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ORIGINAL ARTICLES

Euroroundups

TRAVEL-ASSOCIATED LEGIONNAIRES' DISEASE IN EUROPE: 2004

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Six hundred and fifty five cases of travel-associated legionnaires' disease with onset in 2004 have been reported to the EWGLINET surveillance scheme by 25 countries. A total of 84.9% of cases were diagnosed by the urinary antigen test, and 37 cultures were obtained. Thirty seven deaths were reported, giving a case fatality rate of 5.6%.

Eighty six new clusters were detected, 45% of which would not have been detected without the EWGLINET scheme. Ninety four accommodation sites were investigated and the names of four sites were published on the EWGLI website. Fifteen sites were associated with additional cases after a report was received to say that investigations and control measures had been satisfactorily carried out.

Further improvements could be made in the data collected on deaths due to travel-associated legionnaires' disease, and on the number of samples taken for culture throughout Europe.

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Key words: Europe, legionnaires' disease, travel

Introduction

In 1976, an outbreak of a pneumonic illness at a hotel in Philadelphia in the United States led to the identification and recognition of legionnaires' disease. By the late 1980s, it was clear that international collaboration would be required to facilitate exchange of information about this disease and to identify clusters of cases associated with individual accommodation sites. The European Working Group for Legionella Infections (EWGLI) was formed in 1986 and, in 1987, EWGLI established a surveillance scheme for travel-associated legionnaires' disease (EWGLINET) that aims to track all cases of the disease in European travellers. When a cluster of cases is suspected to be associated with an accommodation site, EWGLINET initiates and monitors immediate control measures and investigations at the site, and ensures that international standards are adhered to. The history and current activities of EWGLI are described further on its website (http://www.ewgli.org).

The number of cases reported to national surveillance schemes across Europe has been increasing. In 2004, 4588 cases were recorded in 35 countries [1] (including hospital-acquired and community-acquired cases, as well as travel-associated cases), compared with only 242 in 1993 from 19 countries. This increase in numbers can be attributed to an increasing awareness of the disease, a rise in the number of contributing countries, and strengthening of national and international surveillance systems. Of the total cases recorded in 2004, 396 (8.6%) died.

This paper provides results and commentary on cases of travel-associated legionnaires' disease with onset in 2004 reported to EWGLINET.

Methods

The addition of Andorra during 2004 brought the number of collaborators participating in EWGLINET to 59, representing 51 collaborating centres in 37 countries [FIGURE 1] which report all travel-associated cases fulfilling EWGLI's case definitions and detected by their national surveillance systems to the European database. Some countries host more than one collaborating centre. Collaborators are encouraged to report cases in people who travel within their own countries as well as those who travel abroad, and an increasing number are doing so.

Standard case definitions have been agreed by the collaborating countries in EWGLINET and are used for the purposes of international surveillance. A single case is defined as a person who, in the two to

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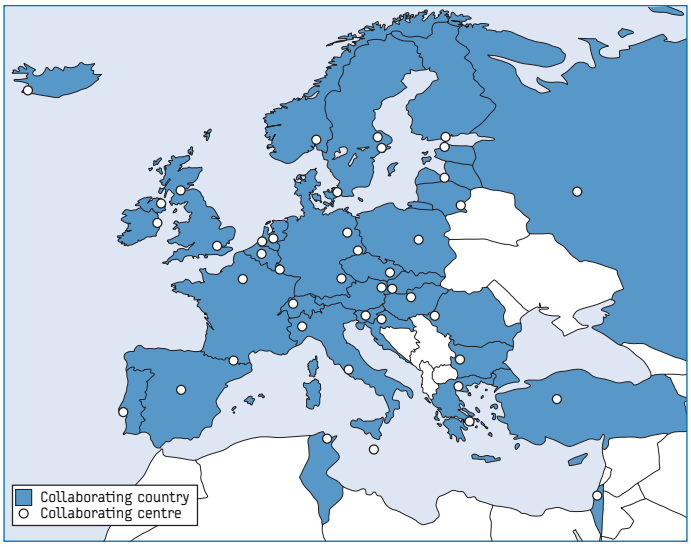
ten days before onset of illness, stayed at or visited an accommodation site that has not been associated with any other cases of legionnaires' disease, or cases who stayed at an accommodation site linked to other cases of legionnaires' disease but more than two years previously [2].

