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ARTICLE INFO

Article history:
Received 6 July 2010
Received in revised form 1 September 2010
Accepted 5 September 2010

Corresponding Editor: Ziad Memish, Riyadh, Saudi Arabia

Keywords:
Legionnaires’ disease
Legionella
Epidemiology
Control
Surveillance

SUMMARY

Background: In France, the notification of Legionnaires’ disease (LD) has been mandatory since 1987. Following a study showing an important under-reporting of the disease, the surveillance system was strengthened in 1997: the urinary antigen detection test was introduced as a new diagnostic tool and guidelines for prevention and control of the disease were implemented. After these measures, the incidence of LD increased gradually, reaching 2.5 per 100 000 in 2005, and then slightly decreased (2.0 per 100 000 in 2008).

Methods: Data from the mandatory notification system and from the national reference centre for Legionella were analysed. Analysis covered the 1998-2008 period.

Results: During the period 1998–2008 a total of 11 147 cases of LD were reported in France through the mandatory system. The majority of cases were diagnosed by urinary antigen test. The median age of cases was 61 years, the male to female ratio was 2.9, and the case fatality rate was 13%. Exposure during travel was documented for 17% of cases. A hospital-acquired infection was suspected for 9% of cases, and this percentage decreased from 21% in 1998 to 7% in 2008. Over this period, 14 community outbreaks were identified involving 380 cases, and cooling towers were the most probable source of infection for 13. No outbreak was reported in 2008. Registration at the regional level of all cooling towers became mandatory at the end of 2004, and the 1997 prevention and control guidelines were updated in 2005. In recent years, several regulations have also been implemented in the hospital setting and care homes for the elderly.

Conclusion: All these measures have contributed to strengthen the French surveillance system and improve our ability to better prevent, detect, and control LD.

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1. Introduction

Since the first large outbreak of pneumonia, which occurred among American Legion members in 1976,1 awareness of the importance of Legionnaires’ disease (LD) has consistently increased among health professionals. LD is a severe pneumonia contracted by inhalation of aerosols contaminated with Legionella species.2 More than 50 species have been identified,3 but Legionella pneumophila serogroup 1 (Lp1) causes the majority of cases reported in Europe4 and in the USA.5 LD is a significant cause of community- and hospital-acquired pneumonia.6 and the case fatality rate (CFR) can be as high as 30%, particularly for hospital-acquired infections or in cases of immunosuppression.7 The majority of cases are considered to be sporadic. However, cases related to outbreaks have enabled the identification of specific sources of infection.8–12 Since Legionella was first identified,13 great advances in knowledge of the disease (clinical presentation, risk factors, outcome), the bacteria (gene regulation, virulence factors, ecology), and the environmental sources have been made. All these elements have allowed a more comprehensive approach to the control of the pathogen.

In France, the objectives of LD surveillance are to monitor trends, to describe cases according to their risk factors and exposure, and to detect clustered cases or outbreaks early in order to implement appropriate prevention and control measures. In 1996, a study showed considerable under-reporting of the disease.14 The first guidelines to strengthen surveillance of the disease, its prevention and control were drawn up in 1997 by the French health authorities. In parallel, the urinary antigen detection test, which provides a rapid and non-invasive diagnosis of Lp1 infection, was also introduced in 1997.

More than 10000 cases have been reported in France since 1998. We describe here the LD trends in France, the characteristics of patients registered in the system from 1998 to 2008, and the implementation of adapted regulations.
2. Materials and methods

2.1. The LD surveillance system

In France, the mandatory notification of LD cases, which was implemented in 1987, is based on a case reporting form that collects the following information: sociodemographic data (age, gender, area of residence), clinical data (date of symptom onset, date of hospitalization, chest X-ray confirmation of the pneumonia, patient outcome), bacteriological data (diagnosis technique, species and serogroup), and risk factors for contracting the disease (tobacco smoking, diabetes, or any immunosuppressive condition such as cancer or hematological disorders or any condition necessitating steroid therapy). Hospitalization status of patients with date of hospitalization has been recorded since 2005. Exposure to any of the following settings during the 10-day period preceding symptom onset (i.e., the incubation period) is also recorded: hospital, thermal centre, whirlpool spa, campsite, hotel, care home for the elderly, and workplace.

