

# Epidemiology of bacterial meningitis among children in Brazil, 1997-1998\*

## Epidemiologia de meningites bacterianas entre crianças no Brasil, 1997 a 1998

Débora PL Weiss, Paul Coplan and Harry Guess

Department of Epidemiology, Merck Sharp & Dohme Research Laboratories, West Point, Pennsylvania, USA

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### Keywords

Meningitis, bacterial, epidemiology.<sup>#</sup>  
Population surveillance.<sup>#</sup> Incidence.  
Retrospective studies. Communicable diseases. *Haemophilus* vaccines.  
Meningitis, bacterial, etiology.  
Meningitis, bacterial, therapy.

### Abstract

#### Objective

To document the incidence and the descriptive epidemiology of bacterial meningitis among individuals under age 20 in a geographically defined region in Brazil during the two-year period immediately preceding the introduction of *Haemophilus influenzae* type b (Hib) vaccines into the national immunization program of Brazil.

#### Methods

Population-based epidemiological study of all cases of bacterial meningitis reported among residents of Campinas, Brazil, under age 20 (n=316,570) during the period of 1997-98, using comprehensive surveillance records compiled by the Campinas Health Department from cases reported among hospital inpatients, outpatients, emergency room visits, death certificates, and autopsy reports.

#### Results

The incidence of bacterial meningitis (n=274) was 334.9, 115 and 43.5 cases/10<sup>5</sup> person-years (pys) for residents of Campinas under age 1, 5 and 20, respectively. All cases were hospitalized, with an average length of stay of 12 days. Documented prior antibiotic use was 4.0%. The case-fatality rate of bacterial meningitis in individuals under age 20 was 9% (24/274) with 75% of deaths occurring in children under the age of five. The incidence of Hib meningitis (n=26) was 62.8 and 17 cases/10<sup>5</sup> pys in children age <1 and <5, respectively.

#### Conclusions

The incidence of Hib meningitis in children under the age of 5 in Campinas during 1997-98 was similar to that reported in the US, Western Europe, and Israel prior to widespread Hib vaccine use in those regions. This study provides a baseline for later studies to evaluate changes in the etiology and incidence of bacterial meningitis in children after introduction of routine Hib vaccination in Brazil.

### Descritores

Meningite bacteriana, epidemiologia.<sup>#</sup>  
Vigilância da população.<sup>#</sup> Incidência.  
Estudos retrospectivos. Doenças transmissíveis. Vacinas anti-*haemophilus*. Meningite bacteriana, etiologia. Meningite bacteriana, terapia.

### Resumo

#### Objetivo

Documentar a incidência e a epidemiologia descritiva de meningites bacterianas entre pessoas com idade inferior a 20 anos em uma região geográfica definida do Brasil. O período foi de dois anos, imediatamente anterior à introdução da vacina contra *Haemophilus influenzae* tipo b (Hib), no Programa Nacional de Imunização do Brasil.

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### Correspondence to:

Débora PL Weiss, MS, RPh  
Merck & Co., Inc.  
10 Sentry Pkwy, Mail Stop, BL 1-7  
Blue Bell, PA 19422, USA  
E-mail: debora\_petersonleite@merck.com

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### **Métodos**

*Estudo epidemiológico populacional dos casos de meningites bacterianas notificados entre residentes em Campinas, SP, Brasil, com idade inferior a 20 anos (n=316.570), entre 1997 e 1998. Baseia-se em dados de notificação da vigilância epidemiológica da Secretaria Municipal de Saúde de Campinas, relatados entre casos provenientes de pacientes hospitalizados, atendimento em pronto-socorros, certificados de óbito, autópsias ou atendimentos em ambulatórios.*