FIGURE 1

EWGLI collaborating countries, 2004



Note: Where more than one collaborating centre is located in a town, only one point is shown

A cluster of travel associated legionnaires' disease is defined as two or more cases in people who stayed at or visited the same accommodation site in the two to ten days before onset of illness and where onset is within the same two year period [2].

Cases are initially reported to their national surveillance schemes, which gather all relevant details on the case, such as information on microbiological diagnoses and travel history, and then report them to the EWGLINET coordinating centre at the Health Protection Agency Centre for Infections in London. There, the details are entered into a central database, which is then searched for other cases that stayed at the same accommodation sites as those visited by the new case. Either a single or a cluster notification will be faxed to collaborators, and the appropriate section of the EWGLINET investigation guidelines will be enacted.

In July 2002, European guidelines were introduced to standardise national responses to EWGLINET notifications [2]. When collaborators are notified of a single case associated with (an) accommodation site(s) in their country, they are expected to issue a checklist to the site(s) to ensure that the risk of legionella infection is minimised. For cases associated with clusters, a more extensive response is required. Within two weeks the country of infection is expected to have returned a 'Form A' to the coordinating centre, stating that a risk assessment has been carried out and control measures are in progress. After a further four weeks (six weeks in total) the coordinating centre will expect to have received a 'Form B' stating that control measures and sampling have been carried out, giving the results of the sampling, and saying whether the accommodation site remains open or has been closed. If these forms are not received within the appropriate time periods, EWGLINET will publish the details of the site on its public website (http://www.ewgli.org), stating that the coordinating centre cannot be confident that the accommodation site has adequate control measures in place. This notice is removed once the relevant form(s) have been received, confirming that measures to minimise the risk of legionella infection at the site have been taken.

Results

Cases and outcomes

A total of 655 cases of travel-associated legionnaires' disease with onset in 2004 were reported by 25 countries (including the United States, which is not a member of EWGLINET, but which reported a small number of cases in patients who had fallen ill with legionnaires' disease following travel to Europe). This is an increase on the 632 cases reported with onset in 2003 [3], but falls short of the 676 cases reported with onset in 2002 [4]. As in 2003, the countries that reported most cases in 2004 were England and Wales (172 cases), France (135), the Netherlands (119) and Italy (66) [TABLE 1].

TABLE 1

Countries reporting more than 10 cases of travel-associated legionnaires' disease in 2004, EWGLI

Country of report	Number of cases
England & Wales	172
France	135
The Netherlands	119
Italy	66
Denmark	33
Spain	22
Sweden	22
Scotland	17
Austria	16
Belgium	12

Note: In addition, a number of countries reported fewer than 10 cases, and are not listed here

The cases reported in 2004 generally fit the distinctive age and gender profile seen in previous years, with male cases outnumbering female cases by 2.9 to 1. The median age for male cases was 57 years (age range 23-96) and for female cases was 60 years (age range 29-84).

The usual pattern of a seasonal peak in summer was repeated in 2004, though with a single peak in August, rather than the July and September peaks witnessed in 2002 and 2003.

Deaths

Thirty seven deaths were reported to EWGLINET in 2004, representing a case fatality rate of 5.6% (6% in 2003), and an additional 41.5% of cases reportedly recovered from their illness (38% in 2003). Together these categories (death and recovery) are considered to be the 'known' outcomes, as opposed an 'unknown' outcome (52.8% of cases in 2004); the known outcomes making up a larger proportion of cases in 2004 (47.2%) than in 2003 (44%) or 2002 (36.1%). This continues to reverse the trend seen between 1995 and 2002 of a falling rate of known outcomes versus unknowns.

