

Epidemiology of bacterial meningitis in Lombardy Region in the period 2000-2006

Anna Pavan¹, Spinello Antinori¹, Annamaria Belloni¹, Antonio Boccazzi¹, Francesco Castelli¹, Maria Gramegna¹, Enrico Magliano¹, Piero Marone¹, Cristina Montomoli², Marco Tinelli¹, Gianvincenzo Zuccotti¹, Luigi Macchi¹

¹Regional Working Group on Surveillance and Control of Bacterial Meningitis Regional Health Office, Lombardy, Italy

²Department of Applied Health Sciences, University of Pavia, Italy

SUMMARY

Epidemiological study of bacterial meningitis, particularly those forms susceptible to vaccination, is an indispensable tool in choosing vaccination strategies. Lombardy Region, where approximately 20% of the Italian population resides, has conducted an in-depth study on invasive meningococcal diseases and pneumococcal meningitis using available health statistics and performing a control of single cases to achieve complete knowledge of the phenomenon. The results, relating to the period 2000-2006, indicate limited incidence rates both for the general population and childhood age groups that do not justify hypotheses of a universal offering of the specific vaccines. However, the healthcare system must equip itself with additional tools for the identification of the serogroups and serotypes responsible for disease as a further support for possible choices modifying the current vaccination policies.

KEY WORDS: Bacterial meningitis, Pneumococcal disease, Meningococcal disease

INTRODUCTION

In the past few years, in Europe and in Italy, increasing attention has been devoted to bacterial meningitis and to invasive meningococcal diseases in general. This is due both to actual epidemiological changes and to the social impact that these clinical pictures determine.

Although these are diseases known to and well understood by medicine, especially from the standpoint of diagnosis and treatment, it is undeniable that many aspects, especially of an epidemiological nature, require further study.

In Lombardy Region the phenomenon had an epicrisis in the course of 2003, reaching a high

incidence of invasive meningococcal disease and with a modification of the serogroups involved that led to a relative increase of Group C *Neisseria meningitidis*.

As a result, it was decided to review the case statistics of the most recent period in order to evidence aspects of the diffusion and epidemiological characteristics of the subjects affected so as to be able to delineate the best ways of implementing a specific surveillance system, the interventions to adopt in relation to individual cases or outbreaks, and finally the prevention strategies with the utilisation of the new vaccine preparations available.

MATERIALS AND METHODS

The study of bacterial meningitis suffers from the limits of the available information systems. Currently the data sources in Italy are comprised of:

Corresponding author

Anna Pavan

Unit for Prevention

Hygiene and Infectious Diseases of the Health's General Office
Lombardy, Italy

E-mail: Anna_Pavan@regione.lombardia.it

- notification of infectious diseases: this is a well-established flow between local health units and the Region and from the regions to the Ministry of Health, which provides for registration of cases of meningococcal meningitis only;
- special surveillance system on bacterial meningitis and meningococcal sepsis: set up by the ISS and the Ministry of Health in 1994, it collects from the centres where the hospital admissions occur reports of cases and bacterial strains (*Neisseria meningitidis* and *Haemophilus influenzae*) for their typing;
- hospital discharge abstracts: indicate, for each hospitalisation, a principal diagnosis and any secondary diagnoses, up to a maximum of four; analysis of the abstracts enables extrapolation of cases where a diagnosis of bacterial meningitis was made.

For the 2000-2006 period the above information systems were therefore analysed and all cases with a diagnosis of bacterial meningitis (defined as compatible clinical pictures and ascertainment of cloudy cerebrospinal fluid) and those of sepsis from *Neisseria meningitidis* or *Streptococcus pneumoniae* were considered.

For each of the cases considered the complete personal information was collected, the starting date of the first symptoms and consequently the age at onset of the disease, the bacterial agent isolated and relative typing available, the city and

local health unit of residence, the presence of specific risk factors, and the outcome of the disease. The data were reprocessed with the applications Access and Excel to arrive at the annual incidence rates and those by age group using the resident population of 2003 as denominator.

RESULTS

Table 1 indicates the identified cases by year and pathogen. Note that, after substantial stability in the years 2000-2002, in the ensuing years there was an increase, attributable especially to *Streptococcus pneumoniae* and *Neisseria meningitidis*.

The recorded increments are also to be considered in the light of increased sensitivity on the part of physicians to reporting and greater attention by local health units to the consultation of current health statistics. Analysis of the different aetiologies does not confirm a rising trend, as the overall number of cases is lower; and therefore the year-to-year oscillations, both upward and downward, are notable, as can be seen in Figure 1.