### **Resultados**

*A incidência de meningites bacterianas (n=274) foi de 334,9; 115 e 43,5 casos por 10<sup>5</sup> pessoas-ano entre residentes, em Campinas, com idade inferior a 1,5 e 20 anos, respectivamente. Em todos os casos houve hospitalização com uma média de permanência no hospital de 12 dias. O uso prévio de antimicrobianos notificado foi de 4,0%. A taxa de mortalidade total devida a meningites bacterianas entre pessoas com idade inferior a 20 anos foi de 9% (24/274), com 75% das mortes ocorrendo entre crianças com idade inferior a 5 anos. A incidência de meningites causadas por Haemophilus influenzae tipo b (Hib) (n=26) foi de 62,8 e 17 casos por 10<sup>5</sup> pessoas-ano em crianças com idade inferior a 1 e 5 anos, respectivamente.*

### **Conclusões**

*A incidência e a epidemiologia descritiva de meningites causadas por Haemophilus influenzae tipo b (Hib), entre crianças com idade inferior a 5 anos, em Campinas, SP, Brasil, durante o período de 1997 a 1998, foram semelhantes às relatadas pelos Estados Unidos, Europa Ocidental e Israel no período anterior ao extenso uso da vacina contra o Haemophilus influenzae tipo b nessas regiões. O estudo fornece valores de referência para outras pesquisas posteriores que avaliem mudanças na etiologia e na incidência de meningites bacterianas em crianças, depois da introdução de vacinação rotineira contra Haemophilus influenzae tipo b, no Brasil.*

## **INTRODUCTION**

Bacterial infections remain an important cause of morbidity and mortality in children despite the availability of highly effective antibiotics. In many countries where vaccination against *Haemophilus influenzae* type b (Hib) disease is not yet widely adopted, this organism is responsible for a substantial fraction of the cases of meningitis in children under five years of age.<sup>4,16,20,23</sup> In the United States, before the era of Hib vaccines, more than 70% of bacterial meningitis among children less than five years old was attributable to Hib.<sup>19</sup> Published data from the U.S. show that the incidence of Hib meningitis among children under 5 years of age decreased from 25 cases per 10<sup>5</sup> in 1984, to less than 2.5 cases per 10<sup>5</sup> in 1993 after the introduction of conjugate vaccines since 1988.<sup>21</sup>

In Brazil, several studies have been performed over the past ten years evaluating the etiology, treatment, or outcomes of bacterial meningitis in newborns and children.<sup>2,5,7,10,14,18</sup> However, only limited information on the etiology, incidence and treatment outcomes of bacterial meningitis in geographically defined regions are available. The present study was conducted to provide an overview of the etiology, incidence rates, antimicrobial use, and outcome of reported bacterial meningitis cases among children in Campinas, SP,

Brazil, during a two-year period immediately preceding the implementation of the Hib vaccination as a part of the national immunization program in July 1999. The information may serve as a baseline for further studies to evaluate the effectiveness of the Hib vaccination program.

## **METHODS**

### **Geography and study population**

In 1998, Campinas, in southeast Brazil, had 930,659 residents of which 316,570 were under 20 years of age (50.8% male) and 77,150 were under 5 years of age (51.3% male).\*

### **Epidemiological surveillance**

The "Secretaria de Saúde do Município de Campinas" (Campinas Health Department) was in charge of the epidemiological surveillance. There was a mandatory requirement for all cases of meningitis to be reported to the Campinas Health Department. All reports of meningitis arising from hospital inpatients, emergency room patients, death certificates, autopsies, outpatients, and telephone calls were recorded in a standardized meningitis abstract form. Information collected included: demographics, date of onset, previous contact with similar cases, type of contact, clinical manifestations,

\*Personal communication: Seade (Sistema Estadual de Análises de Dados Estatísticos); <http://www.seade.gov.br>

laboratory data, final diagnosis, criteria used to define diagnosis, hospitalization, prior antimicrobial use, antimicrobial treatment, and outcome. The notifications were regionally computerized and submitted to the coordinating center (CoVISA – Coordenadoria de Vigilância e Saúde, Health and Surveillance Coordinating Center), where the information was centralized into the notification system database (SINAN – Sistema de Informações de Agravos de Notificação).