Thirty of the deaths were in men (81%), and seven in women (19%). All of the individuals who died were between 41 and 83 years old. Twenty five of the deaths were associated with single cases (68%), 12 with cluster cases (32%).

Microbiology

The proportion of cases in which detection of legionella urinary antigen was the main method of diagnosis increased to 84.9% in 2004 (81.5% in 2003). Diagnoses where the main method of detection was serology continued their decline on previous years, falling to 8.7% in 2004 (10.0% in 2003); the diagnoses were composed of 3.7% by four-fold rise and 5.0% by single high titre. The number of culture proven cases dropped to 37 (48 in 2003), representing just 5.6% of all cases. Five cases (0.8%) were diagnosed primarily by other methods.

Of the 37 deaths in 2004, seven were diagnosed primarily by culture (19%), 27 primarily by urinary antigen (73%), two by serology (four-fold rise) (5%), and one by direct immunofluorescence (3%). Twenty two of the deaths were caused by '*L. pneumophila* serogroup 1' infection (69.4%), one was due to '*L. pneumophila* other serogroup' (2%), nine were attributed to '*L. pneumophila* serogroup unknown', four to 'Legionella unknown' (11%), and one to 'Legionella other species' (3%) (the species was not specified).

The main category of organism detected in 2004 was '*L. pneumophila* serogroup 1' (454 cases, 69.3%). The remaining cases were reported

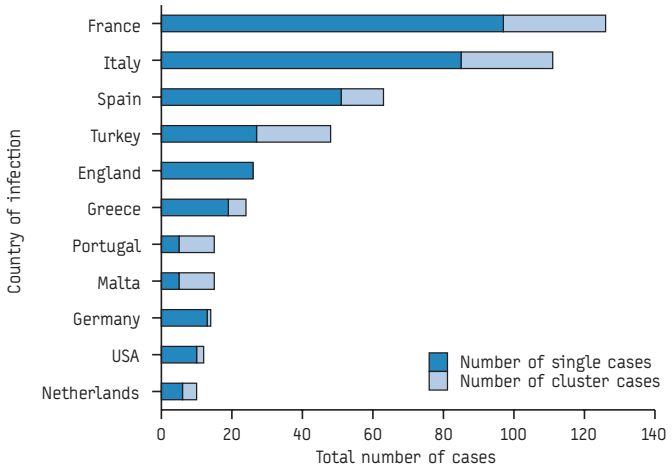
as '*L. pneumophila* other serogroup' (13 cases, 2.0%), '*L. pneumophila* serogroup unknown' (154 cases, 23.5%), 'Legionella other species' (2 cases, 0.3%), and 'Legionella species unknown' (32 cases, 4.9%).

Travel

Although cases in 2004 visited around 60 different countries, over half (53%) were associated with travel to the four main countries of infection: France (126 cases), Italy (111), Spain (63), and Turkey (48) [FIGURE 2]. A large proportion of the cases visiting sites in France were French nationals (88) travelling internally in their own country, and likewise with Italian nationals visiting sites in Italy (54 cases). For cases involving travel in Spain, the proportion associated with clusters was 19%; for cases involving travel to France and Italy the figure was 23% for each, while for Turkey it was 44% (although this proportion is higher than that seen in the other three countries, it further consolidates the improvements seen on the 71% of cases in Turkey which were associated with clusters in 2002).

FIGURE 2

Countries visited by more than 10 cases of travel-associated legionnaires' disease in 2004, by case type, EWGLI 2004



Fifty five cases visited more than one European country, and ten cases visited more than one country outside Europe. An additional 66 cases (10.1%) visited countries outside the EWGLINET scheme.

