

Epidemiological characteristics associated with specific sequence types ST1, ST23, ST47 of legionnaires' disease cases in France, 2008 – 2012

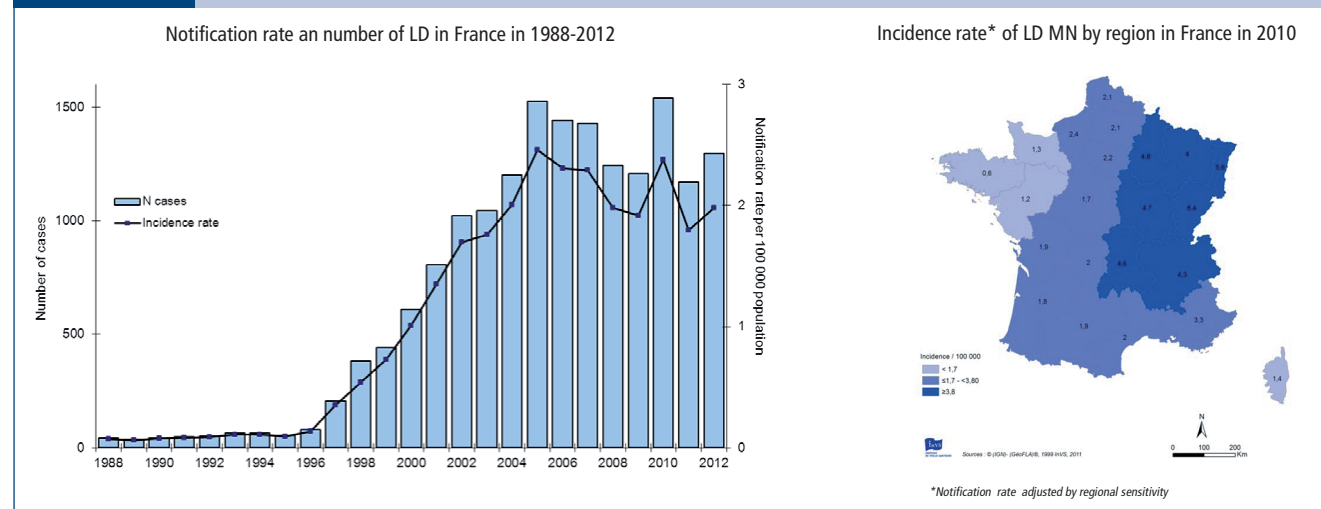
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Background

- In France, around 1,200 cases of Legionnaires' disease (LD) are notified annually.
- A geographical west-east gradient of LD incidence rate is observed.

FIGURES 1&2 LEGIONNAIRES' DISEASE IN FRANCE



- Almost all cases (99%) in France are due to *Legionella pneumophila* (Lp).
- Isolates are available for approximately 20% of cases since 2000.
- More than 200 strains of Lp1 are isolated each year.
- All isolates are characterized by sequence based typing method at the National Reference Centre for *Legionella*.
- Among all isolates, some ST are more frequently identified: ST1, ST23, ST47.

Our study objective was to describe cases according to their sequence types (ST).

Method

- Case definition: all cases of LD with an Lp1 isolate notified in France from 2008 to 2012.
- Statistical methods
 - We compared cases characteristics according to their ST:
 - ST1 versus ST23;
 - ST47 versus ST23;
 - ST1 or ST23 or ST47 versus other ST.
 - A multivariable modified Poisson regression model was constructed to:
 - estimate an incidence rate ratio (IRR);
 - identify risk factors and exposures potentially associated with specific ST: ST1; ST23; ST47.

Results

- 6,467 LD cases were notified from 2008 to 2012.
- A total of 1,217 were included in the study.