Information is initially collected by the clinician or the biologist in charge of the patient, who sends the reporting form to the district health authority (Direction Départementale des Affaires Sanitaires et Sociales, DDASS) in accordance with national ethics guidance. The DDASS is in charge of the rapid implementation of epidemiological and environmental investigations. Cases (or their relatives) are systematically interviewed by the DDASS using a standardized questionnaire. The objectives are to assess risk factors for contracting LD, to identify a possible source of exposure, and to detect other LD cases potentially related to a common source. If necessary, the DDASS environmental team investigates the potential sources of contamination and collects water samples for laboratory analysis. The notification form is sent by the DDASS to the national level (Institut de Veille Sanitaire, InVS), which monitors trends, documents the epidemiological characteristics of LD patients, and detects clustered cases that are not identified at the local level, especially when cases exposed to a common source are reported by different districts (or different countries).

The national reference centre for Legionella (NRC-L) plays a key role in the epidemiological surveillance of LD, through the confirmation of uncertain cases and the molecular typing of isolates. When a sample is taken or a Legionella strain is isolated, the sample or isolate is sent to the NRC-L for characterization and molecular analysis. The NRC-L reports all results to InVS and to the corresponding DDASS.

Hotels, campsites, and other travel-related accommodation are recognized to be high-risk settings for LD. Exposure to these settings is monitored through the EWGLI network (European Working Group for Legionella Infections), a network of 36 participating countries that has included France since 1997 (in April 2010, the EWGLI network moved to ECDC, Stockholm, and has been renamed the European Legionnaires Disease Surveillance Network – ELDSNet). Any LD case in whom contamination may have occurred at one of the above accommodation sites is reported to EWGLINET, which in turn informs the country where the case has stayed during the 10-day exposure period. A cluster, defined as two or more LD cases in the same setting within a 2-year period, implies a systematic environmental investigation, in accordance with the 2002 EWGLINET recommendations (http://www.ewgli.org). In addition, EWGLINET collects annual data on all LD (travel- and non-travel-related) cases from participating countries in order to monitor trends at the European level.

2.2. Milestones in national regulations and guidelines

In France, the first guidelines on surveillance and prevention of Legionella infection were introduced in 1997 by the Ministry of Health. In 1998, specific regulations related to the control and the surveillance of the water networks were implemented in healthcare facilities. As the number of cases was increasing and several outbreaks had occurred, new regulations were issued regarding the strict monitoring and control of cooling towers: in 2003 for the cooling towers in hospitals and in 2004, in collaboration with the Ministry of the Environment, these rules were extended to all wet cooling towers. Their registration at the regional level was also made mandatory. Then, in 2005, the existing guidelines for investigation and surveillance were extensively updated. The objective was to standardize all procedures from the detection of cases to the implementation of control measures. These revised and comprehensive guidelines provide additional guidance on investigation and surveillance in care homes for the elderly. Finally, in 2006, regulations on the organization of the response to outbreaks were issued (http://www.sante.fr/).

2.3. Case definitions

A confirmed case of Legionnaires’ disease is a patient presenting clinical and/or radiological signs of pneumonia associated with at least one of the following laboratory criteria: (1) isolation of Legionella species from a culture of bronchopulmonary secretions, or (2) a four-fold increase in antibody titers for any Legionella species with a second titer ≥1:128, or (3) a positive urinary antigen test. A presumptive case is a patient presenting clinical and/or radiological signs of pneumonia associated with a single elevated antibody titer ≥1:256.

In healthcare settings (hospital, care home for the elderly), a definite healthcare-associated case is an LD case that occurred in a patient continuously hospitalized during the 10-day period prior to symptom onset. If hospitalization has not been continuous, the case is considered as a probable healthcare-associated case.

A travel-associated cluster is defined by two or more cases who stayed at or visited the same accommodation site in the 2–10 days before symptom onset and whose symptom onset was within the same 2-year period.

An outbreak is defined as the occurrence of at least 10 cases of LD who are linked in terms of time and place and may involve a common source of contamination.