Clusters

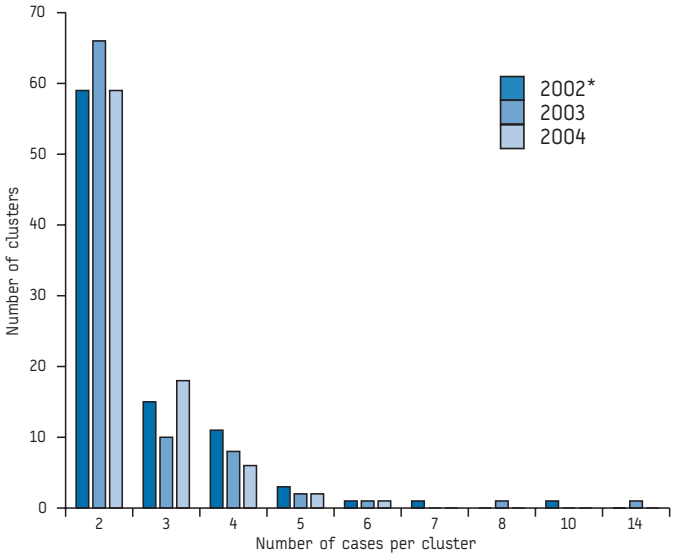
Eighty six new clusters were identified in 2004, compared with 89 in 2003 and 94 in 2002 (this does not include clusters which were identified in previous years and were associated with a subsequent case in 2004; these clusters are included in the previous years' figures). The size of these clusters varied less than in previous years, with the largest cluster involving six cases (down from 17 cases in 2003), although, as in previous years, the majority of clusters (59 in 2004) involved just two cases. There was a slight shift towards clusters involving three cases (up from nine in 2003 to 18 in 2004), but in 2004 the proportion of clusters involving only two or three cases reached almost 90%, compared with 84% in 2003 and 81% in 2002 [FIGURE 3]. Of the 86 clusters, 39 consisted of a single case reported by each of two or more countries. National surveillances schemes do not normally detect clusters that involve fewer than two of their citizens, and therefore would not ordinarily have detected these clusters.

In 2004, clusters were located in 24 countries, and one cluster was associated with a cruise ship [TABLE 2]. Italy and France were associated with the most clusters (17 clusters each, plus another cluster involving sites in both Italy and Germany), followed by Spain and Turkey which were each associated with nine clusters. Of the remaining clusters, the number occurring in countries outside EWGLINET, or in EWGLINET countries not officially signed up to follow the European guidelines, was 14 (representing 16%, an increase on the 13% seen in 2003, and following the trend of increased cluster detection outside the area of operation of the European guidelines). Five clusters involved two or more accommodation sites, including the one mentioned above which spanned two countries (Italy and Germany).

Most of the clusters in 2004 occurred during the summer months (66 between May and September, representing 77% of the full year figure). January was the only month in 2004 during which no clusters were detected.

FIGURE 3

Number of cases of travel-associated legionnaires' disease per cluster, by year, EWGLI 2004



* 2002 figures include clusters both pre- and post- guidelines

TABLE 2

Countries associated with clusters of travel-associated legionnaires' disease in 2004, EWGLI

Country of infection	Number of clusters
Austria	2
Bulgaria	1
Channel Islands	1
Cruise	1
Cuba	2
Dominican Republic	1
France	17
Germany	1
Greece	2
Hungary	1
Italy	17
Italy/Germany	1
Jordan	1
Malta	4
Mexico	1
The Netherlands	1
Poland	1
Portugal	4
Russia	1
Spain	9
Sri Lanka	2
Tunisia	3
Turkey	9
UAE	1
USA	1
Uzbekistan	1

Investigations and publications

A total of 96 sites were involved in the 86 new clusters in 2004. Of these sites, 17 were in countries not signed up to follow the European guidelines, and one site was already under investigation, leaving 78 that required EWGLINET investigations. Additionally, 15 sites that had been involved in clusters in previous years were associated with extra cases during 2004 ('cluster updates') and so needed to be re-investigated (one twice, resulting in a need for 16 re-investigations). These sites had been previously investigated under the guidelines, and are known as 're-offending' sites.