FIGURE 3 SCHEME OF CASES INCLUSION IN THE STUDY

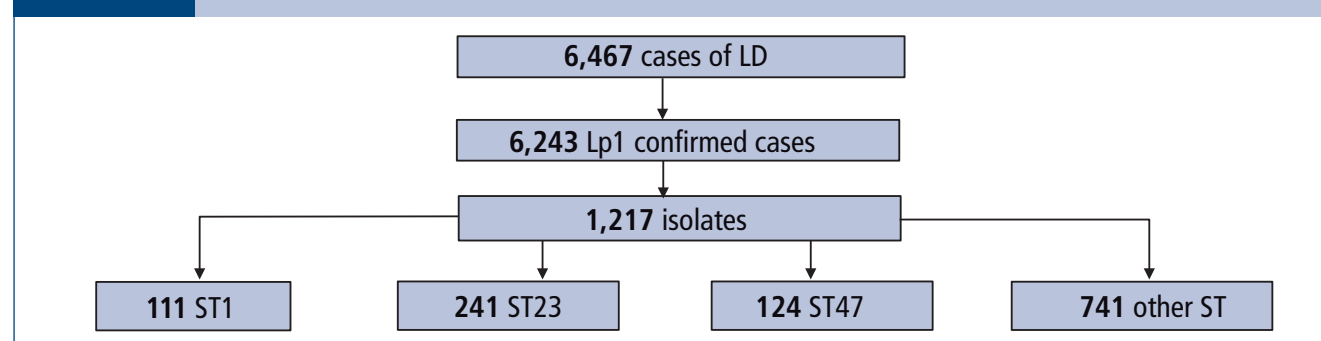


TABLE 1 CHARACTERISTICS OF CASES BY ST

Characteristics	ST1 111		ST23 241		ST47 124		Others ST 741	
	n	(%)	n	(%)	n	(%)	n	(%)
Male	81	(73.0)	194	(80.5)	102	(82.3)	586	(79.1)
Mean age (years)	63.1		59.1		60.5		58.6	
Death	30	(30.6)	35	(15.8)	15	(13.2)	128	(18.7)
Risk factors: at least 1	84	(75.7)	175	(72.6)	86	(69.4)	552	(74.5)
Cancer	26	(23.4)	19	(7.9)	13	(10.5)	81	(10.9)
Steroid therapy	25	(22.5)	10	(4.2)	12	(9.7)	69	(9.3)
Tobacco	32	(28.8)	127	(52.7)	56	(45.2)	376	(50.8)
Diabetes	14	(12.6)	42	(17.4)	24	(19.4)	110	(14.9)
Exposures								
Hospital acquired infection	35	(31.5)	7	(2.9)	3	(2.4)	46	(6.2)
Travel (<10 days before onset)	13	(11.7)	32	(13.3)	21	(16.9)	152	(20.5)
Elderly setting	6	(5.4)	9	(3.7)	0	(0)	14	(1.9)

1) MULTIVARIABLE ANALYSIS: ST1 VERSUS ST23

TABLE 2 CASE CHARACTERISTICS ASSOCIATED WITH ST1 VERSUS ST23

Variable	IRR	IC95%	p value
Age	1.00	(0.99 - 1.01)	0.41
Male	0.97	(0.72 - 1.31)	0.87
Hemopathy	1.33	(0.95 - 1.86)	0.10
Steroid therapy	1.73	(1.29 - 2.32)	<0.001
Tobacco	0.73	(0.51 - 1.05)	0.09
Diabetes	0.81	(0.52 - 1.26)	0.36
Hospital acquired infection	2.63	(1.90 - 3.65)	<0.001
Travel	1.27	(0.76 - 2.11)	0.36
Elderly setting	1.33	(0.67 - 2.66)	0.42

2) MULTIVARIABLE ANALYSIS: ST47 VERSUS ST23

TABLE 3 CASE CHARACTERISTICS ASSOCIATED WITH ST47 VERSUS ST23

Variable	IRR	IC95%	p value
Age	1.00	(0.99 - 1.01)	0.73
Male	1.09	(0.74 - 1.58)	0.67
Hemopathy	1.08	(0.70 - 1.68)	0.73
Steroid therapy	1.65	(1.07 - 2.53)	0.02
Tobacco	0.87	(0.63 - 1.20)	0.83
Diabetes	1.08	(0.76 - 1.54)	0.43
Hospital acquired infection	0.73	(0.29 - 1.86)	0.52
Travel	1.20	(0.82 - 1.74)	0.35

