Travel-associated Legionnaires' disease in Europe in 2008

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In 2008, the European Surveillance Scheme for Travel Associated Legionnaires' Disease (EWGLINET) received reports of 866 cases of travel-associated Legionnaires' disease, 42 of whom were reported to have died. 824 of the cases were classified as confirmed and 42 were presumptive. As in previous years, a very low proportion of clinical isolates were obtained (63 cases, 7.3%). Males outnumbered females by 2.8:1 in the 2008 dataset and had a median age of 60 years compared with women, whose median age was 63 years. Travel outside Europe was reported for 12% of the cases. The scheme identified 108 new clusters in 2008. Sixteen were located in countries outside EWGLINET and 38 (35.2%) involved only one case from each reporting country, and would not ordinarily have been detected by national surveillance schemes alone. The largest cluster (six cases) was associated with travel to Spain. The 108 clusters were associated with 144 environmental investigations, 35 of which were at re-offending sites, (sites which had previously been investigated and where additional cases had subsequently occurred). At 61 (42.1%) of the sites Legionella species were detected. The names of 12 sites were published on the EWGLINET website.

Introduction

EWGLINET (the European Surveillance Scheme for Travel Associated Legionnaires' Disease) is a disease-specific network which aims to detect clusters of Legionnaires' disease associated with accommodation sites across Europe. It was established in 1987 by EWGLI (the European Working Group for Legionella Infections) in order to better protect the health of travellers by improving the detection and control of sources of infection in European countries.

Travel-associated clusters are unusual in that they often involve residents from more than one country and as such may not be identified by national surveillance systems alone. EWGLINET collates and coordinates the information held by each country, and communicates with the country in order to initiate investigations and control measures at sites of potential exposure.

In 2002, EWGLI introduced The European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease [1]. These guidelines are designed to ensure a common standard of response to single cases and clusters of travel-associated Legionnaires' disease across Europe, and 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 2008.

Methods

National surveillance systems collect data on all cases of Legionnaires' disease that occur within their countries. Cases that have stayed overnight in a public accommodation site during their incubation period, and that meet EWGLINET's case definition [2] are reported to the scheme.

Basic epidemiological, microbiological and exposure information for each reported case is entered into a database held by the coordinating centre at the Health Protection Agency Centre for Infections in London. A database search is performed for each new case, to determine whether it should be classified as a single case or as part of a cluster. These are defined as follows [1]:

- **Single case:** A person who stayed, in the two to 10 days before onset of illness, at a public accommodation site that has not been associated with another case of Legionnaires' disease within two years.
- **Cluster:** Two or more cases who stayed at the same accommodation site in the two to 10 days before onset of illness and whose onset is within the same two-year period.

This classification determines the response that is expected from the country of infection under the

European guidelines [2]. A single case may have contracted Legionnaires' disease at any time during their incubation period of two to 10 days, and as such the accommodation site will often be only one of many potential sources. Therefore, the only required response to single cases is that the collaborator in the country of infection must send the accommodation site a checklist for minimising the risk of Legionella infections, to encourage the site to follow best practice. Further investigations may be conducted locally at the discretion of the national collaborator.

However, if the site is identified as a cluster site, a full investigation is required. Within two weeks a risk assessment must have been conducted and control measures initiated. These actions are reported back to the coordinating centre in London using a 'Form A'. Within a further four weeks, environmental sampling must have been carried out and control measures completed; a 'Form B' report is then submitted to the coordinating centre. If any of these actions are not completed within the time frame allowed, or if the report states that control measures are unsatisfactory, EWGLINET will publish the details of the accommodation site on its website. This is done so that individual travellers and tour operators can determine for themselves whether or not to contract with these sites. The notice is removed once investigations have been completed satisfactorily.

If the investigation of a cluster site has been completed, but the site is subsequently linked to additional cases within a two-year period, these are termed 're-offending sites' 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 determine which site was responsible for the infections and both will be subject to investigation; these are termed 'complex clusters'.

The number of clusters reported in this paper do not include those that were identified in previous years and were associated with a subsequent case in 2008 ('cluster updates'); such clusters are included in the previous years' figures.

