The Italian Multicentric Study on Legionnaires' disease

Paola Borella

Dipartimento di Scienze Igienistiche e Microbiologiche, Università degli Studi di Modena e Reggio Emilia, Modena, Italy

Correspondence to: Paola Borella, Dipartimento di Scienze Igienistiche e Microbiologiche, Via Campi 287, 41100 Modena, Italy.
E-mail: borella.paola@unimore.it

Report presented at *Legionellosi: un rischio crescente,* 18-19 June 2004, Roma, Italy

Abstract

The general objective of the Italian Multicentric Study on Legionnaires' disease is the investigation of some of the critical aspects of this emerging disease, with a specific interest in the Italian situation. An epidemiological study is being conducted in different Italian localities to evaluate the diffusion of *Legionella* spp in the environment and the efficiency of some of the control strategies to detect cases, study their related risk factors and to establish the frequency of infection within groups at different exposure levels. The first results obtained from the research project are presented below.

Introduction

From a public health point of view, the key issues concerning Legionnaires' disease are: insufficient knowledge regarding the prevalence of infection/disease, difficulties in detecting and associating cases with the environmental sources, poor identification of risk factors involved in infection/disease, scant information on environmental risk factors and events allowing the survival of *Legionella* spp in the environmental reservoirs and finally, problems in controlling the microorganism by applying long-term efficient disinfecting methods.[1-9]

In response to this the Italian Multicentric project aims to: a) to deepen the knowledge on *Legionella* spp diffusion in water systems, the most common source of infection in Italy and to evaluate the efficacy of the control measures; b) to investigate the prevalence of anti-legionella spp antibodies within subgroups exposed at different risk levels; c) to evaluate the frequency of nosocomial and community-acquired legionellosis among patients with pneumonia from large hospitals located in various Italian localities (a case-control study is used to define both exposure and personal risk factors associated with the disease, with special reference to the basal immune situation and genetic markers involved in host resistance/progression to infection); d) to draw an epidemiological map of *Legionella* serotypes and genotypes collected throughout the epidemiological survey, identifying the diversity in *Legionella* strains and the degree of correlation between serotypes, genotype and virulence.[10-14]

Methods

A multicentric survey of public and private buildings (hospitals, hotels, homes) was conducted to search, isolate and subtype *Legionella* strains from hot water systems. The sampling sessions included a detailed investigation of the environmental and structural factors associated with the presence of *Legionella.* The prevalence of anti-legionella antibodies (Indirect Fluorescent Antibody test, IFA test) within subgroups exposed at different risk level was investigated and subjects working in contaminated structures were recruited. Since 2001, a surveillance protocol was activated to evaluate the frequency of nosocomial and community-acquired legionellosis among patients with pneumonia from large hospitals located in Milan, Reggio Emilia, Bologna, Rome, Neaples, and Bari. This active surveillance is based on the search for the urinary antigen *L. pneumophila* (Enzime Immuno Assay, EIA), followed (when possible) by isolation of the germ from a sputum culture, and sero-conversion as the confirming test on a substantial and representative number of the patients. Subjects are included in a case-control study to evaluate environmental, clinical and personal characteristics associated with the disease and are compared with both healthy subjects and patients affected by other types of pneumonia.

Results

Legionella spp, predominantly *L.pneumophila*, was detected in 22.4% of domestic hot water systems, in 69% of hotels and in all the examined hospitals. The main risk factors for contamination

were structural, such as to have a centralised and old water distribution system, instead of a more recent one with high copper levels in the water were protective against *Legionella* contamination.

By conducting a large surveillance of pneumonia cases between 2002 and 2003, the study detected 165 cases of legionellosis from 4340 examined patients with a frequency of 3.8% for community acquired case and 5% for nosocomial cases.

In the first group of patients recruited for the case-control study, only pre-existing immunopathologies were found to be associated with the disease, whereas smoking habits and co-morbidity were risk factors for all pneumonia. A significant decrease in CD16 (natural killer) cell numbers was found in the affected patients in comparison to the control group. Furthermore, significant alterations in iron metabolism were associated with the disease.

