

Haemophilus influenzae meningitis in Sweden 1981-1983

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SUMMARY Four hundred and seventy cases of meningitis caused by *Haemophilus influenzae* in children and 30 cases in adults were identified in Sweden between 1981 and 1983. The age specific incidence in the most susceptible age group (0-4 years) was 31/100 000/year (440 cases), which is higher than previously reported from Europe. A further 30 cases were seen in children aged 5-14. The risk of developing *H influenzae* meningitis before the age of 15 was 1 in 669. There were 11 deaths (2%) and five cases of serious neurological sequelae among the children. Only 18 children (4%) had predisposing diseases. All but one of the 294 strains of *H influenzae* from children that had been serotyped were type b. Infections in adults differed from infections in children. Five of the adults died (17%), 12 had important predisposing diseases, and at least six of the infections were caused by non-typable strains. It is concluded that research into the prevention of invasive *H influenzae* infections in children should have high priority.

The incidence of *Haemophilus influenzae* meningitis in children aged less than 5 years has been comprehensively studied in the United States. The age specific incidence in this group varied between 19 and 71/100 000/year in the general population,¹⁻³ but three groups of native Americans had high incidences: 173-409/100 000/year.^{1 4 5} The variations in incidence can be explained partly by racial and socioeconomic differences.

In contrast, little is known about the incidence of *H influenzae* meningitis in children outside North America. Two studies from England reported incidences in children less than 5 years old of only 11 and 18/100 000/year, respectively.^{6 7} In The Netherlands,⁸ Finland,⁹ and a region of Sweden,¹⁰ the incidences were 22, 27, and 27/100 000/year, respectively, in the same age group.

Even though most *H influenzae* infections occur in young children, several recent reports have shown that the organism may also be the cause of meningitis in older children and adults.^{7 9 11-13} The present study aimed to estimate the incidence and mortality of *H influenzae* meningitis in children and adults in Sweden.

Patients and methods

We attempted to identify all Swedish residents who

had *H influenzae* meningitis between 1 January 1981 and 31 December 1983. All departments of paediatrics, infectious diseases, internal medicine, and neurosurgery in Sweden were contacted about patients with *H influenzae* meningitis. Case records of these patients were examined by the authors at hospitals covering more than 20% of the population. The information from the remaining hospitals was obtained from the respective clinicians; 482 patients with *H influenzae* meningitis were identified.

Letters were then sent to all departments of clinical bacteriology and to the National Bacteriological Laboratory requesting that all patients in whom *H influenzae* had been isolated from cerebrospinal fluid should be reported to us. Because some laboratories had not kept complete records for the period being studied, this search yielded only 360 patients, 17 of whom had not been found through the hospital search. Their case records were also examined. The departments of medicolegal medicine, where patients who die outside hospital have necropsies carried out, reported an additional patient with *H influenzae* meningitis. Thus a total of 500 cases were found in 498 patients, as two patients had the disease twice at intervals of one and eight months, respectively. These episodes have been counted separately.

In 490 cases the diagnosis was confirmed by

isolation of *H influenzae* from cerebrospinal fluid and in one case by isolation of *H influenzae* from the meninges and several other organs at necropsy. The remaining nine patients all had clinical meningitis and the cerebrospinal fluid was purulent. *H influenzae* was isolated from blood in eight cases. From one, *H influenzae* type b capsular antigen was detected in the cerebrospinal fluid by coagglutination and Gram negative rods were seen on microscopy of the cerebrospinal fluid.

Four of the adult patients described here have been included in a previous report.¹¹ Sweden has three regions, one in the south with 12 counties, one in the middle with seven counties, and one in the north with five counties. Population data from the 24 counties were obtained from official statistics.¹⁴

Results

CHILDREN 14 YEARS OLD AND UNDER

The age distribution of the 470 patients who were 14 years old or younger is shown in table 1. Of the 470, 440 children (94%) were younger than 5 years old, 272 (58%) were younger than 18 months, and 17 (4%) were younger than 3 months. There were 252 boys (54%) and 218 girls (46%).

The age specific incidence in five year intervals is

Table 1 Age distribution related to serotype of isolate in 500 cases of *H influenzae meningitis*

Age	Type b	Type f	Non-typable	Unknown	Total
Months:					
0-2	8	0	0	9	17
3-5	33	0	0	22	55
6-8	42	1	0	28	71
9-11	46	0	0	13	59
12-14	23	0	0	15	38
15-17	22	0	0	10	32
18-20	18	0	0	9	27
21-23	16	0	0	10	26
Years:					
2	39	0	0	24	63
3	19	0	0	19	38
4	7	0	0	7	14
5	7	0	0	2	9
6	4	0	0	4	8
7	1	0	0	1	2
8	2	0	0	2	4
9	3	0	0	0	3
10-14	3	0	0	1	4
15-19	3	0	0	1	4
20-29	2	0	0	1	3
30-39	4	1	2	0	7
40-49	1	0	1	1	3
50-59	1	1	0	1	3
60-69	1	0	1	3	5
70-79	1	0	1	2	4
80-89	0	0	1	0	1

shown in table 2. The incidence in the most susceptible age group (0-4 years) was 31/100 000/year. The incidences in the southern, middle, and northern regions of Sweden were 27, 37, and 27/100 000/year, respectively. The incidences in the two counties with the biggest cities—Stockholm and Göteborg—were 32 and 24/100 000/year, respectively.

