Probabilistic Analysis of Legionellosis outbreak data and its potential contribution to microbial risk assessment

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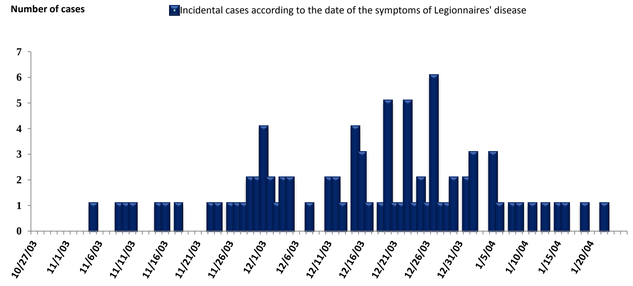
INTRODUCTION

Certain species of bacteria belonging to the *legionella* genus are the etiologic agent of Legionnaire's disease and its non-pneumonia form, Pontiac fever. Legionellosis is a public health problem with a high rate of mortality (11%). Managing at-risk facilities (showers, cooling towers) relies on a *legionella* concentration threshold in water but not air, which is the route of exposure.
Using probabilistic methods, we took data from a well-documented legionellosis outbreak to analyse the risk related to each installation identified as the potential cause of the epidemic. By taking into consideration some hypotheses and factors related to the functioning of the installation, this study enabled us to suggest a ranking of the potential sources.

THE LEGIONELLOSIS OUTBREAK

The data used for the study come from the most extensive Legionellosis outbreak that France has ever experienced. There were 86 Legionellosis cases recorded from 5 November 2003 to 22 January 2004 over a 12-kilometer area of the Harnes commune in the Pas-de-Calais department of France. The male/female ratio was 1.5 and the median age was 76. Eighteen cases (21%) died.
An environmental investigation helped list and inspect all potential sources of contamination for the purposes of identifying the source of the outbreak.
The microbiological investigation provided clinical and environmental samples from all analysed sites. All of the isolated strains were identified using PFGE (Pulsed Field Gel Electrophoresis). Atmospheric samples were also taken. The epidemic *legionella* strain (Lp1) was found in 23 clinical cases and four installations: factory cooling towers, an aerated waste treatment basin and a car wash station. The fourth facility was the use of a high-pressure water cleaner on cooling towers, since this may have aerosolised *legionella*-contaminated biofilm.
A special support mission and epidemiological investigations of the *Institut de Veille Sanitaire* (the French institute for public health surveillance) concluded that the outbreak had two waves and that the most likely source was a cooling tower at a plant located in the Harnes commune (1, 2). There was also a review of the management methods employed during the outbreak (3).



METHODS

Description of the method employed
Starting with the number of cases identified each day, we determined the contamination date by taking into consideration the incubation period modelled according to various laws of probability.
Then, an analysis of potential contamination sources was performed by determining, for each wave, the number of victims that were exposed to a potential source when that source was operational.
This was followed by a ranking of potential sources using a scoring system for different parameters and according to the various hypotheses mentioned below.

Hypotheses considered when ranking the sources
Four parameters were used to rank the sources and each parameter was divided into several classes for scoring purposes:
•The entry of legionella into the atmosphere for each installation (seven classes). The legionella concentrations correspond to the values found during the environmental study. For the basin, the concentrations were extrapolated by correlating them with the quantities of delivered sludge based on a measurement performed in January 2004. The characteristics taken into consideration for this parameter during the third wave and are summarised in the following table:

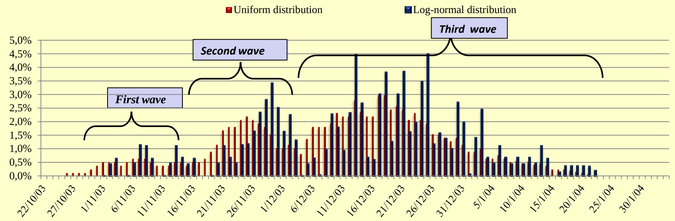
Installation	Caractéristics	Contamination (CFU/L)	Legionella movement (CFU/S)	**Comments** on the assumptions*
Car wash	500 l/h	1,600	200*	The entire flow was aerosolised
High-pressure water cleaner	500 to 1,500 l/h	100,000	700 to 4,000*	5 to 10% of the flow was aerosolised
Cooling tower	2 * 90 l/h*	100,000	5,000	Aerosol emission
Basin	40 CFU/s/m^2 2,600 m^2 *	Approximately 2 10^8	100,000	Inverse modelling using Screen 3 based on air concentrations measured on 14 Jan 2004.

•Aerosol dispersion capacity (three classes). This parameter depends upon the speed with which the aerosol spray is ejected as well as the height of the installation. These parameters were empirically established as 1 for the basin and car wash, 10 for the high-pressure water cleaner and 100 for the cooling tower.
•Number of victims who may have been exposed by contamination date (five classes)
•Duration of aerosol emission by installation operational period (five classes).