### Data collection

The Campinas Health Department provided a copy of the SINAN database with data on meningitis for this study. Respecting standard ethical procedures, this study reviewed all reported cases of bacterial meningitis reported in Campinas among individuals under 20 years of age, notified from January 1, 1997 to December 31, 1998. All cases whose residence was Campinas, but who were eventually seen by a health professional outside the city were reported by this system, since the complete investigation process and control measures were responsibility of the Campinas Health Department. Cases whose residence was outside Campinas were excluded. Sex, age, date of onset, laboratory data, final diagnosis, criteria used to define diagnosis, hospitalization, prior antimicrobial use, antimicrobial treatment, and outcome were extracted, reviewed and analyzed.

### Case definition and diagnostics

The diagnostic criteria for bacterial meningitis included at least one of the following:

1. Cerebral spinal fluid (CSF) positive bacterial culture.
2. CSF positive Gram's stain with negative cultures (i.e., a gram stain revealing only gram-negative diplococci was classified as *Neisseria meningitidis* even if CSF cultures remained negative) in the presence of clinical manifestations.

3. Positive bacterial culture or Gram's stain from blood, petechial lesion or sputum in the presence of clinical manifestations of meningitis.
4. Positive antigen detection with latex agglutination or counterimmunoelectrophoresis (CIE) in the CSF or blood.
5. CSF profile demonstrating significant cytochemical changes such as white blood cells  $\geq 1,000/\text{mm}^3$ , neutrophils  $\geq 60\%$ , protein  $\geq 100 \text{ mg/dL}$  and glucose  $\leq 50 \text{ mg/dL}$  in the presence of clinical manifestations of meningitis.

### Statistical analysis

Two years of collected data (1997-1998) were analyzed for this study. Overall incidence and age-specific incidence rates were calculated in cases per  $10^5$  pys (person-years) according to the Campinas population during the two-year period. Tests of statistical significance were performed using chi-square, Fisher's exact test, *t*-Test and ANOVA and 95% confidence intervals were computed when applicable.

## RESULTS

### Epidemiology and etiology

Over the two-year period 274 cases of bacterial meningitis were found. *N. meningitidis* was the most common cause of bacterial meningitis (19.3%), followed by Hib, (9.5%), *Streptococcus pneumoniae* (*S. pneumoniae*) (7.7%), and other etiologic agents (8.0%). No specific organisms were isolated in 152 cases (55.5%). Table 1 shows the diagnostic criteria were used to identify the different organisms. Most of the Hib cases were identified by antigen detection with latex agglutination in the CSF.

### Sex and age distribution

One hundred and sixty cases were male (58.4%).

**Table 1** - Diagnostic criteria used to identify the different etiologic organisms.

| Diagnostic criteria   | <i>H influenzae</i> type b<br>(%) (n=26) | <i>N meningitidis</i><br>(%) (n=53) | <i>S pneumoniae</i><br>(%) (n=21) | Other etiology<br>(%) (n=22) | Unspecified<br>(%) (n=152) |
|---|--|-------------------------------------|-----------------------------------|------------------------------|----------------------------|
| CSF culture   | 88.5                                     | 64.2                                | 85.7                              | -                            | -                          |
| Blood culture   | -  | 15.0                                | -                                 | -                            | -                          |
| Detection of antigen with latex agglutination in the CSF                | 96.2                                     | 3.8                                 | 14.3                              | -                            | -                          |
| Detection of antigen with counterimmunoelectrophoresis (CIE) in the CSF | 3.8                                      | 3.8                                 | -                                 | -                            | -                          |
| Gram stain revealing only gram-negative diplococci                      | -  | 13.2                                | -                                 | -                            | -                          |
| CSF and/or blood culture  | -  | -                                   | -                                 | 100                          | -                          |
| CSF positive bacterial Gram's stain                                     | -  | -                                   | -                                 | -                            | 5.3                        |
| CSF, blood or both positive bacterial culture                           | -  | -                                   | -                                 | -                            | 9.2                        |
| Alterations of CSF profile in the presence of clinical manifestations   | -  | -                                   | -                                 | -                            | 85.5                       |