Regarding the *Neisseria meningitidis* forms and the serogroups involved, Figure 2 shows a gradual increase in relation to serogroup C, a phenomenon also registered at national level.

Figure 3 reports the incidence rates, per 100,000

TABLE 1 - Cases of bacterial meningitis by year and agent - 2000-2006.

Year of notification	Invasive meningococcal disease	Invasive pneumococcal disease	Bacterial meningitis HIB	Bacterial meningitis other agent	Bacterial meningitis not ID	Overall total
2000	51	61	6	38	62	218
2001	53	64	4	36	53	210
2002	56	67	8	37	51	219
2003	100	91	5	52	63	311
2004	78	91	6	53	39	267
2005	94	65	14	75	44	292
2006	49	104	6	99	32	290
Total	481	543	49	390	344	1807

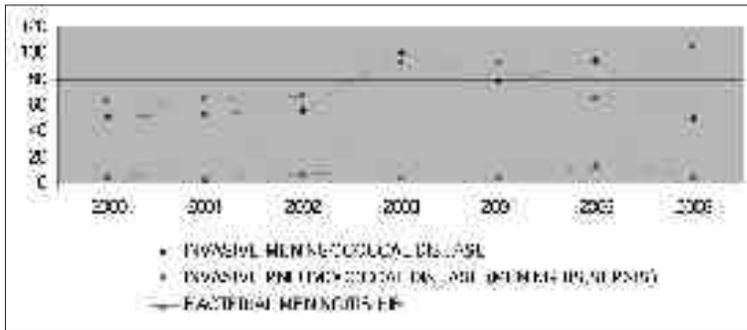


FIGURE 1 - Cases of meningitis/sepsis from principal agents – 2000-2006.

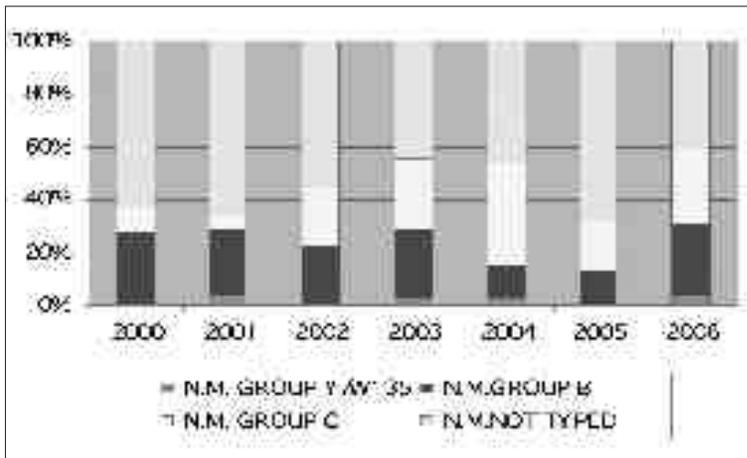


FIGURE 2 - Percentage breakdown by serogroups of meningitis/meningococcal sepsis.

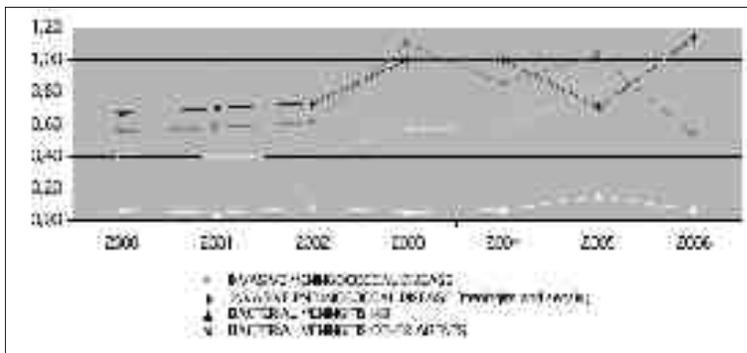


FIGURE 3 - Annual incidence rates per 100000 inhabitants of meningitis/sepsis from principal agents.

inhabitants, of the main clinical pictures. The values display a stable trend in the seven years considered, with a tendency to increase for the forms from *Streptococcus pneumoniae* and other bacterial agents.

