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Clusters of travel-associated Legionnaires' disease in Italy, Spain and France, July 2002 - June 2006

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For several years, over 50% of the cases of travel-associated Legionnaires' disease (TALD) reported to the European Working Group for Legionella Infections (EWGLINET) have been among travellers to France, Italy, and Spain. We describe clusters of TALD cases reported in these countries during a four-year period. We analysed data from EWGLINET and from the individual countries. In all three countries, upon notification of a cluster, local health authorities are alerted by the national collaborator and immediately begin an environmental investigation at the accommodation site, which includes risk assessments and analysis of water samples.

From July 1, 2002 to June 30, 2006, 2,101 accommodation sites were associated with TALD cases and reported by EWGLINET to Italian, Spanish and French collaborators. Of these, 252 sites (12%) were associated with clusters: 13.8% (96/697) in Italy, 13.2% (81/615) in Spain and 9.5% (75/789) in France. Overall, 641 cases were reported. Hotels, camping sites and ships and other sites represented respectively 83%, 10% and 7% of the total accommodation sites, with similar proportions in the three countries. In 99% of the sites, samples were collected; 62% of them were found to be positive for *Legionella*.

The findings of this study highlight that disinfection and long-term preventive measures were correctly implemented by the large majority of sites. However, additional efforts must be made to further reduce the percentage of re-offending sites so as to reduce the number of accommodations that are contaminated by *Legionella*.

Introduction

The European Working Group for Legionella Infections (EWGLINET) was established in 1987 to identify cases, clusters and outbreaks of travel-associated Legionnaires' disease (TALD). Collaborators in the scheme are usually national or regional representatives from the public health and microbiology institutes in each country and they report cases of travel-associated legionnaires' disease to EWGLINET's coordinating centre in London. National surveillance schemes detect and follow up each case within the country of residence and then report the case, travel and microbiology details to the EWGLINET coordinating centre at the Health Protection Agency's Communicable Disease Surveillance Centre (CDSC) in London. The details are entered onto a database, and the database is searched to check whether that case should form or become part of a cluster, or whether it is a single case.

The number of cases reported to EWGLINET has increased, from 11 in 1988 to 916 in 2006, in part due to the increase in the number of collaborating countries, which is currently 35 with 62 collaborators from 52 centres [1] and improvement in legionnaires' disease (LD) surveillance in most countries. For a number of years, over 50% of the reported cases have been among travellers to France, Italy, and Spain, while the remaining cases occurred mainly in Turkey, Greece, United Kingdom, Germany, and the United States.

Before July 2002, the procedures for responding to and reporting clusters of TALD were not standardized. To standardize these procedures, a group of experts began to prepare European guidelines in 2000 [2], which were approved and endorsed by the European Union's Committee for the Epidemiological Surveillance and Control of Communicable Diseases in the Community [3]. In this article, we summarize the findings of the epidemiological investigations performed according to these guidelines, for clusters identified in France, Italy, and Spain in the past four years.

Methods

We considered cases reported to France, Italy and Spain in the period from 1 July 2002 to 30 June 2006. The data used were those collected by EWGLINET and from the individual countries.
The incubation period for LD usually ranges from 2-10 days. According to the European guidelines, a cluster of TALD is defined as two or more cases represented by persons who stayed at or visited an accommodation site between two and 10 days before onset of illness and whose onset was within the same two-year period.
Sites in which a cluster occurred and which were associated with additional cases after a report was sent to EWGLI to say that investigations and control measures had been satisfactorily carried out were defined as 're-offending' sites .

When a cluster is identified, an immediate response is required, including risk assessment, sampling and control measures. The European guidelines also require that two reports are sent by the national collaborator in the country of infection to the EWGLINET coordinating centre in London, one within two weeks of the notification of the cluster alert and one within six weeks [4]. These reports have to confirm that measures have been taken to minimize the risk at the site. If one or both of these two reports are not received, or they state that control measures have not been taken or are not appropriate, EWGLINET publishes the name of the accommodation site on its public website (www.ewgli.org). This notice is removed only once satisfactory reports of control measures are received.