2.4. Characterization of Legionella strains

Comparisons of genomic profiles from clinical and environmental isolates are performed by pulsed-field gel electrophoresis (PFGE) according to standard procedures. Since 2008, two additional methods have routinely been used: sequence-based typing (SBT) and Dresden monoclonal antibody (MAb) subgrouping. Typing of clinical Legionella isolates by PFGE and SBT in combination with epidemiological data has identified several epidemiological groups that are used to classify clinical strains: (1) sporadic strains are defined as isolates with non-previously identified genotype and that are epidemiologically not linked; (2) epidemic strains share a genotype specific to an identified outbreak; (3) endemic isolates, which also share a previously observed genotype and are responsible for at least 30 epidemiologically unrelated cases of legionellosis. Isolates sharing a previously identified genotype but which are non- endemic are classified as ‘known strains’.

2.5. Data analysis

We indirectly estimated the incidence rate by calculating the notification rate using population estimates from the 1999 national census as the denominators. Crude and age-specific
Incidence rates were calculated using the average annual number of cases and the corresponding population estimates. We considered age over 70 years as an additional risk factor for acquiring LD, as published elsewhere. Regarding the geographic distribution of cases, we restricted the analysis to the period 2002–2008. This was to ensure that the widespread use of the urinary antigen test across the country had been achieved, thus reducing the variability due to different diagnostic procedures by region and limiting the impact of the changing sensitivity of the surveillance system.

Data were analyzed using Epi Info software (US Centers for Disease Control and Prevention, Atlanta, GA, USA). Comparisons between groups were performed using Fisher’s exact test or the Student’s t-test whenever appropriate, with a p-value of <0.05 considered as statistically significant.

3. Results

3.1. Incidence and trends

From 1998 to 2008, a total of 11 147 cases of LD were reported in France, corresponding to a yearly average incidence rate of 1.6 per 100 000 population. Between 1998 and 2005, the incidence rate increased by an average of 20% per year, reaching 2.5 per 100 000 in 2005; it has since slightly decreased (2.0 per 100 000 in 2008) (Figure 1).

3.2. Case characteristics

During the study period, 50% of cases were identified during the four summer months from June to September (Figure 2). The male to female ratio was 2.9 and incidence rates in males exceeded rates in females for all age groups. The median age of cases was 61 years (range 0–103 years) and it differed by gender: 59 years (range 0–100 years) in males and 68 years (range 3–103 years) in females. Incidence increased with age, from 0.1 cases per 100 000 persons/year among people aged below 30 years to 5.1 cases per 100 000 persons/year among people aged 80 years and above. Less than 0.1% of all cases were reported among children aged less than 15 years. The sex ratio and the distribution of cases by age group remained stable over the study period. As shown in Figure 3, the incidence rate increased with age in both genders.

Among the 11 147 reported cases, 7834 (70%) presented at least one known risk factor for contracting LD, and in most cases a combination of several risk factors was reported. Tobacco smoking was the leading risk factor, reported in 6396 (57%) patients. Diabetes was reported in 1433 (13%) cases, cancer in 1123 (10%) cases, and immunosuppressive conditions in 1068 (10%) cases. Other risk factors including chronic respiratory or cardiac diseases, HIV infection or alcoholism were reported in 2181 (20%) cases. Finally, 3776 (34%) cases were older than 70 years, and among them, 42% had no known risk factors (vs. 22% in cases aged <70 years; p < 10^{-6}).

3.3. Outcome

The outcome was known for 9307 (84%) cases. The CFR was 13% (1237/9307) over the study period. It decreased from 22% in 1998 to 11% in 2008 (p < 10^{-6}) and did not significantly differ by gender. LD patients who died were older than those who recovered (70.4 years vs. 60.2 years; p < 10^{-6}) and their infections were more often healthcare-associated (20.5% vs. 6.7%; p < 10^{-6}). Among the 1537 confirmed cases aged ≤70 years without known risk factors, the CFR was 5.1%.

Since 2006, 93 out of 4102 cases for whom data were available (2%) did not require hospitalization. These cases were younger...
than cases requiring hospitalization (57 vs. 64 years; \(p < 10^{-6}\)) and only one patient died (CFR = 1.1%). No other differences regarding risk factors were noted.