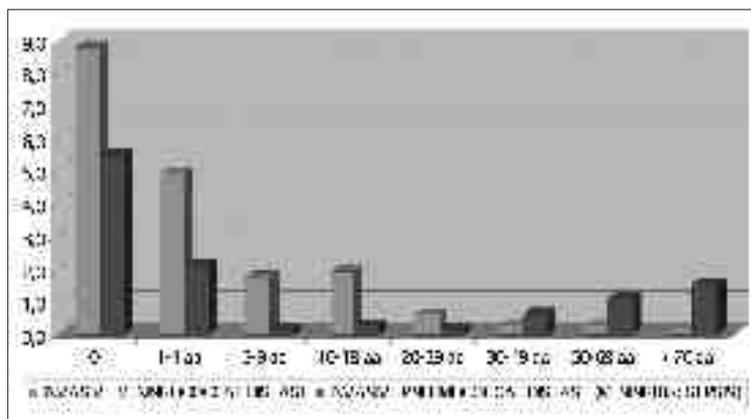
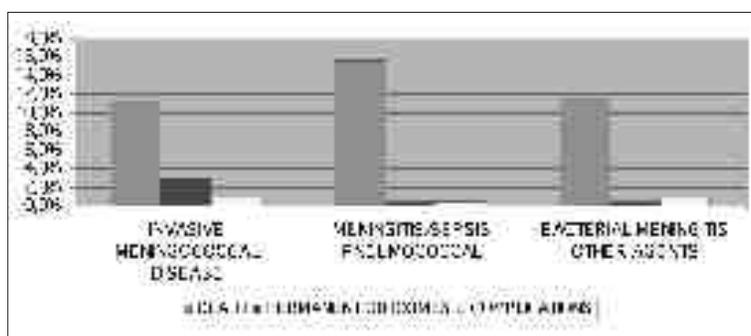
Considering the incidence rates by age group (Figure 4), the data in the literature are confirmed, with *Neisseria meningitidis* prevalent up to 20 years of age and *Streptococcus pneumoniae* with high values, somewhat below *Neisseria meningitidis*, in the first five years and in adults over the age of 50.

Table 2 and Figure 4 respectively represent the absolute number of cases, divided by age class, and relative rate of incidence.

The examination of the cases from *Neisseria meningitidis*, *Streptococcus pneumoniae*, other agents from the standpoint of the outcome (Figure 5) shows that the overall mortality, evaluated on the cases of the entire period, places itself at values in the range of what is foreseen in the literature; the mortality in patients from 0 to 4 years is 7% for the forms from meningococcus and 10.8% from pneumococcus.

TABLE 2 - Number of cases in 2000-2006 period divided by age and agent.

Age	Invasive meningococcal disease	Invasive pneumococcal disease (meningitis; sepsis)
0	53	33
1-4 aa	115	50
5-9 aa	48	4
10-19 aa	108	15
20-29 aa	46	13
30-49 aa	57	122
50-69 aa	41	178
>70 aa	13	128

FIGURE 4 - Average annual incidence rates by age group of meningitis/sepsis from *Neisseria meningitidis* and *Streptococcus pneumoniae*.FIGURE 5 - Percentage of severe outcome from *Neisseria meningitidis*, *Streptococcus pneumoniae*, other agents.

DISCUSSION

The problem of bacterial meningitis, especially in infancy, has taken on notable social relevance in Italy in the last decade, also in view of greater availability of specific vaccines, which

for the health authorities poses the obligation of attentive examination of the epidemiological data and the consequent impact of different vaccination strategies.

Neisseria meningitidis and *Streptococcus pneumoniae* are the main causes of bacterial menin-

gitis, after the reduction of the cases due to *Haemophilus influenzae* type B as a result of the introduction of conjugate vaccines, of the cases from *Listeria* thanks to the efforts made to reduce food contamination, and of the cases from *Streptococcus* B for the use of intrapartum prophylaxis in screened women (Harrison, 2006). Invasive meningococcal disease, presenting itself exclusively with forms of meningitis and sepsis, is well known: in the United States it has an incidence of approximately 0.5-1.1/100,000, while in Europe, according to the latest EU-IBIS report (Ramsay *et al.*, 2005), the average rate for the 1999-2004 period is 1.64 per 100,000, with a range from 0.18 to 11.86.

In Europe and in North America, serogroups B, C and Y predominate (American Academy of Pediatrics, 2005); the proportion of infections due to *Neisseria meningitidis*- serogroup C in Europe varies from 6 to 56%, with a resulting difference in the incidence (range 0.05-3.71/100,000) (Schrauder *et al.*, 2006). Naturally, the European epidemiological profile has undergone profound modifications as a result of the impact of the specific vaccine, widely introduced in the countries that, prior to 1999, reported the highest rates (EU-IBIS Network, 2006).