Italy and France have applied this procedure since July 2002 and have notified EWGLINET of all cases of TALD, whether acquired internally or abroad. Due to legal issues, Spain only began to apply this procedure in January 2006 and prior to this date only notified EWGLINET of the cases acquired by Spanish citizens abroad, although the cases acquired within Spain were fully investigated in accordance with the European Guidelines. In any case, in the present analysis, data on all Spanish clusters for the entire study period were available.

In countries participating in EWGLINET, when a cluster is identified, local health authorities are alerted by the national EWGLINET collaborator and immediately begin the environmental investigation, which includes identifying the risk and collecting and analysing water samples. Water samples are analysed by accredited regional or local environmental laboratories, and the isolation of *Legionella* is based on standard methods (ISO 11731). Local authorities report the results of the investigation to the EWGLINET collaborator, who in turn notifies the EWGLINET coordinating centre. Lastly, available clinical and environmental strains are compared by the national Legionella reference laboratories by performing molecular analyses [pulsed-field gel electrophoresis (PFGE) of genomic restriction fragments, sequence-based typing, amplified fragment length polymorphism, etc.), to confirm that the site is the source of the cluster.

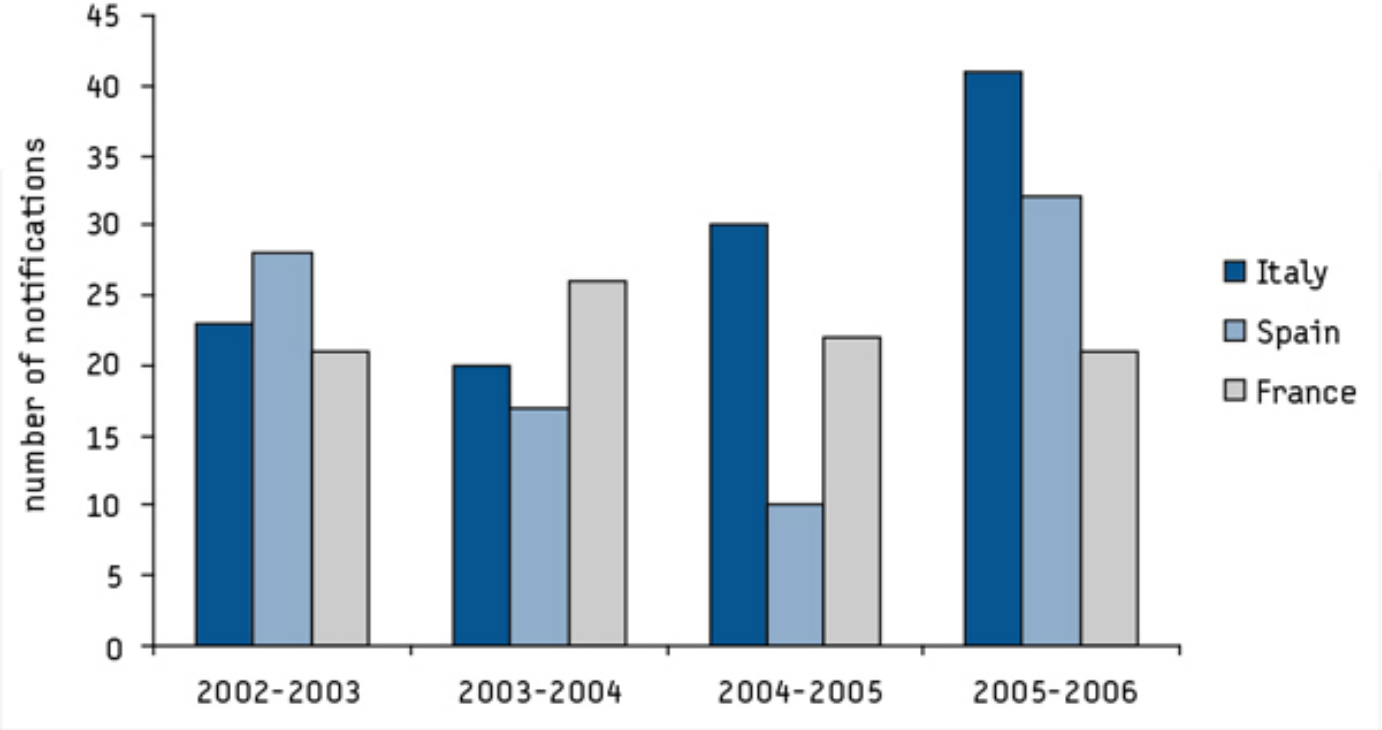
Results

In the study period, 2,101 accommodation sites were associated with TALD cases and reported by EWGLINET to the Italian, Spanish and French collaborators. Of these, 252 sites (12%) were associated with clusters; 13.8% (96 of the 697 sites with cases) in Italy, 13.2% (81/615) in Spain and 9.5% (75/789) in France. Overall, in the period 2002-2006, from 48% to 61% of the clusters reported to EWGLINET were located in Italy, France and Spain.

The distribution of the clusters, by year and country during the study period is shown in Figure 1. Overall, 641 cases were reported to be associated with the 252 accommodation sites; in particular, 276 cases reported to Italy, 179 cases reported to Spain, and 186 cases reported to France. The median number of days of stay of cases was five in Italy, seven in Spain and two in France; the mode was one day in Italy and France and seven days in Spain.

FIGURE 1

Clusters of travel-associated Legionnaires' disease in Italy, Spain and France, July 2002 - June 2006: distribution of cluster notifications by year and country