RESULTS

Outbreak in three waves

The distribution of potential contamination days after consideration of the incubation period revealed three successive waves during the outbreak, and not two as was indicated in the reports.
The figure shows the results using two laws of probability to model the incubation period: a uniform distribution and a truncated lognormal distribution, giving an incubation period of two days at least and ten days at most.



Daily distribution of incident cases according to the date of contamination under the probability law used for incubation period

Type of probability law	Wave of the outbreak	Period (days)	Dates	Number of cases	Nonzero probability of exposure to the source (Number of cases – percentage of cases per wave)			
					Cooling tower	High pressure water cleaner	Basin	Car wash station
Uniform distribution	Wave 1	16	26/10/2003 to 10/11/2003	7	7 (100%)		7 (100%)	
	Wave 2	23	11/11/2003 to 03/12/2003	26	23 (88%)		26 (100%)	
	Wave 3	50	04/12/2003 to 22/01/2004	53	26 (49%)	32 (60%)	53 (100%)	33 (62%)
	Total duration of the outbreak	89	**26/10/2003 to 22/01/2004**	86	56 (65%)	32 (37%)	86 (100%)	33 (38%)
Lognormal distribution	Wave 1	9	01/11/2003 to 09/11/2003	4	4 (100%)		4 (100%)	
	Wave 2	23	11/11/2003 to 03/12/2003	23	23 (100%)		23 (100%)	
	Wave 3	50	04/12/2003 to 22/01/2004	59	23 (39%)	16 (27%)	59 (100%)	24 (41%)
	Total duration of the outbreak	82	**01/11/2003 to 22/01/2004**	86	50 (58%)	16 (19%)	86 (100%)	24 (28%)

Analysis of potential contamination sources

The analysis of potential contamination sources revealed, for the three waves, that:

- **65 % of all** 86 cases *(uniform law)* and **58 %** of all 86 cases *(lognormal law*) have a nonzero probability of having been exposed to the cooling tower. This means that **35%** of all 86 cases *(uniform law*) and **42%** of all 86 cases *(lognormal law*) have a zero probability of having been exposed to the cooling tower aerosols.
- **100 % of all** 86 cases *(uniform law and lognormal law*) have a nonzero probability of having been exposed to aerosols released by the basin surface aerators.

Ranking of potential sources

First wave of the outbreak:
The combination of two potential sources (cooling tower and basin) was the most likely cause of the contamination during this first wave.

Second wave of the outbreak:
The cooling tower was the most likely source of the contamination during this second wave. However, the investigation of this source demonstrated that 12% of the 26 cases of this wave had a zero probability of having been exposed and therefore of being likely to have been infected by the cooling tower. In other words, the cooling tower could not be the only source of the second wave of the outbreak. The underlying hypotheses must therefore be reviewed.

Third wave of the outbreak:
The basin was the most likely (96.98%) source of the contamination in this third wave. The investigation of this source demonstrated that 100 % of the 53 cases of this wave had a nonzero probability of having been exposed and therefore were likely to have been infected by the basin.

Sources	*Wave 1*		*Wave 2*		*Wave 3*		
	Potential Risk (uniform law and lognormal law)	Maximal legionella flow	Potential Risk (uniform law and lognormal law)	Maximal legionella flow	Potential Risk (uniform law)	Potential Risk (lognormal law)	Maximal legionella flow
Basin	**50%**	**200**	**0,1%**	**794**	**96,98%**	**96,96%**	**105 000**
Cooling tower	**50%**	**4,95**	**99,9%**	**7 625**	**2,91%**	**2,91%**	**19,96**
High pressure water cleaner					**0,10%**	**0,03%**	**192**
Car wash station					**0,01%**	**0,10%**	**1 000**

DISCUSSION - CONCLUSION

Analysing epidemic data using probabilistic methods helps determine the probability that a potential source contributed with some robustness. Taking the operation of the installations into consideration, the distribution and probability of exposure help rank the potential sources of the outbreak. The various results of this study demonstrated that the cooling tower could not have been the only cause of all *legionella* cases. However, the aerated basin may have been directly responsible for the most of the cases of the third wave. The direct involvement of this type of installation in epidemics has been published since the outbreak discussed here occurred (4, 5). The review of the ranking of sources was based on hypotheses that need to be revised: numerous data pertaining to the operation of certain installations, such as car washes, high-pressure water cleaners and basins (*legionella* flow, dispersion) are not known with enough precision.
Many improvements can be made, particularly to the consideration of possible aggregates (6), a parameter that may change with the type of installation and could have a role on legionella survival or to the consideration of contamination only once the epidemic strain has been identified.
This type of analysis can help us learn more about these phenomena and develop a method for quantitatively assessing risks so that appropriate management methods can be implemented.

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