### 3.4. Diagnostic tests

Among the 11 147 cases during this 11-year period, the great majority were confirmed cases (93%) according to our case definition, and 9417 cases (84%) were diagnosed by a positive urinary antigen test. The distribution of diagnostic techniques used for confirmation evolved over time with an increasing proportion of urinary antigen testing (39% in 1998 vs. 95% in 2008; \(p < 10^{-6}\)). The remaining LD cases were diagnosed either by culture (3%) or by other techniques (serology, PCR, direct fluorescent antibody staining; 13%). The species was available for 10 763 cases (97%). The majority were confirmed cases (93%) according to our case definition, and 9417 cases (84%) were diagnosed by a positive urinary antigen test. The distribution of diagnostic techniques used for confirmation evolved over time with an increasing proportion of urinary antigen testing (39% in 1998 vs. 95% in 2008; \(p < 10^{-6}\)). The remaining LD cases were diagnosed either by culture (3%) or by other techniques (serology, PCR, direct fluorescent antibody staining; 13%). The species was available for 10 763 cases (97%). The majority were confirmed cases (93%) according to our case definition, and 9417 cases (84%) were diagnosed by a positive urinary antigen test. The distribution of diagnostic techniques used for confirmation evolved over time with an increasing proportion of urinary antigen testing (39% in 1998 vs. 95% in 2008; \(p < 10^{-6}\)).

### 3.5. Strains

The NRC-L received 1916 isolates for further identification and molecular typing. The proportion of previously identified strains (endemic and other) has increased in recent years (Figure 4). Endemic strains represented 29% and 34% of all isolates in 2007 and 2008, respectively. The diversity of endemic strains increased between 1998 and 2008 and five major endemic strains were characterized in 2008. Among these, Paris clone isolates were detected in 9% of culture-proven cases (164/1916; 42% were healthcare-associated and 58% were community-acquired). The Paris clone grouped with sequence type (ST) 1 or ST1-related isolates had a specific PFGE pattern and different MAb subgroups: Philadelphia (MAb 3/1-positive), or France/Allentown (MAb 3/1-positive), or Olda (MAb 3/1-negative). The Lorraine strain was isolated anecdotally before 2002 (three isolates). Since 2002, the prevalence of this strain has increased considerably and it accounted for 11% (23/202) of clinical isolates in France in 2008. All Lorraine clone isolates analyzed were ST47 and MAb France/Allentown. The most prevalent ST in culture-confirmed cases was ST23. In 2008, isolates of ST23 were cultured in 40 of the 197 culture-proven cases (20%). None of these were hospital-acquired cases.

### 3.6. Delays in notification

As one of the aims of surveillance is the early implementation of prevention and control measures, efforts were also put towards improving delays in case reporting. The median delay between symptom onset and notification to the DDASS decreased from 28 days in 1998 to less than 7 days in 2006. As a consequence, the proportion of cases reported within one incubation period (i.e., 10 days) rose from 9% in 1998 to 73% in 2008 and the proportion of cases reported within two incubation periods (20 days) rose from 33% to 91% between 1998 and 2008. From 2005, the median delay between the date of hospitalization and the date of notification was 3 days for cases diagnosed by positive urinary antigen test.

### 3.7. Geographic distribution

From 2002 to 2008, the average annual incidence rate of LD was 2.1 per 100 000 population in France. Cases were reported from all 22 administrative regions, but a west–east gradient in the incidence rates over the study period was noticed (Figure 5).

### 3.8. Exposure

The distribution of exposures among the 11 147 cases was: 7820 (70%) community-acquired confirmed, 1921 (17%) travel-related, 1002 (9%) hospital-acquired, and 404 (4%) acquired in a care home for the elderly. The percentage of hospital-acquired cases decreased over the 11-year period from 21% in 1998 to 7% in 2008 \( (p < 10^{-5}) \) (Table 1). The dates of hospitalization and onset were available for 89% \( (n = 989) \) of cases. Among them, 39% \( (n = 345) \) were definite healthcare-associated LD cases. Since 2001, information concerning care homes for the elderly shows that about 5% of annual LD cases live in such residences.