A large proportion of clusters consisted of French nationals travelling within France (39%), whereas in Spain and Italy this proportion was lower (28% and 24%, respectively). The proportion of clusters involving only foreign citizens was lower in France (19%) compared to Italy and Spain (56% and 58%, respectively) (Figure 2). Of the 252 clusters, 85 consisted of a single case reported by two or more different countries.

FIGURE 2

Clusters of travel-associated Legionnaires' disease in Italy, Spain and France, July 2002 - June 2006: country of origin of cases

In the three countries, the size of the clusters did not greatly vary; the majority of clusters (68%) involved just 2 cases. In only 4% of the sites, more than four cases were involved.

Hotels, camping sites and ships and other sites represented, respectively, 83%, 10% and 7% of the total accommodation sites, with similar proportions in the three countries. For 38 (15%) of the sites with a cluster, an additional case was reported within two years of the last case (thus increasing the size of the cluster); for five (2%) sites, more than one additional case was reported.

Environmental investigations

In all three countries, environmental investigations were started within one to two days after cluster notification, and control measures were implemented or reinforced in all of the accommodation sites. In some cases, investigations were already ongoing before the EWGLI notification. The results of the environmental investigations are summarized in Table 1. In nearly all of the sites (99%), samples were collected. In Spain, in one site water samples were not collected because the hotelier had already carried out disinfection before health authorities performed their inspection; in France, the information was not available in one site.

TABLE 1

Clusters of travel-associated Legionnaires' disease in Italy, Spain and France, July 2002 - June 2006: number of sites sampled by country and by result

Country	Number of sites	Sites sampled No. (%)	Negative samples No. (%)	Positive, but unknown Legionella concentration No. (%)	Legionella concentration CFU/ L <10^3 No. (%)	Legionella concentration CFU/ L >10^3 No. (%)
Italy	96	96(100)	36 (37)	3 (3)	6 (7)	51 (53)
Spain	81	80 (99)	33 (41)	37 (46)	3 (4)	7 (9)
France	75	74 (99)	20 (27)	4 (5)	14 (19)	36 (49)
Total	252	250 (99)	89 (36)	44 (18)	23 (9)	94 (37)

In more than one third (36%) of the sites, no legionella was found. In Spain, for 46% of the sites, the concentration of legionella was not known, compared to 3% of the sites in Italy and 5% in France. Concentrations of legionella equal to or greater than 1,000 cfu/litre (the threshold set by European Guidelines as requiring actions) were found in 50% of the sites in Italy and in France and in only 9% in Spain.