CSF=Cerebral spinal fluid

The percent of cases that were male with Hib, *N. meningitidis*, and *S. pneumoniae* were 53.8%, 54.7%, and 57.1% respectively. Sixty-four percent of the cases occurred in children under five years old and 35% in children less than one year old (Table 2). The median age among all bacterial meningitis cases was two years (range 3 days – 19 years). All Hib cases occurred in children less than five (69.2% in children under one). Of all *N. meningitidis* cases, 69.8% were in children less than five (30.2% in children under one). Regarding *S. pneumoniae* cases, 61.9% were in children less than five (42.9% in children under one). For other etiologies, 72.7% of the cases were in children less than five (54.5% in children under one). And for unspecified cases, 58.6% were in children less than five (27% under one).

**Other etiologic agents**

Other reported etiological agents included: *P. aeruginosa* (4 cases, age 7 days-5 months), *K. pneumoniae* (4 cases, age 3-7 months), and 14 cases with a variety of organisms typical of skin contaminants.

**Incidence rates**

The incidence rate ratio of males to females for

unspecified bacterial meningitis was 1.6:1 (p<0.01), 95% CI (1.1, 2.2) and for all bacterial meningitis was 1.4:1 (p<0.01), 95% CI (1.1, 1.7). The male to female incidence rate ratios for *N. meningitidis*, Hib, *S. pneumoniae*, and other etiologies were 1.2:1, 95% CI (0.7, 2.0), 1.1:1, 95% CI (0.5, 2.5), 1.3:1, 95% CI (0.6, 3.1) and 1:1, 95% CI (0.4, 2.2), respectively (not significant).

From 1997 to 1998 the overall incidence of bacterial meningitis increased by 61%, from 33.2 cases/10<sup>5</sup> pys to 53.4 cases/10<sup>5</sup> pys (Table 3). For Hib, the incidence rates overall and for children <5 were stable. The incidence rate of Hib for children under age one decreased by 62%. The incidence rates for *N. meningitidis*, *S. pneumoniae*, other etiologies, and unspecified meningitis increased across nearly all age groups and overall, ranging from an increase of 32% for *N. meningitidis* to 118% for other etiologies.

**Morbidity and mortality**

There were 24 deaths among the population studied. The total case fatality rate (CFR) was 8.8%. Seventy-five percent of deaths occurred in children less than five years old and 45.8% occurred in children less than one year old. There were four deaths among the Hib cases (CFR=15.4%, 100% <5 years old, 50% <1

**Table 2** - Age-specific incidence rates\* by category of bacterial meningitis among children in Campinas, SP, Brazil, over a two-year period (1997-1998).

| Age groups | <i>H influenzae</i> type b |      | <i>N meningitidis</i> |      | <i>S pneumoniae</i> |      | Other etiology |      | Unspecified |       | Total |       |
|------------|----------------------------|------|-----------------------|------|---------------------|------|----------------|------|-------------|-------|-------|-------|
|            | N                          | Rate | N                     | Rate | N                   | Rate | N              | Rate | N           | Rate  | N     | Rate  |
| up to 2m   | 3                          | 38.3 | 2                     | 25.5 | 1                   | 12.8 | 7              | 89.3 | 20          | 255.2 | 33    | 421.1 |
| 3 to 5m    | 6                          | 56.8 | 9                     | 85.2 | 3                   | 28.4 | 3              | 28.4 | 12          | 113.6 | 33    | 467.5 |
| 6 to 11m   | 9                          | 65.4 | 5                     | 39.3 | 5                   | 39.3 | 2              | 14.5 | 9           | 65.4  | 30    | 217.8 |
| 1y         | 6                          | 20.9 | 8                     | 27.9 | 2                   | 7.0  | 2              | 7.0  | 8           | 27.9  | 26    | 90.6  |
| 2y         | 1                          | 3.5  | 5                     | 17.3 | -                   | -    | -              | -    | 10          | 34.6  | 16    | 55.3  |
| 3y         | -                          | -    | 6                     | 20.4 | -                   | -    | -              | -    | 12          | 40.8  | 18    | 61.2  |
| 4y         | 1                          | 3.4  | 2                     | 6.7  | 2                   | 6.7  | 2              | 6.7  | 13          | 43.7  | 20    | 67.3  |
| 5 to 9y    | -                          | -    | 7                     | 4.7  | 1                   | 0.7  | 3              | 2.0  | 46          | 30.8  | 57    | 38.2  |
| 10 to 19y  | -                          | -    | 9                     | 2.7  | 7                   | 2.1  | 3              | 0.9  | 22          | 6.6   | 41    | 12.4  |
| Total      | 26                         | 4.1  | 53                    | 8.4  | 21                  | 3.3  | 22             | 3.5  | 152         | 24.1  | 274   | 43.5  |