Results

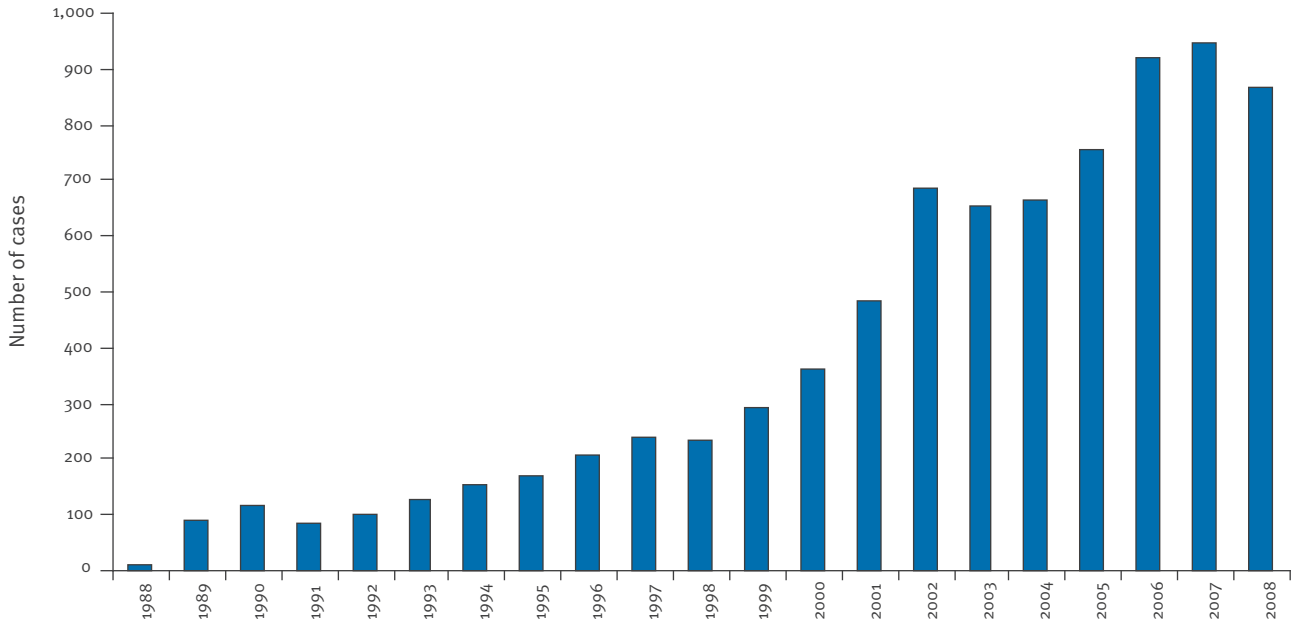
A total of 866 cases were reported to the EWGLINET surveillance scheme with onset during 2008. Among these cases, 853 were reported by 19 of the 35 countries who officially collaborate in the scheme. The remaining 13 cases were reported by Australia and the United States (not part of the official network). The overall number of cases with onset in 2008 was lower than the number with onset in 2007 (946 cases) (Figure 1). The mean interval between onset and report to EWGLINET in 2008 was 27 days (range: 1–300 days).

The highest numbers of cases were reported by France (190 cases), the United Kingdom (UK) (166 cases), Italy (127 cases) and the Netherlands (127 cases), and in total represented 70.4% (610 cases) of case reports (Table 1).

The sex and age distribution reflected the classical distribution for cases of Legionnaires' disease with a ratio of 2.8:1 (641 males and 225 females) and a median age of 60 years for men and 63 years for women. The age group with the most cases for men was 50-59 years and for women 60-69 years. Outcomes were provided for 427 cases (49.3%, the same proportion as in 2007), and 42 were reported to have died (9.8%). Overall, the case fatality for reported cases was 4.8% compared with 3.0% in 2007. The deaths occurred in 36 men and

Figure 1

Travel-associated Legionnaires' disease cases reported to EWGLINET since the scheme began in 1987 (n=8,161)



six women aged 26 to 85 years and 15 were associated with clusters (35.7%).

Cases of Legionnaires' disease tend to peak during late summer, and in a travel-associated scheme this seasonality is exaggerated, although cases occurred in all months of the year. September was the peak month for onset for cases reported to EWGLINET in 2008 (136 cases, 16.6%) and similar to the peak in September 2007 (157 cases, 15.7%).

