases each year [3], and 17 of EWGLINET's 35 member countries reported no travel-associated cases to the scheme in 2006. Other factors that should also be considered as contributing to the increase in case numbers include climate change and generally warmer temperatures [4], and perhaps improved environmental conditions for growth of the legionella bacteria and therefore more opportunities for infection in travellers. In addition, it is known that leisure travel has increased markedly in recent years and that many active elderly (a more susceptible age group), are embarking on holidays further afield and outside Europe, increasing their risk of exposure to infection in countries where control and prevention programmes may be less well developed compared with European holiday destinations. The data set for 2006 showed that among the cases aged 70-79 years, 12.1% travelled outside Europe (19 out of 157 cases) compared with only 6.3% in this age group in 2005 (8 out of 127 cases*) (odds ratio=2.74, p=0.098). Among all cases associated with travel outside Europe, 24.0% were aged 70 or more in 2006 (25 out of 104 cases) compared with 11.8% in 2005 (10 out of 85 cases*) (odds ratio 4.64, p=0.031). (*Note that the figures for 2005 presented in this paragraph use data amended since last publication [3], and as such are not comparable with the other data for 2005 presented throughout this paper.)

The proportion of cases diagnosed by culture remained very low but relatively stable in comparison with 2005 although a rise in the absolute number of isolates was seen in 2006. Three quarters of the isolates came from single cases, a similar proportion to that observed in 2005 (73.7%) and were reported mainly by countries with a strong background in this methodology. Countries should be encouraged to increase the number of specimens taken for culture from cases associated with clusters in order to support the findings of epidemiological and environmental investigations, in addition to those collected prospectively and in advance of any case becoming part of a cluster. The number of isolates associated with cases that are known to have died is much higher than for other cases and was similar for 2005 and 2006 (13.2% in 2005 and 12.5% in 2006). This probably reflects the greater importance placed on thorough investigation of the illness when it has had a fatal outcome.

As case numbers have increased, so has the proportion of diagnoses conducted by urinary antigen detection. This has implications for investigators seeking to identify the source of an infection, since urinary antigen tests are mostly specific to *L. pneumophila* serogroup 1 infections and cannot distinguish between other serogroups or different strains within serogroup 1. Because *Legionella* spp. are ubiquitous in the environment, this is often insufficient evidence for legal purposes and compensation claims by cases. Also, if additional tests are not conducted on urine-negative cases, it is possible that non-serogroup 1 infections will be missed.

The case fatality rate decreased slightly in 2006, whilst the number of cases reported without a definitive outcome (i.e. reported as 'unknown outcome' or 'still ill') has increased. These two trends are probably linked, and it is likely that the 'unknown' or 'still ill' outcomes include some cases that died following the report to EWGLINET.

There has been a large increase in the number of clusters detected in 2006. This is due in no small part to Spain's retrospective reporting of 35 cases, most of which were associated with Spanish clusters; the majority of these case reports were submitted early

in 2007, which in turn accounts for the longer period between onset and report to EWGLI in 2006 compared with 2005. 2006 was the first year when Spain was able to report Spanish cases that had travelled internally within their country, following the relaxation of local reporting regulations. Spain should ordinarily have investigated these sites even without a EWGLINET cluster alert, since their public health authorities would have been notified of all of the cases associated with the particular accommodation site (whether through their national reporting scheme or through EWGLINET). Therefore we expect that the public health impact of Spain's change of reporting policy will be minimal for EWGLINET and the standards laid down in the European guidelines [1] since these in practice do not vary greatly from Spain's national investigation standards [5]. However, due to Spain's improved reporting, EWGLINET's case and cluster numbers are now more complete than in previous years.

The increase in cluster numbers has implications both for work load of EWGLINET's collaborators and the relevant national health authorities, and for the impact of Legionnaires' disease on the tourist industry. Tour operators are informed of clusters of three or more cases with onset of infection within three months of each other and about all clusters outside Europe. With the rise in travel to non-European countries, more clusters are expected to occur in countries where experience of legionella control and prevention is limited compared to Europe. When these happen it is costly for tour operators to relocate their guests, but the prevention of further, possibly fatal, cases of Legionnaires' disease is a public health priority and should be executed regardless of all costs.

Whilst the overall number of clusters has increased, those located in Turkey have decreased (seven in 2006 compared with 15 in 2005) and the number of reoffending sites has also decreased (five compared with 11 in 2005). This is very encouraging since Turkey has had difficulties with Legionnaires' disease in the past [6].

The proportion of positive environmental samples from cluster sites increased from 57.4% in 2005 to 67.8% in 2006. Since 2004, EWGLINET has been funded to hold annual training courses for collaborating countries in legionella outbreak management, risk assessment, sampling and control. Courses will also be held in 2008 and 2009. These training courses have led to an improvement in legionella detection and diagnosis in Europe and have positively contributed to higher quality surveillance programmes in many countries. However, as more cases are entered into the EWGLINET database, there is an increased likelihood of clusters occurring by chance, but with better microbiological expertise, we would expect these to return negative sampling results.

Despite the increase in the number of clusters and the related investigations, there was a reduction in the number of clusters published on the EWGLI website in 2006. This is encouraging, and indicates the timely investigation of these sites by EWGLINET collaborators and other public health professionals in the countries of infection.

Note: The data presented throughout this paper for 2005 (except where indicated by an asterisk) reflects case numbers as they appear in previous publications [3].

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*The list of EWGLINET collaborators is available at the following URL address: http://www.ewgli.org/collaborators.htm

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