\* Expressed as cases per 10<sup>5</sup> pys

**Table 3** - Age-specific incidence rates\* of bacterial meningitis among children in Campinas, SP, Brazil, by year.

| Rates by age group | <i>H influenzae</i> type b |      | <i>N meningitidis</i> |      | <i>S pneumoniae</i> |      | Other etiology |      | Unspecified |       | Total |       |
|--------------------|----------------------------|------|-----------------------|------|---------------------|------|----------------|------|-------------|-------|-------|-------|
|                    | 1997                       | 1998 | 1997                  | 1998 | 1997                | 1998 | 1997           | 1998 | 1997        | 1998  | 1997  | 1998  |
| <1y                |                            |      |                       |      |                     |      |                |      |             |       |       |       |
| N                  | 13                         | 5    | 8                     | 8    | 3                   | 6    | 2              | 10   | 18          | 23    | 44    | 52    |
| Rate               | 91.3                       | 34.6 | 56.2                  | 55.4 | 21.1                | 41.6 | 14.1           | 69.3 | 126.5       | 159.4 | 309.1 | 360.3 |
| <5y                |                            |      |                       |      |                     |      |                |      |             |       |       |       |
| N                  | 13                         | 13   | 16                    | 21   | 4                   | 9    | 5              | 11   | 33          | 56    | 69    | 107   |
| rate               | 17.1                       | 16.9 | 21.0                  | 27.2 | 5.2                 | 11.7 | 6.6            | 14.3 | 43.3        | 72.6  | 90.5  | 138.7 |
| 5-19y              |                            |      |                       |      |                     |      |                |      |             |       |       |       |
| N                  | 0                          | 0    | 7                     | 9    | 4                   | 4    | 2              | 4    | 21          | 42    | 39    | 62    |
| rate               | 0                          | 0    | 3.0                   | 3.8  | 1.7                 | 1.7  | 0.8            | 1.7  | 8.7         | 17.5  | 15.0  | 25.9  |
| Total              |                            |      |                       |      |                     |      |                |      |             |       |       |       |
| n                  | 13                         | 13   | 23                    | 30   | 8                   | 13   | 7              | 15   | 54          | 98    | 105   | 169   |
| rate               | 4.1                        | 4.1  | 7.2                   | 9.5  | 2.5                 | 4.1  | 2.2            | 4.8  | 17.0        | 31.0  | 33.2  | 53.4  |
| % Δ**              | 0%                         |      | 32%                   |      | 64%                 |      | 118%           |      | 82%         |       | 61%   |       |

\*Expressed as cases per 10<sup>5</sup> pys

\*\*\*Δ refers to percent change in the total rates from 1997 to 1998.

year old); nine among *N. meningitidis* cases (CFR=15%, 66.7% <5 years old, 22.2% <1 year old); two among *S. pneumoniae* meningitis (CFR=9.5%, 100% <1 year old); two among other etiologies (CFR=9.1%, 50% for ages 1-4 years old) and seven among unspecified bacterial meningitis (CRF=4.6%, 71.4% <1 year old). Data on death were missing for 15 cases (5.5%).

