Travel-associated Legionnaires' disease in Europe in 2007

C A Joseph (Carol.Joseph@HPA.co.uk)[1], R Yadav[1], K D Ricketts[1], on behalf of the European Working Group for Legionella Infections[1]
1. Respiratory and Systemic Infections Department, Health Protection Agency Centre for Infections, London, United Kingdom

Nine hundred and forty six cases of travel-associated Legionnaires' disease were reported to the European Surveillance Scheme for Travel Associated Legionnaires' Disease (EWGLINET) with onset during 2007; 890 were confirmed and 56 were presumptive. Twenty eight cases died, giving a case fatality rate of 3.0%. 8.2% of cases were diagnosed by culture, an important increase from 5.2% in 2006.

One hundred and twelve new clusters were identified; the largest involved nine cases. Sixteen of these clusters (14.3%) occurred in countries outside EWGLINET, and three involved cruise ships. Twenty nine of the new clusters (25.9%) would not have been detected without the EWGLINET scheme. A total of 151 investigations were conducted in Europe, 42 of which were conducted at 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 13 accommodation sites were published on the European Working Group for Legionella Infections (EWGLI) website; 11 of these were situated in Turkey.

Introduction

Cases of Legionnaires' disease are often associated with overnight stays in public accommodation sites which may be visited by individuals from all over the world. As such, a cluster of cases of Legionnaires' disease at a public accommodation site may involve nationals from more than one country and if the countries concerned do not share information on their cases, these clusters can go undetected. In 1987, the European Working Group for Legionella Infections (EWGLI) established a surveillance system known as 'The European Surveillance Scheme for Travel Associated Legionnaires' Disease' (EWGLINET) with the aim of identifying clusters of travel-associated cases in Europe that may not be detected by national surveillance systems alone, and initiating investigation and control measures at such sites.

In 2002, EWGLI members introduced the European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease [1], to standardise investigation and control measures conducted at cluster sites. These were endorsed by the European Commission in 2003. 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 2007.

Methods

Each of the countries that participate in the EWGLINET scheme run their own national surveillance schemes for Legionnaires' disease, which collect information on cases occurring in their residents. In order to ensure that every country reports their data to EWGLINET in a consistent manner, standardised case definitions have been developed [2]. When a travel-associated case is identified that meets these definitions, it is reported to EWGLINET's coordinating centre at the Health Protection Agency Centre for Infections in London. The coordinating centre maintains a database of all cases that have been reported to the scheme since its inception, and this is searched each time a new case is added to determine whether it is a single case or part of a cluster. These are defined in the following way [2]:

- A single case: 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 another case of Legionnaires' disease within two years.
- A cluster: 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.

In 2002, EWGLI determined that the investigations conducted in response to EWGLINET single and cluster case notifications should be standardised. To this end, the group introduced the European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease [1]. In response to the notification of a single case of Legionnaires' disease associated with an accommodation site, the collaborator in the country of infection is informed and is required to send the site a checklist for minimising risk of legionella infections so that the site can ensure it is following best practice. At this stage no further actions at the international level are required because the epidemiological evidence suggesting that the site is the source of infection is relatively low, although further investigations may be conducted locally.

However, if a collaborator receives a EWGLINET notification of a cluster associated with an accommodation site in their country, they are required to initiate a full investigation of the site. First, a risk assessment and initial control measures must be implemented within two weeks, and a 'Form A' report returned to the coordinating centre to record that preliminary measures have been completed. Second, environmental sampling must be carried out and control measures completed within a further four weeks, and a 'Form B'

report returned to the coordinating centre to record the completion and results of the investigation.

Because these measures are deemed to be important for the protection of public health across Europe, EWGLINET will publish details of any cluster site which is not properly investigated, or where the investigation is not completed on time, on its public website (www.ewgli.org). The information is then in the public domain and individual travellers or tour operators can choose for themselves whether or not to contract with these sites. The notice is removed once the relevant forms have been received.

If a site has been associated with a cluster and investigated under the guidelines, but is subsequently linked with a further case within a two year period, it is termed a 're-offending' site and a complete re-investigation is required. If two cases have more than one accommodation site in common during their incubation periods, it is not possible to know which site may have caused the infections. This situation is termed a 'complex cluster', and each site involved is investigated separately.