Microbiology

Under the EWGLINET case definition, 824 (95%) of the 866 cases were confirmed and 42 were presumptive [2]. The confirmed cases consisted of 754 cases diagnosed primarily by urinary antigen detection (87.1%, an increase from 85.1% in 2007), 63 cases diagnosed by culture (7.3%, compared with 8.2% in 2007), and seven cases diagnosed by a fourfold rise in serology titre as L. pneumophila serogroup 1 (0.8%, compared with 0.7% in 2007). Of the 63 culture-confirmed cases, 57 were identified as L. pneumophila serogroup 1, one was serogroup 2, one was serogroup 3, three had unknown serogroups, and one had unknown species. The presumptive cases consisted of a further four cases (0.5%) diagnosed by a fourfold rise in serology titre, 25 cases (2.9%) diagnosed by a single high titre, and 13 diagnosed primarily by PCR (1.5%, an increase from 1.1% in 2007).

In addition to the 13 cases diagnosed primarily by PCR in 2008, 16 of the confirmed cases had a positive PCR test result in conjunction with other tests, to give a total of 29 cases with a positive PCR result. Fourteen of these were reported by Denmark, seven by the Netherlands, five by Sweden, and one each from Belgium, Finland and Scotland. The first PCR-positive cases were reported to EWGLINET in 1994; since then a total of 241 PCR-positive cases have been reported by fifteen countries. Over half of these (147 cases) were reported by Denmark.

Table 1

Countries reporting more than 10 cases of travel-associated Legionnaires' disease to EWGLINET in 2008

	Number of cases	
Reporting country	2007	2008
France	181	190
United Kingdom	236	166
Italy	153	127
The Netherlands	137	127
Spain	68	97
Denmark	31	38
Sweden	41	35
Norway	17	21
Austria	21	20
United States	4	12
Belgium	15	11

A further ten countries (including Australia) reported fewer than 10 cases and are not listed here.

Travel

A total of 60 different travel countries were reported in 2008 (Figure 2), with 104 cases (12.0%) visiting countries outside the EWGLINET scheme. Eleven cases were associated with cruise ships, and 62 cases visited more than one country during their incubation periods. The four countries in this dataset most frequently associated with infection were Italy (182 cases, 21.0%), France (151 cases, 17.4%), Spain (144 cases, 16.6%) and Turkey (62 cases, 7.2%); together they accounted for 62.2% of the total 2008 dataset.

The numbers of cases associated with travel to Italy, France and Spain include a high proportion of persons infected when travelling in their own country, in contrast to cases acquired as a result of travel abroad: 57.7% of the infections associated with Italy occurred among Italian nationals travelling in their own country (105 cases). For France this proportion was higher, at 72.2% (109 cases), and lower for Spain at 44.4% (64 cases). In contrast, there were no Turkish nationals among the cases reported with travel to Turkey.

Clusters

108 new clusters were identified in 2008, occurring in 24 countries and on one cruise ship. The highest numbers of clusters were associated with Italy (n=31), followed by France (n=17), Turkey (n=12), Spain (n=11), Greece (n=5), and Germany (n=3) (Table 2). Sixteen of the remaining clusters (14.8%) occurred in countries outside EWGLINET, a similar proportion to the 14.2% in 2007.

Altogether, 252 (29%) cases were associated with the clusters in 2008. For travel to Italy the proportion was 39.0% (71 cases), for France it was 23.2% (35 cases), and for Spain 20.8% (30 cases). The proportion of cases associated with travel to Turkey that were part of clusters continues to remain high. It was at its highest in 2005 when 53% of cases were part of clusters and at its lowest in 2006 (38%). In 2008 the proportion was 43.5% (27 cases).

The largest new cluster in 2008 involved six cases and occurred in Spain. Thirty-eight of the new clusters (35.2%) consisted of single cases that were reported by two or more countries; these would not ordinarily have been detected by national surveillance systems alone. The proportion of such clusters was higher in 2008 compared with 2007 (29 clusters, 25.9%) (p=0.13).

Clusters were detected in every month of the year in 2008 (by date of onset of the second case in the cluster). Following the seasonality seen in cases of Legionnaires' disease, there was also a seasonal pattern in the onset of clusters: 81 (75.0%) occurred between May and October.