In Italy, five sites (5.2%) were temporarily closed for implementing control measures; one (1%) site was closed shortly after the investigation for renovation and 19 (20%) accommodation sites were seasonal and were closed during the winter season. In Spain, four (5%) of the sites were temporarily closed; two (2.5%) were closed for renovation; and two (2.5%) were seasonal. In France, 10 sites (13%) were closed for renovation, 12 (16%) sites were closed for the winter season. For all of the sites that had closed, the local health authorities conducted another environmental investigation before re-opening.

The names of eight French sites (seven hotels and one campsite), two Italian hotels and no Spanish sites were published on the EWGLI website during the study period for failure to comply with the European guidelines.

Microbiological investigations

Clinical isolates were available for 20 of the 186 cases (9.3%) in France, for four of the 234 cases (2%) in Italy, and for two of the 179 cases (1%) in Spain. In France, clinical isolates were available from patients who visited 18 sites (24%), and in 10 sites environmental isolates were available for comparison with clinical isolates. Comparison was made by PFGE or Sequence Based Typing (SBT), and in each instance the environmental and clinical isolates were found to have had identical genomic profiles. Two clinical isolates were obtained from two cases who stayed in the same accommodation site; in one site, all isolates were identical and in another site the clinical isolates were compared and found to have been identical by SBT, but no environmental isolates were available for further comparison [5].

In both Spain and Italy, clinical and environmental isolates were also available for two sites, and the comparison showed a similar genomic profile.

Discussion

The results of the analysis reveal some differences among the three countries considered. In Italy and France, the length of stay in each accommodation site was shorter than that observed in Spain. In Spain and Italy, there was a higher proportion of clusters comprised exclusively of foreigners than in France, which probably indicates different patterns of tourism in the three countries. However, the investigations performed and the results were very similar: in fact, though a huge number of accommodation sites were reported to the three countries during the study period, epidemiological and environmental investigations were carried out in more than 99% of clusters, and control measures were satisfactorily implemented in 96%, as demonstrated by the negligible number of sites published on the EWGLI website. Criteria for closure of accommodation sites are not identified in the European guidelines, and the decision is left to individual countries, according to their national laws; this explains the differences found among the three countries.

Overall, more than 60% of the sites sampled were found to be positive for legionella, and, in particular in Italy and France, where the concentration of legionella was known for most sites, approximately 50% of them were found to be positive at concentrations greater than 1,000 cfu/litre. Although disinfection and long-term preventive measures were correctly applied by most sites, 43 sites (17%) reported additional cases after the cluster and thus required further investigation during the study period. This indicates that additional efforts must be made to further reduce the percentage of 're-offending' sites, so as to reduce the number of hotels that are contaminated by *Legionella* [6]. The fact that no legionella was found in more than one third of the investigations could be because culture of water samples for *Legionella* spp may not be highly sensitive, or because cases did not acquire infection in the accommodation site under investigation.

Between 2002 and 2006, there appears to have been a trend of increase in notifications for Italy and Spain. The increase in the number of clusters in these two countries seems to reflect the improved reporting and ascertainment of cases in 2005-2006, both at the national level (in Italy and in Spain) and at the European level, as demonstrated by the increased number of TALD cases reported to EWGLI. The matching of environmental *Legionella* strains with clinical strains was only possible for a very limited proportion of cases in Italy and Spain, and in a slightly higher proportion in France. This is due to the low proportion of clinical isolates available, as a result of the diagnosis of legionellosis mainly being performed by urinary antigen detection. Efforts should therefore be made to encourage practitioners to collect clinical specimens.

The findings of this study highlight the importance of collaboration among all European countries, given that the surveillance network detected 33% more clusters than would have been detected by individual countries alone. Furthermore, the European guidelines have led to a more standardised approach to investigations across all European countries and to a greater awareness of the importance of proactive interventions. It is thus expected that in the next few years, in spite of the continuously increasing number of travellers, there will be a decline in the number of accommodation sites associated with clusters.

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