Figure 1

Number of travel-associated Legionnaires' disease cases reported to EWGLINET since the scheme began in 1987 (n=7,295)

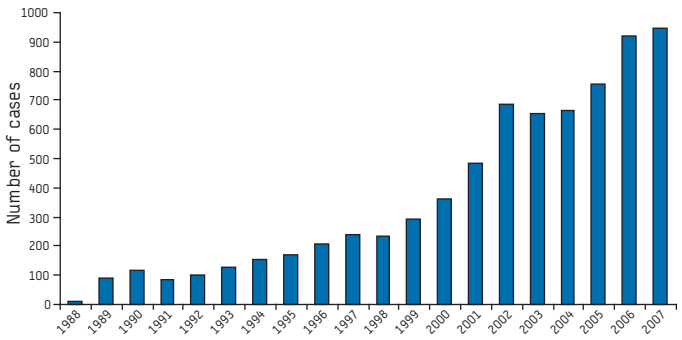


Table 1

Countries reporting more than 10 cases of travel-associated Legionnaires' disease to EWGLINET in 2007

	Number of cases	
Country of report	2006	2007
United Kingdom	250	236
France	174	181
Italy	130	153
The Netherlands	158	137
Spain	73	68
Sweden	28	41
Denmark	26	31
Austria	14	21
Norway	12	17
Belgium	16	15
Finland	6	14
Ireland	9	11

Note: In addition, ten other countries (including the United States), reported fewer than 10 cases and are not listed here

Results

Cases and outcomes

In 2007 the EWGLINET surveillance scheme had 35 collaborating countries of which 21 reported a total of 942 cases of travel-associated Legionnaires' disease with onset during 2007 (England and Wales, Scotland and Northern Ireland have been counted as one country). This compares with 18 countries that reported 921 cases in 2006. The United States, a country not part of the official network, reported a further four cases in American citizens who had travelled to Europe. This brought the total number of cases reported to the EWGLINET scheme with onset in 2007 to 946, a small increase of 2.7% on the number reported in 2006 and a 25.3% increase on the number of cases in 2005 (Figure 1). The mean interval between onset and report to EWGLINET was 28 days in 2007 compared with 36 days in 2006 (due to the late report of some cases from Spain) and 29 days in 2005.

The majority of the cases reported in 2007 were from the following countries: United Kingdom (236 cases), France (181), Italy (153) and the Netherlands (137) (Table 1). This represents 74.7% (707 cases) of the total number of cases for the year.

The high occurrence of infection in males continues, with cases in males outnumbering those in females at a ratio of 2.6:1 (686 males and 260 females, compared with a ratio of 2.8:1 in 2006). As in previous years, cases in 2007 mainly occurred in the older age groups with peaks in the 50-59 year age group for men (median 59 years) and the 60-69 year group in women (median 61 years).

In 2007 the peak month for onset of cases was September (157 cases), compared with August in 2006 (162 cases), continuing the established pattern of high incidence during the summer period often seen with this travel-associated disease specific network.

Outcomes were provided for 470 (49.7%) cases, and 28 deaths were notified (3.0% of the total cases). This case fatality rate is slightly less than that in 2006 (33 deaths, 3.6%). The 28 deaths were reported for cases aged 42 to 86 years (median 69 years); 23 were male and five were female. The majority of deaths in 2007 were associated with single cases (17 cases, 60.7%), although less than in 2006 when 87.9% of the reported deaths were linked to single cases. The remaining deaths in each year were associated with clusters.

Microbiology

The 2007 dataset comprised cases diagnosed by urinary antigen detection, culture, serology and PCR. Under the EWGLINET case definition, 890 cases were classified as confirmed and 56 were classified as presumptive [2]. The confirmed cases consisted of 805 cases diagnosed primarily by urinary antigen detection (85.1%, a decrease from 89.2% in 2006), 78 cases diagnosed by culture (8.2%, compared with 5.2% in 2006), and seven cases diagnosed by serology fourfold rise as *L. pneumophila* serogroup 1 (0.7% compared with 0.5% in 2006). The presumptive cases consisted of a further eight cases diagnosed by serology fourfold rise as the main method of diagnosis (six diagnosed as *L. pneumophila* serogroup unknown and two as non-serogroup 1) (0.8% compared with 0.7% in 2006), 38 diagnosed primarily by single high titre (4.0%, compared with 3.6% in 2006) and 10 diagnosed primarily by PCR (1.1%, up from 0.8% in 2006).