Serotyping of the infecting organism was performed by latex agglutination or coagglutination in 294 of the cases in children (63%). All strains but one were type b; *H influenzae* type f was isolated from a child aged 6 months with no known predisposing diseases. The serotypes of the isolates from the two children with two episodes of *H influenzae meningitis* were not known.

Only 18 children (4%) had any predisposing disease: congenital brain disease (n=10), traumatic head injury (n=4), Down's syndrome (n=3), and malignant lymphoma (n=1). One infant aged 3 months had been born at a gestational age of 30 weeks. All 17 infants aged 0-2 months were born at gestational ages of 37 weeks or more. Only one had a predisposing disease (encephalocele), and this child had a second attack of *H influenzae meningitis* eight months later.

Eleven children (including two neonates) with no known underlying diseases died. Five children developed serious neurological sequelae, such as hemiplegia, diplegia, or tetraplegia, in combination with mental retardation, blindness, or epilepsy. The mean time spent in hospital was 12 days.

PATIENTS 15 YEARS OLD AND OLDER

There were 30 adults (6% of all patients) aged between 17 and 82 years. Eleven were men and 19 women. Their ages and the serotypes of the isolates are shown in table 1. The adults differed from the children in serotype distribution, predisposing diseases, and outcome. Of the 21 strains that were

Table 2 Age specific incidence (cases/100 000/year) of *Haemophilus influenzae meningitis* in Sweden 1981-1983.

Age (years)	Mean population	Documented cases of <i>H influenzae meningitis</i>	Age specific incidence
0-4	477 461	440	30.7
5-9	530 926	26	1.6
10-14	563 927	4	0.2
0-14	1 572 314	470	10.0
15 and over	6 752 610	30	0.1
Total	8 324 924	500	2.0

serotyped, only 13 were type b, two were type f, and six were non-typable. Predisposing diseases were known in 12 adults (40%) and comprised head injury (n=11) and acute lymphatic leukaemia (n=1). Five (17%) of the adult patients died. Among those were two patients aged 29 and 36 years with type b infections and no known predisposing disease.

β lactamase producing strains

Twenty nine strains (6%) (from 12 of the 24 counties) produced *β* lactamase.

Discussion

Like all previous estimates of the incidence of *H influenzae* meningitis in children¹⁻¹⁰ the results of the present study are based on a retrospective search for patients; the true incidence of *H influenzae* meningitis in Sweden is probably higher than that reported here. Some episodes of meningitis might never have been diagnosed, and some patients might have become ill abroad.

The incidence of *H influenzae* meningitis in children aged 0-4 years in Sweden from 1981-1983 that we report (31/100 000/year) is higher than that previously reported in Europe⁶⁻¹⁰—11-27/100 000/year. The incidence in Europe seems to be similar to or somewhat lower than that reported from white middle class North American populations, and considerably lower than in North American black and American Indian populations.¹⁻⁵ The risk of developing *H influenzae* meningitis in Sweden is, according to our data, 1/669 before the age of 15 years.

The impact of invasive *H influenzae* type b disease on morbidity and mortality in children is considerable. The mortality from *H influenzae* meningitis in Sweden is 1-2%.¹⁰ The 11 fatal cases described here comprise 0.4% of all deaths (2822) in children aged 0-14 years during the same time period; the mortality reported from other countries (5-8%) is higher.⁵⁻⁷

There were five children with serious neurological sequelae. The prevalence of less severe sequelae could not be estimated in this study, but other studies have described auditory impairment, mental retardation, motor abnormalities, visual impairment, language disorders, and behavioural or psychological problems, alone or in combination, in 27-33% of survivors.²⁰⁻²² In addition children who seem to recover completely from meningitis have a lower mean intelligence quotient and perform less well than their siblings at intellectual and neurophysiological tests.^{23 24} There are also other manifestations of *H influenzae* infection,

notably epiglottitis, which in Sweden seems to be more common than *H influenzae* meningitis,²⁵ septicaemia, pneumonia, osteitis, and arthritis.

The purified *H influenzae* type b capsular polysaccharide vaccine could only have prevented 31-42% of the cases described here because it is only immunogenic in children over the age of 18 to 24 months.^{15 16} The experimental vaccines comprising the *H influenzae* type b polysaccharide conjugated to proteins are of great interest as they will probably induce immunity from the age of 3 months.¹⁷⁻¹⁹

Although *H influenzae* type b meningitis is mainly a disease of young children, the infection is also seen in adults.^{7 11-13} In the present study nine adults aged 17-55 years with no known predisposing diseases had *H influenzae* type b meningitis, indicating that some apparently healthy adults in Sweden lack protective antibodies against *H influenzae* type b. The finding of 17 infants born at term who got *H influenzae* meningitis before the age of 3 months indicates that women of childbearing age in Sweden do not always have protective amounts of *H influenzae* type b antibodies in their blood. There are many differences between *H influenzae* meningitis in children and adults. In adults the disease is more often related to predisposing diseases and the mortality is high¹¹⁻¹³; in the present study it was 17%. In older patients with predisposing diseases non-typable strains of *H influenzae* are also important pathogens as we have shown both here and previously.¹¹⁻¹³

In conclusion, research into the prevention of invasive *H influenzae* infections in children by immunisation should have a high priority because of the high incidence, the prevalence of sequelae, and the low but nevertheless important mortality.

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