We also documented that workers of a contaminated hospital have a higher frequency of antibodies against *Legionella* spp compared with a control group. However, no subject declared the disease and no association was found between seropositivity and the known risk factors for Legionnaires' disease.

Conclusions

Our active clinical surveillance scheme was able to detect numerous cases between 2002 and 2003, thus contributing to the increase in reported cases from Italy. The rate of infection amongst pneumonia cases was about 4%, confirming results of other similar surveys. The preliminary results of the case-control study show that cases have peculiar although not sufficiently studied alterations in both immune and biochemical parameters.

The identification of environmental, immune, genetic and personal risk factors and the quantification of their role in determining the infection/disease will offer a relevant scientific contribution, so far scarcely studied by other research programmes. The project is also focused on the mechanisms of transmission and control from the environment to human subjects, with particular attention being paid to the risk for communities such as hospitals.

References

1) Borella P, Bargellini A, Pergolizzi S, et al. Surveillance of legionellosis within a hospital in northern Italy: May 1998 to September 1999. Eurosurveillance 1999; 4:118-20.
2) Borella P, Bargellini A, Pergolizzi S, et al. Prevention and control of nosocomial legionnaires' disease. Ann Ig 2000;12:287-96.
3) Leoni E, Legnani PP, Bucci Sabbatini MA, Righi F. Prevalence of Legionella spp in swimming pool environment. Water Res 2001;35(15):3749-53.
4) Ditommaso S, Biasin C, Giacomuzzi M, Zotti CM, Ruggerini Moiraghi A. Prevenzione della legionellosi: confronto tra linee guida europee ed extraeuropee. Giornale It. delle Infezioni Ospedaliere 2003;10(1):7-24.
5) Fields BS, Benson RF, Besser RE. Legionella and Legionnaires' disease: 25 years of investigation. Clin Microbiol Rev 2002;15(3):506-26.
6) Kim BR, Anderson JE, Mueller SA, Gaines WA, Kendall AM. Literature review-efficacy of various disinfectants against Legionella in water systems. Water Res 2002;36(18):4433-44.
7) Rota MC, Castellani Pastoris M, Ricci ML, Caporali MG, Salmaso S. Rapporto annuale sulla legionellosi in Italia nel 2002. Notiziario ISS 2003;16(12):3-8.
8) Yu VL, Plouffe JF, Pastoris MC, et al. Distribution of Legionella species and serogroups isolated by culture in patients with sporadic community-acquired legionellosis: an international collaborative survey. J Infect Dis 2002;186(1):127-8.
9) Stout J, Yu VL. Hospital-acquired Legionnaires' disease: new developments. Curr Opin Infect Dis 2003;16(4):337-41.
10) Borella P, Montagna MT, Romano-Spica V, et al. Environmental diffusion of Legionella spp and legionellosis frequency among patients with pneumonia: preliminary results of a multicentric Italian survey. Ann Ig 2003;15:493-503.
11) Borella P, Montagna MT, Romano-Spica V, et al. Relationship between mineral content of domestic hot water and microbial contamination. J Trace Elem Med Biol, 2003;17(Suppl.1):37-43.
12) Borella P, Montagna MT, Romano-Spica V, et al. Legionella infection risk from domestic hot water. Emerg Infect Dis 2004;10(3):457-64. Erratum in : Emerg Infect Dis 2004:10(7): 1353
13) Romano-Spica V, Montagna MT, Stancanelli G, et al. Genetic polymorphisms as susceptibility factors to Legionella pneumonia. Proceedings of 19th Annual Meeting of the EWGLI Group 15-18 May 2004 Chamonix Mont Blanc, France (abs).
14) Boccia S, Romano-Spica V, Neglia R, et al. Molecular typing of environmental isolates of Legionella pneumophila collected in Italy over a four years period. 19th Annual Meeting of the EWGLI Group 15-18 May 2004 Chamonix Mont Blanc, France (abs).