3) MULTIVARIABLE ANALYSIS: ST1/ ST23/ ST47 VERSUS OTHER

TABLE 4 CASE CHARACTERISTICS ASSOCIATED WITH ST1 VERSUS OTHER ST

Variable	IRR	IC95%	p value
Age	1.00	(0.99 - 1.01)	0.28
Male	1.00	(0.70 - 1.42)	0.98
Hemopathy	1.19	(0.78 - 1.81)	0.43
Steroid therapy	1.37	(0.90 - 2.09)	0.14
Tobacco	0.64	(0.41 - 0.99)	0.047
Diabetes	0.77	(0.46 - 1.28)	0.31
Hospital acquired infection	3.40	(2.25 - 5.15)	<0.001
Travel	0.84	(0.47 - 1.50)	0.55
Elderly setting	2.30	(1.09 - 4.86)	0.03

TABLE 5 CASE CHARACTERISTICS WITH ST23 VERSUS OTHER ST

Variable	IRR	IC95%	p value
Age	1.00	(0.99 - 1.01)	0.75
Male	1.07	(0.81 - 1.42)	0.60
Hemopathy	0.82	(0.53 - 1.25)	0.36
Corticotherapy	0.54	(0.30 - 0.99)	0.047
Tobacco	0.99	(0.77 - 1.26)	0.90
Diabetes	1.13	(0.85 - 1.51)	0.40
Hospital acquired infection	0.60	(0.29 - 1.22)	0.16
Travel	0.63	(0.45 - 0.89)	0.008
Elderly setting	1.40	(0.80 - 2.45)	0.24

TABLE 6 CASE CHARACTERISTICS WITH ST47 VERSUS OTHER ST

Variable	IRR	IC95%	p value
Age	1.00	(0.99 - 1.02)	0.38
Male	1.24	(0.80 - 1.92)	0.33
Hemopathy	0.96	(0.56 - 1.65)	0.88
Steroid therapy	1.14	(0.66 - 1.99)	0.64
Tobacco	0.84	(0.57 - 1.24)	0.39
Diabetes	1.25	(0.83 - 1.90)	0.27
Hospital acquired infection	0.36	(0.12 - 1.13)	0.08
Travel	0.77	(0.50 - 1.20)	0.25

ST1 OR ST47 VERSUS ST23

- ST1 cases were associated with hospital acquired infection (IRR: 2.6; $p < 10^{-3}$) and use of steroid therapy (IRR: 1.7; $p < 10^{-3}$) compared with ST23 cases.
- ST47 cases were associated with use of steroid therapy (IRR: 1.7; $p < 0.02$) compared with ST23 cases.

ST1 - ST23 - ST47 VERSUS OTHER ST

- ST1 cases were associated with hospital acquired infection (IRR: 3.4; $p < 10^{-3}$) and elderly settings (IRR: 2.3; $p < 0.03$) compared with other ST cases.
- ST23 cases were associated with a lesser use of steroid therapy (IRR: 0.54; $p < 0.047$) and a lesser exposure during travel (IRR: 0.63; $p < 0.008$) compared with others ST cases.

GEOGRAPHIC DISTRIBUTION

- ST1 cases were more observed in the Ile de France region (Paris and suburbs).
- ST47 cases were more observed in the Eastern and Northern regions of France.
- ST23 cases were widely observed across France.

Discussion

- In France, a large number of LD cases are identified each year, but an isolate is available for only 20% of cases.
- The result of these findings should not be extended to all LD cases, especially those with no strain available.
- Nevertheless:
 - ST1 is associated with hospital acquired infection and elderly setting as already suggested in other study [1].
 - Despite a large number of cases with ST23, we did not identify any risk factor specific to this ST but ST23 cases are less frequently associated with travel and use of steroid therapy.
 - The geographic distribution of cases needs additional studies to better explore specific spatial distribution for some ST.

Conclusion

- Compared with other ST and ST23 this study identified independent associations between ST1 and hospital acquired infection and elderly setting.
- It is important to maintain clinician awareness of the need to collect sputum samples in order to document LD cases and to better understand the disease.

Reference
 [1] Ginevra C, Duclos A, Vanhems P, Campese C, Forey F, et al. Host-related risk factors and clinical features of community-acquired legionnaires disease due to the Paris and Lorraine endemic strains, 1998-2007, France. Clin Infect Dis. 2009 Jul 15;49(2):184-91.