The mortality rate reported in the literature is 10%-14%, which reaches 20% between the ages of 1 and 4 years and 25% between the ages of 5 and 14 (Michael *et al.*, 2005). The EU-IBIS report indicates estimated mortality percentages that range from 6.9% in 1999 to 7.2% of 2004. In Italy the incidence is around three times lower than the European average, with levels constant in the last seven years. Examination of the available data from 1994 to 2002 shows that serogroup B has always clearly predominated over serogroup C; however, since 2002 there has been a steep change in the C/C+B ratio: from 25% in 2001 the ratio rose to 40% in 2002, 42.9% in 2003, and 58.66% in 2004 (ISS, 2006). The data for Lombardy Region, albeit with significant variability in the various years, confirm incidence rates in line with the national average and, therefore, lower than those of European countries that have introduced mass vaccination for newborns.

Epidemiological study of invasive pneumococcal disease is more complex on account of the dif-

ferent clinical forms that, for what regards Italy, have not yet been put under surveillance.

Limiting ourselves therefore to meningitis in order to have more homogeneous data, a recent systematic review (Jefferson *et al.*, 2006) indicates that in Western Europe the incidence of meningitis from pneumococcus is 8 to 9 cases per 100,000 children below two years of age. The most recent surveillance report on bacterial meningitis (European Bacterial Meningitis Surveillance Project, 2002) reports the incidence of pneumococcal meningitis in the general population, relative to the years 1999-2000, of nine European countries, with rates varying from 0.07 per 100,000 for Poland to 1.06 for Holland. On the basis of the data of the surveillance system on bacterial meningitis (ISS, 2006), the average rate of incidence of pneumococcal meningitis, in the 2000-2004 period, is 0.4 cases per 100,000 inhabitants; in the first year of life the incidence is just over 4 cases per 100,000. The regional data display a slightly higher level than the national average but in any case well below the European mean, both in the general population and in children younger than two years of age.

Epidemiological study of bacterial meningitis susceptible to vaccination proves itself necessary both prior to the implementation of a universal offering and subsequently, in order to monitor the positive effects and possible impacts on the bacterial ecology (Pebody, 2006).

The analysis conducted on the statistics available in our region indicates the need for further study, especially from the qualitative standpoint: typing of serogroups and serotypes is indispensable for careful monitoring of the phenomenon of bacterial meningitis.

The incidence of invasive meningococcal disease and of pneumococcal meningitis, which thanks to the implementation of additional information sources can be considered descriptive of the phenomenon in its entirety, displays a steady trend in Lombardy in the past few years, with incidence rates comparable to the national ones and lower than for European countries in which mass vaccination has been introduced.

Continuous monitoring of bacterial meningitis, with further study of serogroups and serotypes,

will make it possible to assess the need for putting new vaccination strategies in place with the active offering of specific vaccines aimed at achieving coverage percentages that ensure a real benefit to the public.

REFERENCES

- AMERICAN ACADEMY OF PEDIATRICS. (2005). Prevention and control of meningococcal disease: recommendations for use of meningococcal vaccine in paediatric patients. *Committee on Infectious Disease. Pediatrics* **116**, 496-505.
- EUROPEAN BACTERIAL MENINGITIS SURVEILLANCE PROJECT. Surveillance of Bacterial Meningitis in Europe 1999/2000, February 2002.
- EU-IBIS NETWORK. (2006). Invasive *Neisseria meningitidis* in Europe 2003/2004. *Health Protection Agency*, London.
- HARRISON, L.H. (2006). Prospects for vaccine prevention of meningococcal infection. *Clinical Microbiol Reviews* **19**, 142-164.
- ISTITUTO SUPERIORE DI SANITÀ (2006). Meningiti batteriche: sintesi dei dati raccolti attraverso il sistema di sorveglianza.
- JEFFERSON, J., FERRONI, E., CURTALE, F., GIORGI ROSSI, P., BORGIA, P. (2006). *Streptococcus pneumoniae* in Western Europe: serotype distribution and incidence in children less than 2 years old. *Lancet Infectious Diseases*, **6**, 405-410.
- MICHAEL, E., PICHICHERO, M.D. (2005). Meningococcal conjugate vaccine in adolescents and children. *Clin Pediatr* **44**, 479-489.
- PEBODY, R.G., HELLEBRAND, W., D'ANCONA, F., RUUTU, P. (2006). Pneumococcal disease surveillance in Europe Eurosurveillance. **11**, 171-177.
- RAMSAY A., CHANDRA M., TROTTER C. Epidemiology and surveillance of meningococcal disease in Europe: collaboration between EU-IBIS and EU-MenNet, 8th EMGM Meeting, Royal College of Surgeons Ireland, Dublin, 7th-9th September 2005.
- SCHRAUDER A, CLAUS H, ELIAS J, VOGEL U, HAAS W, HALLENBRAND W. (2006). Capture-recapture analysis to estimate the incidence of invasive meningococcal disease in Germany, 2003. *Epidemiol Infect* **29**, 1-8.