Investigations and publication

Some clusters were complex and involved more than one accommodation site. The 108 clusters were associated with 129 accommodation sites. Twenty of these sites (15.5%) were situated in countries that had not signed up to follow the European guidelines, leaving 109 sites that required EWGLINET investigations. In addition, 35 're-offending sites' were reported in 2008 (compared with 40 in 2007), 16 situated in Italy, six in France, four in Spain, four in Turkey, two in Greece, one on a cruise ship and one each in Austria and Malta.

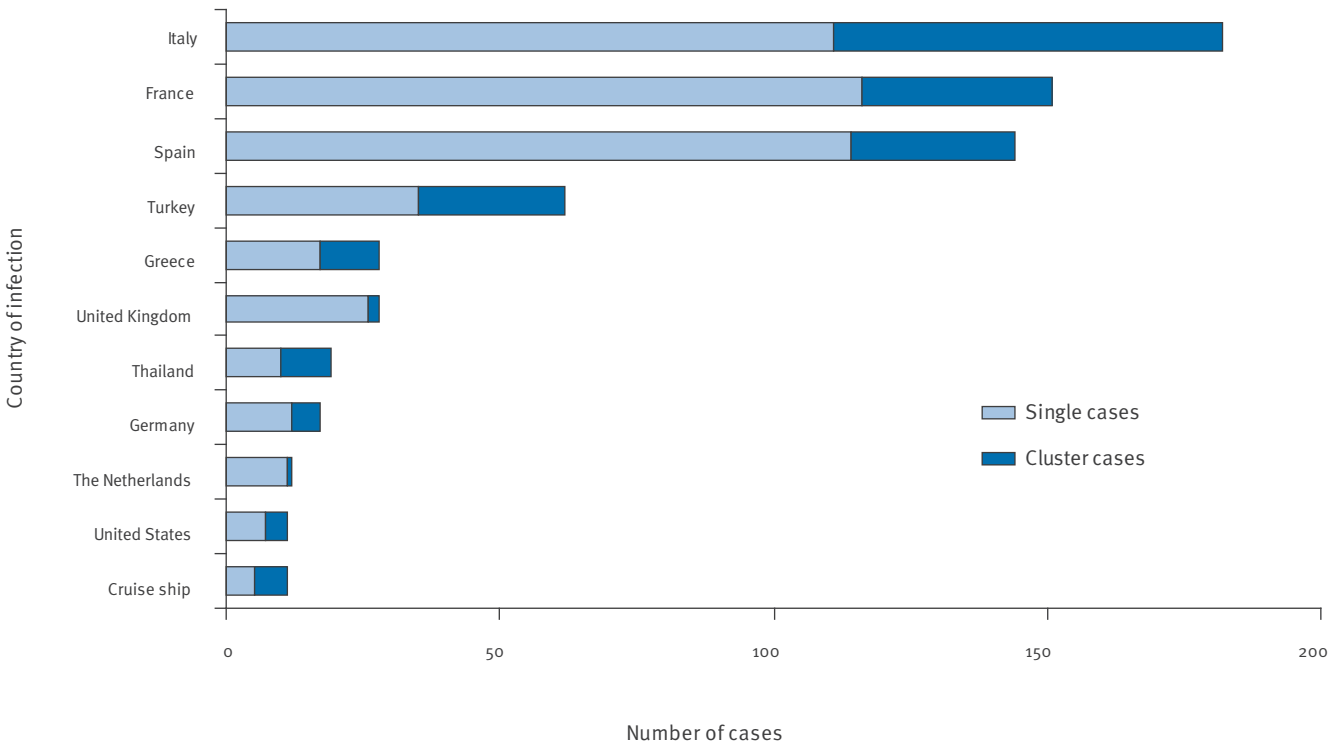
EWGLINET therefore requested a total of 144 environmental investigations in 2008 (109 new cluster sites in Europe and 35 re-offending sites). Four of these Form B reports have not been returned to date: one of the sites is closed and a Form B will be required prior to reopening, and three are published on the EWGLI website for failure to return a Form B report in time. Reports were submitted for the remaining 140 sites, 59 (42.1%) of which reported that Legionella spp. had been isolated from water samples taken at the accommodation sites. This positivity rate is lower than that reported in 2007 (54.3%) and in 2006 (66.4%). Seventy-eight (55.8%) of these forms reported that Legionella was not detected in samples, and three (2.1%) reported 'unknown', i.e. delayed results due to site closures (in these situations the site investigation would be delayed until immediately prior to the site reopening, in order to ensure optimal protection for travellers). When the investigation results for re-offending sites are considered separately, 13 of 35 (37.1%) returned positive samples (compared with 54.8% in 2007).