From 1998 to 2008, an exposure during travel was documented for 17% \( (n = 1921) \) of cases. Among them, 65% \( (n = 1250) \) were notified to EWGLINET, with 65% \( (n = 815) \) of cases having traveled within France. The remaining 671 travel-associated Legionnaires’ disease (TALD) cases had stayed in private accommodation or had not been notified to EWGLINET because their places or dates of stay were not correctly reported. EWGLINET also notified InVS of 362 cases. These cases were diagnosed in other countries and had traveled in France during the incubation period. Between 2002 and

### Table 1 Evolution of risk exposures of Legionnaires' disease cases in France, 1998–2008

<table>
<thead>
<tr>
<th>Year</th>
<th>Hospital-acquired</th>
<th>Acquired in care home for the elderly</th>
<th>Travel-associated</th>
<th>Community-acquired, confirmed and assumed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>(n = 381), %</td>
<td>21</td>
<td>16</td>
<td>63</td>
</tr>
<tr>
<td>1999</td>
<td>(n = 440), %</td>
<td>17</td>
<td>15</td>
<td>68</td>
</tr>
<tr>
<td>2000</td>
<td>(n = 610), %</td>
<td>20</td>
<td>12</td>
<td>68</td>
</tr>
<tr>
<td>2001</td>
<td>(n = 807), %</td>
<td>13</td>
<td>17</td>
<td>70</td>
</tr>
<tr>
<td>2002</td>
<td>(n = 1021), %</td>
<td>10</td>
<td>17</td>
<td>73</td>
</tr>
<tr>
<td>2003</td>
<td>(n = 1004), %</td>
<td>9</td>
<td>17</td>
<td>74</td>
</tr>
<tr>
<td>2004</td>
<td>(n = 1202), %</td>
<td>6</td>
<td>18</td>
<td>76</td>
</tr>
<tr>
<td>2005</td>
<td>(n = 1527), %</td>
<td>7</td>
<td>18</td>
<td>76</td>
</tr>
<tr>
<td>2006</td>
<td>(n = 1443), %</td>
<td>6</td>
<td>17</td>
<td>76</td>
</tr>
<tr>
<td>2007</td>
<td>(n = 1428), %</td>
<td>7</td>
<td>17</td>
<td>76</td>
</tr>
<tr>
<td>2008</td>
<td>(n = 1244), %</td>
<td>7</td>
<td>20</td>
<td>73</td>
</tr>
</tbody>
</table>
2008, there were 123 accommodation sites where clusters occurred. Water samples were collected in 122 sites for identification of Legionella. Among these, 42% were negative, 17% had Legionella titers <1000 CFU/l, and for 41%, the level was ≥1000 CFU/l. At eight sites the clinical and environmental isolates shared identical PFGE profiles.

3.9. Outbreak investigations

From 1998 to 2008, we identified 14 community outbreaks involving 380 (3%) cases. No outbreak was identified in 2008. The first outbreak was identified by EWGLNET during the Football World Cup in Paris in 1998. It involved 20 cases, among whom nine were European tourists, and the investigation showed that one cooling tower was the source of contamination.25 The second outbreak involved 20 cases and was identified in 2000 by the NRC-L, who characterized seven isolates with a unique and identical PFGE pattern (unpublished data). Other outbreaks were detected by the local health authorities. The median number of cases per outbreak was 22 (range 11–86), and only one outbreak involved more than 40 cases.11 The median duration of outbreaks was 44 days (range 10–106). Twelve (86%) outbreaks took place between May and September. During these 14 outbreaks, 5% (19/380) of cases were not hospitalized; in particular 21% of cases were not hospitalized during one outbreak that took place in Lyon in 2005.28 The global CFR was 12.6%, and in four outbreaks, no patient died.

Cooling towers were the most probable source of infection for 13 outbreaks. These sources were confirmed by epidemiological and microbiological evidence in eight outbreaks, and were suspected in five. The largest outbreak occurred in the north of France during the winter 2003–2004 with 86 confirmed cases and 18 deaths. The investigation of this outbreak showed that the aerosol spread from the cooling towers could extend to more than 6 km.11 In September 2006, an outbreak was suspected to be related to a whirlpool spa display at a fair.27

4. Discussion

This analysis of the surveillance data has enabled us to describe the epidemiology of LD and recent trends in France. We found that there was a gradual increase in incidence until 2005 then a steady decrease. The various steps in strengthening our surveillance system, including the introduction of the urinary antigen test in 1997 and improvements in data quality and delays in notification have certainly enhanced our ability to detect, prevent, and control LD, probably leading to the recent fall in notified cases. Since 1998, the delay in notification has decreased and most cases are now notified very quickly. A shortened notification delay in addition to the systematic investigation of cases at the district level, has contributed to the timely detection of clusters and outbreaks and
to the rapid implementation of control and prevention measures. All this progress was facilitated by the 2005 guidelines, which aimed to standardize all procedures from the detection of cases to the implementation of control measures.