In total, EWGLINET requested the investigation of 94 sites for clusters and cluster updates in 2004. Fifty three 'Form B' reports (56.4%) advised that samples from the accommodation site had tested positive for *L. pneumophila* (at concentrations equal to or greater than 1000 cfu/litre [5]), 38 (40.4%) reported that *L. pneumophila* was not detected in samples, and three 'Form B' reports (3.2%) did not have samples taken for reasons accepted by the coordinating centre.

The names of three French sites and one site in Turkey were published on the EWGLI website during 2004 for failure to return reports on time, or for failure to implement appropriate control measures in time. This represents a significant reduction from the 27 site names published during 2003.

During 2004, investigation reports were received for 149 sites associated with just a single case, even though the EWGLI guidelines do not require these. Of the 145 sites at which sampling was undertaken, 76 (52.4%) were reported positive for *L. pneumophila*.

Discussion

The EWGLINET surveillance scheme for travel-associated legionnaires' disease has now been in operation for 17 years. Each year the scheme detects a large number of clusters that involved no more than one case from any country and would otherwise have gone undetected. Thirty nine such clusters were identified by EWGLINET in 2004 (45%), and were therefore subjected to the high standard of investigation and control demanded by the EWGLI guidelines.

Italy and France continue to report a high proportion of their internal travel cases (for example, cases in French people travelling within France). These cases are important because they allow EWGLINET to detect additional clusters within Italy and France that might otherwise go undetected. EWGLINET encourages other countries to do the same by ensuring that their internal travel cases are reported.

The number of postings on the EWGLI website dropped dramatically in 2004, demonstrating that countries (especially Turkey, who had a much higher number of sites published in 2003 than in 2004) have adapted well to implementing the guidelines in a timely fashion. It is especially promising to note that the proportion of smaller clusters (clusters involving just two or three cases) has increased since the introduction of the EWGLI guidelines, which suggests that the standard of investigation and control outlined in the guidelines has proven sufficient to prevent a large number of further cases developing from those accommodation sites.

There continue to be areas where surveillance could be improved across Europe. Data on deaths is not as detailed as it could be. Cases are often reported to EWGLINET as 'still ill' or 'unknown', and these cases may eventually be fatal. Unfortunately, EWGLINET is rarely updated on the status of these cases, and after a year they become classified as 'outcome unknown'. Collaborators are encouraged to let the coordinating centre know the outcome of cases that were reported while the patient was still ill. The proportion of cases reported to the scheme with known outcomes has been increasing, which is promising.

Cultures were taken for 19% of fatalities, which is an improvement on the cultures taken in only 5.6% of cases overall, but this percentage is still lower than would be liked. Fatal cases are often investigated more thoroughly than cases in patients who recover, and in order to demonstrate that the infection came from a particular source, a clinical culture is required for each case. Clinicians should be encouraged to take samples for culture wherever possible, and especially in fatal cases.

The seasonal pattern typically seen by EWGLI each year, with a concentration of cases during the summer months, can be explained for the most part by the fact that the scheme records only travel associated cases of legionnaires' disease, and the majority of people in Europe choose to take their holidays during the northern hemisphere summer. However, national surveillance systems, which deal with community and hospital-acquired cases as well as travel-associated cases, also often see a marked increase in case numbers over the summer months that cannot be attributed solely to travel patterns. It may be that the warmer ambient temperatures in summer provide a more amenable environment for the legionella bacteria to multiply.

The surveillance scheme continues to expand to cover a greater number of European countries. The addition of Andorra to the scheme in 2004 brought the number of collaborating countries up to 37, but there are areas of eastern Europe that do not yet participate. It should be a priority for the scheme to form a working relationship with these countries with the intent of forming official collaborations with them at the earliest possible date, so that cases of travel-associated legionnaires' disease occurring in their residents can be added to the European dataset.

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* The list of EWGLI collaborators is available at the following URL address: www.ewgli.org/contact/contact_listof_collaborators.asp

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