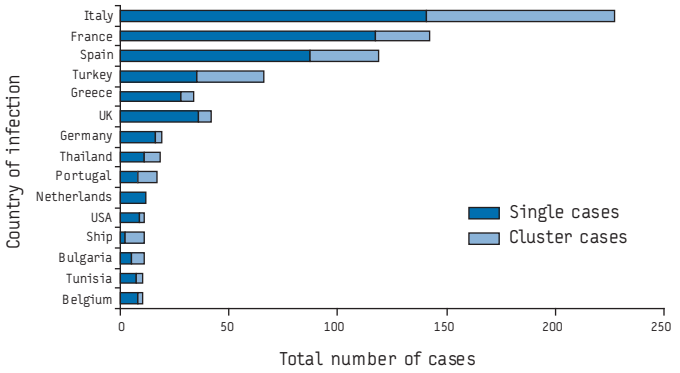
Travel

Cases visited a total of 73 different countries during their incubation periods in 2007 (Figure 2). One hundred and eighteen cases (12.5%) visited countries outside the EWGLINET scheme and 11 cases were associated with cruise ships. Sixty six cases visited more than one European country, and three visited more than one country outside Europe. The four countries most frequently associated with infection were Italy, France, Spain and Turkey and together they accounted for 58.6% of the total 2007 data set (554 cases). Italy accounted for 227 (24.0%) cases, France 142 (15.0%), Spain 119 (12.6%) and Turkey 66 (7.0%).

Of the 227 cases associated with travel in Italy, 48.9% of the infections occurred among Italian nationals travelling in their own country (111 cases). For France this proportion was higher, 69.7% of cases visiting sites in France were French nationals (99 cases). For Spain 33 cases were travelling internally in their own country (27.7%). There were no Turkish nationals among the cases reported with travel to Turkey; 23 cases came from the Netherlands (34.8%) and 22 from the United Kingdom (33.3%). The proportion of cases associated with clusters in Italy was 37.9% (86 cases). In France the proportion was 17.6% (25 cases), and in Spain 26.9% (32 cases). The proportion of cases associated with clusters in Turkey increased to levels seen in previous years, at 47.0% (31 cases).

FIGURE 2

Countries visited by 10 or more cases of travel-associated Legionnaires' disease in 2007, by type of case, EWGLINET data



Note: A further 58 countries were visited by less than 10 cases, and do not feature on this graph.

TABLE 2

Countries where two or more clusters of travel-associated Legionnaires' disease occurred in 2007, EWGLINET data

	Country of infection	Number of clusters
Europe		
	Italy	39
	France	17
	Turkey	12
	Spain	7
	Greece	4
	Portugal	3
	Bulgaria	2
	Germany	2
	Malta	2
	United Kingdom	2
Non-Europe		
	India	3
	Thailand	3
	United Arab Emirates	2
Other		
	Cruise ships	3

Note: In addition eleven other countries were associated with only one cluster and are not listed here

Clusters

The number of new clusters identified in 2007 was 112 compared with 124 in 2006, 94 in 2005 and 85 in 2004 (this does not include clusters which were identified in previous years and were associated with a subsequent case in 2007 ('cluster updates'); these clusters are included in the previous years' figures). This represents a decrease of 9.7% in the number of new clusters notified from 2006. A total of 278 cases (29.4%) were part of clusters in 2007. Twenty nine of the new clusters (25.9%) consisted of a single case that was reported by each of two or more countries; these would not ordinarily have been detected by national surveillance systems alone.

The largest cluster detected during 2007 involved nine cases (the same as in 2006), one of whom died, following a Baltic cruise in July and August. The ship was carrying approximately 723 passengers and 329 crew members. Seven of the cases were females and two were males; the cases were aged between 59-86 years. Investigations showed the ship's water system to be the likely source of infection.

The 2007 clusters were detected across 24 countries and on three cruise ships. Italy was associated with the highest number (39), followed by France (17), Turkey (12), Spain (7), Greece (4) and Portugal (3) (Table 2). Of the remaining clusters, 16 (14.3%) occurred in countries outside EWGLINET, a slight increase on the 12.1% outside EWGLINET in 2006.

The seasonal pattern of clusters remains in line with the high incidence of cases during the summer period, with 93 of the clusters in 2007 (83.0%) occurring between May and October. Clusters were also detected in all the other months of 2007 outside this period (by date of onset of the second case in the cluster).

Investigations and publication

One hundred and thirty one accommodation sites were associated with the 112 new clusters in 2007 (some of the clusters were complex clusters involving more than one accommodation site). Twenty two of the total number of sites (16.8%) were located in countries that had not signed up to follow the European guidelines, leaving 109 new cluster sites that required EWGLINET investigations. In addition, 42 sites were associated with cluster updates issued in 2007 where additional cases were detected after investigations had been completed and control measures were reported as satisfactory ('re-offending sites'). The guidelines require that these sites are re-investigated; accordingly, EWGLINET

requested a total of 151 investigations to be conducted in 2007, a similar number to the 146 investigations required in 2006.