Considering the aforementioned improvements and the increasing sensitivity over time,15,35,36 we consider that at present, our surveillance system enables us to provide a representative description of the epidemiology of LD in France. Nevertheless, in our experience of outbreak management, additional cases that would not have been diagnosed under normal circumstances were identified, suggesting that LD is probably still under-diagnosed and under-notified. However, from 1998 to 2008 the incidence in France remained higher than that in Europe (0.5 to 2.0 per 100 000 from 1998 to 2008 in France vs. 0.43 to 1.2 per 100 000 in Europe; http://www.ewgli.org). This observation may be linked to differences in surveillance sensitivity.29,30 The national guidelines and legislation for registering wet cooling systems and controlling their levels of bacteria also differ between countries.31 The potential impact of exposure density and other environmental factors that can play a role in the development of LD should also be considered. For example, the UK and the Netherlands experienced an unexplained increase in non-TALD cases during the summer of 2006.32 This suggests that notification rates are influenced by many factors, such as practitioner awareness, sensitivity of the surveillance system, impact of legislation for controlling the development of the bacteria in the aquatic environment, and environmental factors. Therefore we must be very cautious when discussing the differences across countries.

Considering the case characteristics, our observations were similar to those at the European level, especially regarding the high proportion of cases among elderly males. Advanced age and male gender are well recognized as risk factors for LD, thus facilitating the diagnosis among these groups. Knowledge of case characteristics has also allowed the implementation of specific regulations aimed at reducing the risk, e.g., in care homes for the elderly in France in 2005. To a much lesser extent, LD can also affect children,33 but the proportion of pediatric cases in our surveillance data is very small, similar to observations in the USA.33,34 It is difficult to establish whether children do not develop LD or whether children with pneumonia are not tested for LD, leading to misdiagnosis and underreporting of pediatric cases.

Other risk factors for acquiring LD have been widely documented15,35,36 and our results confirm that smoking, chronic disorders, and cancer are frequently reported.

Case outcome was well documented in our dataset and the CFR decreased significantly over time. Even if we cannot differentiate between deaths attributable to LD or an underlying disease, this encouraging result is probably due to earlier diagnosis by urinary antigen testing, which has contributed to reduce mortality.37-39 through the prompt initiation of appropriate therapy. It has been shown that delays in appropriate antibiotic treatment have a negative impact on outcome40,41 and that the rapid recognition of the disease, particularly for patients with underlying conditions, is crucial. In order to further reduce the CFR, practitioners should be better informed of the need to systematically use the urinary antigen test for at-risk patients presenting clinical signs of atypical pneumonia.

Nevertheless, the CFR is higher in France than that observed in Europe.4 The outcome of LD cases is known for the majority of cases in France, through the LD routine surveillance scheme. A surveillance system enabling such a follow-up does not exist in all other European countries. Most cases in our data were due to Lp1 and were diagnosed by urinary test. However, this test is specific to Lp1. The diagnosis of LD caused by other serogroups or other species can be made by culture from bronchopulmonary aspirations or secretions and serology, but results are not rapidly available. In accordance with the EWGLI case definitions, diagnosis by polymerase chain reaction (PCR) performed on respiratory samples will soon be introduced to our case definition. This will probably facilitate the diagnosis of LD for patients presenting clinical signs suggesting LD, but with a negative urinary antigen test. In addition, this may contribute to the identification of emerging strains that can cause infections, such as non-pneumophila Legionella.