Among the 252 survivors, 16 (5.8%) had sequelae: three among Hib cases (11.5%, 100% under five years old, 33.3% under one year old); five among *N. meningitidis* cases (9.4%, 100% under five years old, 40% under one year old); three among *S. pneumoniae* cases (14.3%, 66.7% under one year old); and five among unspecified cases (3.3%, 40% under one year old). Data on sequelae were missing for 84 cases (30.7%). The type of sequelae was not recorded.

### Hospitalization

The sum of hospitalization patient-days for all cases was 3,374. The total average length of stay was 12.4 days (SD 9.0, range 1-64). Table 4 shows the average length of stay (ALOS) and ranges of stay for each of the types of meningitis. The difference between these type-specific average lengths of stay was not statistically significant.

### Prior antimicrobial use

Eleven cases (4.0%) had documented prior antimicrobial use.

**Table 4** - Hospitalization of cases of bacterial meningitis among children in Campinas, SP, Brazil, from 1997-1998 by etiologic agent.

| Etiologic agents           | ALOS* | Hospitalization SD | R    | %    |
|----------------------------|-------|--------------------|------|------|
| <i>H influenzae</i> type b | 15.9  | 10.1               | 1-46 | 100  |
| <i>N meningitidis</i>      | 12.1  | 8.6                | 1-45 | 100  |
| <i>S pneumoniae</i>        | 15.6  | 12.4               | 3-62 | 100  |
| Other etiology             | 14.4  | 11.8               | 1-52 | 95.5 |
| Unspecified                | 11.1  | 8.6                | 1-64 | 92.8 |

\*ALOS: average length of stay in days

One hundred and twenty-six cases (46.0%) documented no prior antimicrobial use; for the other 137 cases (50.0%) information was not available.

### Antimicrobial treatment

Antimicrobial treatment was recorded for 67.5% of the cases, including 88.5% of the Hib cases. Ampicillin plus chloramphenicol was the most widely used antimicrobial treatment. Cephalosporins were the second most widely used antimicrobial treatment for all agents, except *S. pneumoniae*, for which penicillin was the second most widely used drug (19.0%). Table 5 provides a more detailed listing by etiologic agent and age group of the various combinations of antibiotics used.

### DISCUSSION

Hib represented a smaller percent of bacterial meningitis among children in Campinas (9.5%) than in previous studies in Bahia, Brazil (23.0% and 26.0%),<sup>2,14</sup> and in several studies from different countries with the highest percent of 47.2% and 51.7% in Ecuador

**Table 5** - Most common received antimicrobial treatments for bacterial meningitis by etiologic agents and age groups among children in Campinas, SP, Brazil, over 1997-1998.

| Antimicrobial treatment by category of bacterial meningitis | Percent of use by age groups |                   |                    | Total % (n=274) |
|---|------------------------------|-------------------|--------------------|-----------------|
|   | <1 y % (n=96)                | 1 to 4 y % (n=80) | 5 to 19 y % (n=98) |                 |
| <i>H influenzae</i> type b                                  | n=18                         | n=8               | -                  | n=26            |
| Ampicillin+ Chloramphenicol                                 | 38.9                         | 60.0              | -                  | 50.0            |
| Ampicillin+Cephalosporin                                    | 27.8                         | -                 | -                  | 11.5            |
| Cephalosporin   | 11.1                         | 20.0              | -                  | 15.4            |
| <i>N meningitidis</i>                                       | n=16                         | n=21              | n=16               | n=53            |
| Penicillin  | 6.3                          | -                 | 25.0               | 9.4             |
| Ampicillin  | 12.5                         | 4.8               | 18.8               | 11.3            |
| Ampicillin+Chloramphenicol                                  | 31.3                         | 33.3              | 6.3                | 24.5            |
| Cephalosporin   | -                            | 28.6              | 6.3                | 13.2            |
| <i>S pneumoniae</i>   | n=9                          | n=4               | n=8                | n=21            |
| Penicillin  | -                            | -                 | 50.0               | 19.0            |
| Ampicillin  | 22.2                         | -                 | 12.5               | 14.3            |
| Ampicillin+Chloramphenicol                                  | 22.2                         | 50.0              | 12.5               | 23.8            |
| Other etiology  | n=12                         | n=4               | n=6                | n=22            |
| Penicillin  | -                            | -                 | 16.7               | 4.5             |
| Penicillin+Cephalosporin                                    | -                            | 25.0              | -                  | 4.5             |
| Penicillin+Other  | -                            | -                 | 16.7               | 4.5             |
| Ampicillin+Chloramphenicol+Other                            | -                            | 25.0              | -                  | 4.5             |
| Cephalosporin   | 8.3                          | 25.0              | 16.7               | 13.6            |
| Other   | 25.2                         | 25.0              | 16.7               | 22.7            |
| Unspecified   | n=41                         | n=43              | n=68               | n=152           |
| Penicillin  | 2.4                          | -                 | 23.5               | 10.5            |
| Ampicillin  | 2.4                          | 4.6               | 10.3               | 5.9             |
| Ampicillin+Chloramphenicol                                  | 14.6                         | 41.9              | 14.7               | 23.0            |
| Cephalosporin   | 9.8                          | 16.3              | 11.7               | 13.2            |
| Other   | 7.3                          | -                 | 4.4                | 3.9             |