Eighty two (54.3%) of the 151 Form B reports submitted to the coordinating centre reported that Legionella spp. was isolated from water samples taken at the accommodation site. This compares with 66.4% of reports with positive sampling results in 2006. Of the remaining 69 sites investigated, 66 (43.7% of the total) reported that legionella was not detected in samples, and three 'Form B' reports (2.0% of the total) reported 'unknown' results due to site closures.

Of the 82 sites where *Legionella* spp. was isolated from the water, *L. pneumophila* serogroup 1 was isolated from 57 sites (69.5%), at 12 sites the isolates were non-serogroup 1 (other species or serogroups) (14.6%), and the reports for 13 sites did not include enough information to categorise them in this way (15.9%).

There were 42 instances where additional cases were associated with a site after it had been investigated ('re-offending sites'). Three of these re-offences occurred at the same site; thus 40 distinct sites were associated with further cases in 2007 subsequent to a previous cluster. This compares with 33 re-offending sites in 2006, two of which re-offended twice (31 distinct sites). Nineteen of the re-offending sites in 2007 were situated in Italy, eight in Spain, six in Turkey, two in France, and one each in Austria, Czech Republic, Germany, Latvia, Portugal. Twenty three of the 42 reinvestigations (54.8%) returned positive samples (compared with 21 out of 35 reinvestigations in 2006 (60.0%). Four of the re-offending sites were part of a complex cluster (where the cases involve more than one accommodation site as a potential source).

Thirteen accommodation sites were published on the EWGLI website during 2007 for failure to return Form A or Form B reports on time, or for failure to implement appropriate control measures within the required period. These sites were located in Turkey (11), Italy (1) and France (1). This represents a significant increase from the four site names published during 2006 (nine publications in 2005, and four in 2004).

The European guidelines do not require an investigation to be carried out at sites associated with a single case report. However Italy, and occasionally other countries, do carry out such investigations and in 2007 reports were received for 107 single case sites (82 sites in 2006), of which 48 (44.9%) were reported positive for *Legionella* spp. One of these reports was received from Turkey, one from Latvia, and the rest from Italy.

Discussion

Travel-associated Legionnaires' disease continues to represent a significant public health burden in many European countries and impacts disproportionately on otherwise healthy individuals as a consequence of their travel abroad or within their own country. Improved ascertainment and better reporting to EWGLINET has increased the number of cases linked to travel from less than one hundred in 1989 to almost one thousand in 2007. Whilst this rise in cases is formidable, it probably remains an underestimate of the true incidence of travel-associated legionella infection since many studies continue to highlight the issues of underdiagnosis and underreporting of Legionnaires' disease [3,4].

As in previous years the four countries most frequently associated with cases continue to be France, Italy, Spain and Turkey. A large proportion of cases from both Italy and France are people travelling internally within their own country. Since both countries have well established surveillance systems, these cases are likely to be due to differences in travel patterns. People from northern Europe will travel to the warmer countries of southern Europe for holidays, whilst those of southern Europe will tend to vacation closer to home.

Because the number of visitors or internal travellers in France, Italy and Spain is large, rates of infection per million visitors are much lower than in Turkey which receives fewer visitors. In 2007, rates of infection per million visitors from the UK were 2.93 for Spain compared with 13.47 for Turkey, reflecting the fact that 41 cases were reported from more than 14 million visitors from the UK to Spain compared with 22 cases from 1.6 million UK visitors to Turkey [5]. Rates of infection for other nationals such as the Dutch are known to be very high in relation to travel to Turkey [6], and more than two thirds of the 66 cases linked to Turkey in this dataset are UK and Dutch residents. The greater number of clusters detected in Turkey (12) than in Spain (7), along with the high rate of infection, suggest that control and prevention measures in tourist accommodations in Turkey are less well managed. This is also borne out by the fact that 11 of the 13 clusters published on the EWGLI website in 2007 were located in Turkey. It is hoped that Turkish health officials will take note of these findings.

The increase in the number of cases diagnosed by bacterial culture is to be welcomed since these may contribute to identifying the source of infection in accommodation sites where positive environmental samples have also been obtained. A legionella-positive environmental sample on its own is not sufficient to determine the source of infection although the likelihood that the accommodation is the source increases when clusters of two or more cases with onset of illness close together in time are linked to a site. The fall in the proportion of cluster sites with positive sampling results in 2007 (54.3% compared with 66.4% in 2006) is a return to the level observed in previous years. These levels can be compared with those reported in a French study of public accommodation sites not known to be linked to cases of Legionnaires' disease, where 18.3% were positive [7]. That the percentage of positive sites was so much higher in the EWGLINET scheme reflects the targeted nature of the cluster investigations.