Strain isolation allows the identification of the source of infection by matching of environmental and clinical strain profiles. Despite the wide-scale use of the urinary tests, cultures were regularly carried out, as shown by the stable percentage of isolates recovered during the study period. In fact, in France, it is recommended that cultures be performed on pulmonary samples for all cases with a positive urinary test, and clinicians are regularly reminded of this recommendation. This pro-active attitude has probably contributed to enlarge the isolate strain collection available at the NRC-L. Since January 2008, all clinical isolates have been routinely characterized by three different typing methods in order to improve the discriminatory capacity. This systematic characterization of strains, associated with available epidemiological and sometimes environmental data, provides a unique opportunity to develop research studies on specific strains. For instance, Ginevra et al. showed that the Lp1 Paris strain was associated with female sex, steroid therapy and history of cancer or hematomatological disease, whereas the Lp1 Lorraine strain was associated with smoking.42 We emphasize that the availability of isolates contributes to the microbiological progress towards a better understanding of the virulence factors,43,44 the ability of Legionella to multiply in host cells,45 and the relationship between host characteristics and clinical presentation of the disease.

Despite the decreased percentage of hospital-acquired cases during the study period, the number of hospital-acquired cases remained stable. Intensive efforts to better assess and control the risk have been made in healthcare facilities and care homes for the elderly, especially with the introduction of new regulations for prevention and control in 2002 and 2005. Hospital-acquired cases highlight the difficulty in eradicating Legionella from complex water systems despite regular maintenance and monitoring.46,47 For better prevention, the environmental long-term monitoring of the water distribution systems appears necessary in such settings.

The percentage of TALD cases has not decreased over the years, suggesting that travel is still an important risk factor for LD.15,36 The majority of TALD cases were in French persons traveling in France, contrary to the northern European countries where the majority of TALD cases have traveled abroad.16,48 EWGLINET single case notification does not require a systematic environmental investigation. The local health authority is only asked to inform the accommodation manager about the LD risk and to give advice on sampling. For clusters, the investigations showed that a majority of sites reported a Legionella contamination of their water networks, but microbiological evidence of the source of contamination was found for only eight clusters out of 123. The percentage of contaminated accommodation sites is similar to that reported in Italy,49 where a large number of TALD cases are also registered. In 2008, specific guidelines on LD risk were distributed to managers of French tourist accommodation to encourage efforts aimed at implementing prevention and control measures. In addition, in 2010, the Ministry of Health introduced new regulations requiring a systematic water network risk assessment and a yearly water sampling in order to reduce the number of TALD cases.

From 1998 to 2008, several community outbreaks of LD occurred in France, most often associated with wet cooling systems. One year after the outbreak that occurred in the north of France,11 new regulations for cooling systems were introduced (end 2004) to reduce the environmental risks linked to aerosol-
generating devices. These new regulations require the registration of all wet cooling systems at the local and regional level, with regular microbiological monitoring and inspection at least every 2 years to ensure that adequate procedures are in place. This outbreak generated considerable media attention, which probably contributed, at least in part, to the rapid introduction of the French legislation. In parallel, awareness and the strong commitment of the public health authorities have undoubtedly played an essential role in improving the identification of cases and outbreak management. Of note, only one outbreak was identified during the last 2 years. This result is very encouraging, and further efforts to maintain the high quality of our surveillance system and our ability to rapidly investigate and control a source of contamination should be made.

Geographic variation in LD incidence rates was observed. This could partly be explained by climate and meteorological conditions, as recently suggested for other acute respiratory tract infections.63–66 Humidity and temperature might have an influence on LD incidence,51–54 but further studies are needed to better understand the impact of these environmental conditions. We know that free-living amoebae could play an important role in the development of Legionella. Ecological studies should be encouraged to better understand the association between exposure density, environmental conditions, and LD incidence.55,56

In recent years, research on Legionella has been widely developed. New findings are especially interesting because they are beginning to suggest associations between host factors, Legionella genomic factors, and environmental factors that influence the occurrence of this disease. If in future years the research continues to progress, it may be possible, particularly in the context of an environmental contamination, to establish if the environmental strain could result in human cases and to identify the populations particularly at risk. At this stage, it is still too early to measure the possible impact of recent research on the epidemiology of Legionnaires’ disease, but risk assessment for human infection appears more than ever an objective to reach.

Acknowledgements

The authors thank the clinicians, microbiologists, and public health professionals involved in LD surveillance in France at the local and regional level. We would also like to thank the team of the National Reference Centre for Legionnaires in Lyon and Lisa King for her helpful comments.

Conflict of interest: No conflict of interest to declare.

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