and China, respectively.<sup>22,23</sup> *S. pneumoniae* was observed as the primary agent in Congo<sup>13</sup> while *N. meningitidis* was ranked the first agent responsible for bacterial meningitis in this study and in recent reports from Italy (Naples), Spain and Russia.<sup>4,11,17</sup> Interpretation of these comparisons is complicated by the varying percentages of cases with unknown etiology. This percentage was higher in the present study (55.5%) than in other populations, including Seville, Spain (14.5%), and Naples, Italy (46.7%).<sup>6,17</sup>

Seasonal peaks were observed for Hib and *N. meningitidis* in this study, which were consistent with those found in other studies.<sup>11,12</sup> Sex and age distribution of cases in this study was consistent with other published studies.<sup>11-13,19,22</sup>

The incidence rate for Hib meningitis among children under 5 (17 cases per 10<sup>5</sup> pys) in this study is comparable to those found in the U.S., Israel and Western Europe before the use of Hib conjugate vaccines, or in recent reports in unvaccinated populations.<sup>3,9,12,15,20</sup> Values from Argentina revealed similar incidence rate among children younger than five.<sup>16</sup> A report from Spain (Valencia) revealed an incidence rate of 14 cases per 10<sup>5</sup> for meningitis caused by Hib among unvaccinated children under five years of age.<sup>12</sup>

The results of the study suggest that the incidence rates of bacterial meningitis increased from 1997 to 1998. In 1998, the notification system for bacterial meningitis underwent improvement. Thus, more complete notification could help explain the higher rates found for 1998. It could not be determined whether the increase in rates for all agents (except Hib) were due to better reporting, a shift in the overall number of cases (all ages) to the younger age groups (age<20), a

true change in the incidence rates, or a combination of these possible explanations.

The clinical course of bacterial meningitis may be complicated by treatment with inadequate dosing of antimicrobials. Symptoms can be temporarily suppressed and delay the diagnosis and provision of effective antibiotic therapy. Thus, poorer outcome may be associated with prior antimicrobial use. In this study the comparison of the outcomes between those with documented prior antimicrobial use versus no prior antimicrobial use was jeopardized by the small number of subjects with documented prior antimicrobial use (4%) and the large amount of under-reporting (50%). While the reported prior antimicrobial use in this study was lower than in Australia, Chile and China, 38%, 41.1% and 100%,<sup>1,8,22</sup> the validity of the comparison of outcomes is limited by potential under-reporting of prior antimicrobial use.

The incidence of Hib meningitis in children under 5 years of age in Campinas during the period immediately preceding the national Hib vaccination program is comparable to rates found in the USA, Israel, and Western Europe before the introduction of Hib conjugate vaccines. It will be of interest to see whether the dramatic declines in incidence, which occurred in those regions with widespread vaccination, will also be found in Campinas over the coming decade.

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