At the time of report, many collaborators do not know the clinical outcome of their cases (almost 50% of cases had an unknown outcome in 2007). Hence the very low mortality rate recorded by the scheme may be the result of these unknown outcomes. Accordingly, the increased proportion of deaths linked to clusters compared with single cases in 2007 could be due to the follow-up of these clusters and better ascertainment of mortality data for this group of cases.

Travel-associated Legionnaires' disease linked to countries outside Europe is continuing to rise, as is the proportion of tourists aged 70 years or more who are visiting these countries [8]. These susceptible active elderly are at increased risk from legionella infections in countries outside the EWGLINET scheme where less well developed legionella control and prevention programmes exist. Although EWGLINET clusters that occur outside Europe are reported by EWGLI via the World Health Organization (WHO) to the ministry of health in the country concerned, minimal information on investigation and control measures is relayed back to the scheme. The Preparedness and Response Unit of the European Centre for

Disease Prevention and Control (ECDC) hosted a meeting in October 2007 between representatives of EWGLINET, the major international tour operators and the European Commission to address how this situation might be improved and several recommendations were made that are now being discussed at the international level. Since tour operators are always informed of clusters outside Europe, their role in supporting local investigations will be crucial in taking forward some of the recommendations.

In January 2010 EWGLINET will move its coordinating centre to ECDC. Transition of the scheme will take place during 2009 in order to ensure a smooth transfer of reporting and responding to cases of travel-associated Legionnaires' disease thereafter.

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

Aknowledgements

This work is funded by the European Centre for Disease Prevention and Control. We would like to thank all of the collaborators* for reporting their cases and all of the people involved in public health control and prevention programmes for travel-associated Legionnaires' disease.

References

1. European Working Group for Legionella Infections. European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease. London: PHLS; 2002. [Accessed 12 January 2009] Available from: http://www.ewgli.org/data/european_guidelines.htm
2. European Working Group for Legionella Infections. Case Definitions. [Accessed 12 January 2009]. Available from: http://www.ewgli.org/ewglinet/case_definitions.htm
3. Rota MC, Cawthorne A, Bella A, Caporali MG, Filia A, D'Ancona F; Legionellosis Working Group. Capture-recapture estimation of underreporting of legionellosis cases to the National Legionellosis Register: Italy 2002. Epidemiol Infect. 2007;135(6):1030-6.
4. Van Hest NA, Hoebe CJ, Den Boer JW, Vermunt JK, Ijzerman EP, Boersma WG, et al. Incidence and completeness of notification of Legionnaires' disease in The Netherlands: covariate capture-recapture analysis acknowledging regional differences. Epidemiol Infect. 2008;136(4):540-50.
5. Office for National Statistics. MQ6 Transport Travel and Tourism. Overseas Travel and Tourism. Quarter 4 2007. Table 23. [Accessed 12 January 2009] Available from: http://www.statistics.gov.uk/downloads/theme_transport/mq6-q4-2007.pdf
6. Dijkstra F, van Gageldonk-Lafeber AB, Brandsema P, Friesema IHM, Robert-Du Ry van Beest Holle M, et al. Jaarrapportage respiratoire infectieziekten 2007/2008 [Annual report on respiratory infections 2007/2008]. RIVM-briefrapportnummer 210231003. Bilthoven: RIVM; 2008. Available from: http://www.rivm.nl/bibliotheek/rapporten/210231003.html
7. Institut de Veille Sanitaire. Pratiques des Ddass devant un cas isolé de légionellose non nosocomiale et non thermale en 2002 [Practices of the Ddass in management of a single case of legionellosis not linked to healthcare or thermal setting in 2002]. Paris : Institut de Veille Sanitaire ; February 2006. [Accessed 12 January 2009] Available from: http://www.invs.sante.fr/publications/2006/legio_ddass_2002/legio_ddass_2002.pdf
8. Office for National Statistics. International Passenger Survey 2000 to 2007. [Accessed 12 January 2009] Available from: http://www.statistics.gov.uk/statbase/Product.asp?vlnk=1905&More=N

This article was published on 7 May 2009.

Citation style for this article: Joseph CA, Yadav R, Ricketts KD, on behalf of the European Working Group for Legionella Infections. Travel-associated Legionnaires' disease in Europe in 2007. Euro Surveill. 2009;14(18):pii=19196. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19196