Of the 59 sites where Legionella spp. was isolated from the water, L. pneumophila serogroup 1 was isolated from 37 sites (62.7%) and non-serogroup 1 isolates were reported for 12 sites (20.3%) (representing other species or serogroups). The reports for ten sites did not include enough information to categorise the isolates in this way (16.9%).

Since sequence-based typing (SBT) became available [3], EWGLINET aims to match clinical and environmental cultures during cluster investigations, thereby strengthening the evidence that the accommodation site was the probable source of infection. The opportunities to do this are rare due to the low percentage of cases with a positive culture. Of the 140 investigations carried out in 2008, 59 (42%) yielded positive environmental isolates, but only 19 (of 140, 14%) had associated clinical isolates. There were 12 sites that had both clinical and environmental isolates available for comparison, and matching was achieved for three of these, representing only 2% of all investigations. In one instance the clinical and environmental isolates were of different sequence types, and for the remaining eight instances, SBT was not undertaken for both isolates.

Figure 2

Countries visited by 10 or more cases of travel associated Legionnaires' disease in 2008, by type of case



A further 49 countries were visited by less than 10 cases and do not feature on this graph.
EWGLINET data.

Twelve accommodation sites were published on the EWGLI website during 2008 for failure to return a Form A or Form B report on time, or for failure to implement appropriate control measures within the required period. These sites were located in Turkey (n=6), Italy (n=3), Bulgaria (n=1), France (n=1) and Greece (n=1). In comparison, thirteen site names were published during 2007, four in 2006, nine 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 some countries do systematically carry out such investigations. In 2008, Italy reported that 150 of their single sites were investigated, of which 61 (40.7%) reported positive sampling results for Legionella spp. There was also one instance of sequence matching being undertaken for a single case of travel-associated Legionnaires' disease [4].

Discussion

EWGLINET received reports of 866 cases of travel-associated Legionnaires' disease with onset in 2008, slightly below the number of cases reported in 2007. Prior to 2007 there had been a steady increase in the number of cases reported to the scheme since its inception in 1987, due in part to improved national surveillance and to an increasing number of countries joining the scheme. There is still significant under-ascertainment of Legionnaires' disease within Europe, especially among the newer Member States of the European Union (EU) which include many countries where surveillance for Legionnaires' disease is less well developed. Therefore there is still potential for case numbers to increase.

The small decline in case numbers in 2008 may reflect the early impact of the economic recession on the tourist industry. As people take fewer holidays abroad, we would expect the proportion of travel-associated cases reported to national surveillance schemes to decrease, and therefore the number of cases reported to EWGLINET to decrease in turn. Whilst data are not available for all European travellers, the UK Office for National Statistics keeps a record of the number of travellers entering or leaving the UK. Between 1999 and 2006, UK travellers increased year on year, but their numbers subsequently declined (2006: 69,536,000; 2007: 69,450,000; 2008: 68,644,000) [5]. With a decrease in foreign travel, it is possible that there may be an increase in domestic travel as people holiday closer to home. EWGLINET does encourage the reporting of domestic travel-associated cases, but historically collaborators have reported these cases with less urgency than cases that travelled abroad. Over the next couple of years, it will be important to ensure that the scheme captures domestic travel as fully as it captures foreign travel.

The use of PCR in the diagnosis of Legionnaires' disease is increasing, although the proportion of travel-associated cases diagnosed by this method is still very low. Where respiratory samples can be obtained, PCR offers a rapid approach to the diagnosis of Legionnaires' disease, and the clinical sensitivity is likely to be higher than that of culture [6].

Over the last three years there has been a decrease in the proportion of cluster sites that yield positive environmental samples. This trend might indicate a change in the range of laboratory services used for investigations across Europe; alternatively it may reflect the high number of cases reported to the EWGLINET database on an annual basis, which inevitably include some cases whose infection was not linked with the accommodation site that they visited during their incubation period.

The number of accommodation sites published on the EWGLI website for failure to meet EWGLI's standards of investigation remained high in 2008, however the number of publications associated with sites in Turkey fell from 11 of 13 in 2007 to six of 12 in 2008. This suggest that there has been improvement in Turkey's response to clusters following discussion of the situation in our last annual report [7].

Also highlighted in Joseph *et al.* [7] were the difficulties faced by EWGLINET when dealing with clusters that occur in countries outside Europe. The proportion of these clusters in 2008 was similar to that in 2007, and there remains a lack of feedback on the environmental investigations carried out as a result of EWGLINET cluster notifications. However, recent discussions with the World Health Organisation have led to renewed efforts to strengthen existing investigation and reporting mechanisms in non-European countries. EWGLINET is continuing to pursue ways to improve the response

Table 2

Countries where two or more clusters of travel-associated Legionnaires' disease occurred in 2008

	Country of infection	Number of clusters
Europe		
	Italy	31
	France	17
	Spain	11
	Turkey	12
	Greece	5
	Germany	3
	Russia	2
Outside Europe		
	India	4
	Mexico	3
	Thailand	2
	United States	2

A further fifteen countries and one cruise ship were associated with only one cluster and are not listed here.

EWGLINET data.

to travel-associated clusters of Legionnaires' disease in these countries.

Within Europe, attention has been focused on the newer EU Member States. With funding obtained from the European Centre for Disease Prevention and Control (ECDC) a training course for health professionals and the tourist industry was held in Bulgaria in September 2008. Several travel associated outbreaks of Legionnaires' disease have occurred in Bulgaria, including one in 2008 which was not satisfactorily investigated and which was published on the EWGLI website. The local Ministry of Health has noted the need for Bulgaria to increase its laboratory and microbiological resources for testing both clinical and environmental specimens.

Efforts are also required within EWGLINET to increase the use made of SBT typing data where both clinical and environmental cultures are available for a cluster site. Countries are regularly reminded to report microbiological updates, such as culture results after the case has been reported. When positive cultures are available, countries are encouraged to carry out SBT typing of any isolates that are known to be part of a cluster and to make greater use of the international SBT database managed by EWGLI [3]. Two of the three matching sets of clinical and environmental isolates came from the same country in 2008, a country with a high proportion of cases diagnosed by culture and a large number of domestic travel-associated cases of Legionnaires' disease among their own residents, providing the opportunity to encourage greater use of SBT methods.

On 1 April 2010, the EWGLINET scheme moved from London to Stockholm and is now coordinated by ECDC. Collaborators are encouraged to maintain their commitment to rapid reporting and cluster management under the new arrangements, in order to ensure the continued success of this highly active and responsive surveillance scheme.

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References

1. European Working Group for Legionella Infections. European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease. London: Public Health Laboratory Service; 2002. Available from: http://www.ewgli.org/data/european_guidelines.htm
2. European Working Group for Legionella Infections. Case Definitions. London: Public Health Laboratory Service. Available from: http://www.ewgli.org/ewglinet/case_definitions.htm
3. Gaia V, Fry NK, Afshar B, Lück PC, Meugnier H, Etienne J, et al. Consensus sequence-based scheme for epidemiological typing of clinical and environmental isolates of Legionella pneumophila. J Clin Microbiol. 2007;45(6):1965-8.
4. Lück PC, Hahn F, Senger M, Boers SA, Brandsema P. European network cooperation to identify hotel as source for pneumonia caused by Legionella pneumophila serogroup 2. Euro Surveill. 2008:13(24). pii=18903. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=18903
5. MQ6 Transport travel and tourism. Overseas travel and tourism Quarter 4 2008. Newport: Office for National Statistics; 2008. Available from: http://www.statistics.gov.uk/downloads/theme_transport/mq6-q4-2008.pdf
6. Mentasti M, Fry N, Tchipeva D, Afshar B, Palepou-Foxley C, Kimmitt P, et al. Utility of a Legionella pneumophila real-time PCR assessed using respiratory and serum samples from proven cases of Legionnaires' disease. Legionella 2009 Conference; 13-17 October 2009; Paris, France (2009).
7. Joseph CA, Yadav R, Ricketts KD. Travel-associated Legionnaires' disease in Europe in 2007. Euro Surveill. 2009:14(18). pii=19196. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19196