

Original articles

Haemophilus influenzae type b disease in the Oxford region

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SUMMARY A prospective survey of children in the Oxford region identified 200 cases of systemic *Haemophilus influenzae* type b disease in the first three and a half years of the study. The annual incidence in children less than 5 years of age was 33.4/100 000. This represents a cumulative incidence of one systemic infection in 600 children before their 5th birthday. The mortality was 5.0%. The risk of *H influenzae* type b meningitis was one in 850 with a mortality of 5.6%, and substantial morbidity among survivors.

From the total live birth rate, about 1300 cases of systemic *H influenzae* type b disease, over 900 cases of *H influenzae* type b meningitis, and 65 deaths would be predicted annually in children in the United Kingdom.

Haemophilus influenzae type b is a leading cause of bacterial meningitis in children in the United Kingdom.¹ It causes epiglottitis and less commonly may present as cellulitis, septic arthritis, pneumonia, empyema, or pericarditis.^{2,3} Vaccines for *H influenzae* type b that are protective in infancy are now at an advanced stage of development.

No comprehensive data exist for the United Kingdom from which reliable estimates of incidence, mortality, and morbidity can be made for these diseases. A survey in an inner city area of Birmingham from 1973-84 estimated the incidence of severe *H influenzae* infection to be at least one in 950 children,⁴ which is equivalent to an annual incidence of 21/100 000 children aged less than 5 years. Reports for 1984-7 to the Communicable Disease (Scotland) Unit indicate an annual incidence of systemic *H influenzae* type b disease of 28/100 000 children aged less than 5 years.⁵ Laboratory data for Gwynedd, Wales from 1981-4 yield an annual incidence of 45.2/100 000 children aged less than 5 years.⁶ These are higher than previous estimates from the United Kingdom^{7,8} and approach the incidence figures for children aged less than 5 years from recent American series (Minnesota, 1982-4: 68/100 000/year⁹ and Monro County, New York, 1982-3: 64/100 000/year¹⁰).

In order to provide accurate epidemiological information before the introduction of any intervention, a prospective survey was established in the Oxford region in 1985, and we report data from the first three and a half years.

Patients and methods

From 1 January 1985, any clinical isolates of *H influenzae* from normally sterile body fluids (for example, blood, cerebrospinal fluid, or joint aspirates) obtained from children under 10 years of age have been sent with brief clinical details from the microbiology laboratories throughout the Oxford region to the Public Health Laboratory Service Laboratory, John Radcliffe Hospital, Oxford. Serotyping, biotyping, and antibiotic sensitivity have been confirmed and thus only data on bacteriologically proved systemic *H influenzae* disease has been included. Isolates from children who have died outside hospital (for example, from unexpected infant deaths undergoing postmortem examination by the coroner) have been included. We have included all cases admitted within the region even if only temporarily resident, but have not included children from the region admitted elsewhere. The geographically defined denominator population was

2 438 000, of which 166 800 were children under 5 years of age according to data from the Office of Population Census and Survey for 1986. The study is still in progress and the data presented here include all cases up to 30 June 1988.

All 35 survivors of meningitis from the first year of surveillance were reviewed two years later by examination of their medical records and by contacting their general practitioners, health visitors, and community paediatricians. This additional study aimed to identify unequivocal serious morbidity among survivors.

The studies were approved by the Central Oxford Research Ethics Committee.

Results

A total of 219 cases of systemic disease caused by *H influenzae* were recorded in a three and a half year period in children less than 10 years old. 200 (91%) were due to serotype b organisms, the rest being due to non-typable (non-capsulated) strains. No other serotypes were implicated as systemic pathogens.

Of the *H influenzae* type b infections, 195 (97.5%) occurred in children under 5 years and 138 (69%) in children under 2 years of age. Only 20 (10%) occurred in children under 6 months, suggesting that this age group is relatively protected. The estimated annual incidence for systemic *H influenzae* type b disease was 33.4/100 000 children aged less than 5 years. The cumulative risk in this mixed rural and urban population for children by their 5th birthday was 1:600.

The clinical presentations of these 200 cases of *H influenzae* type b infection are summarised by age in the table. The annual incidence of *H influenzae* type b meningitis was 23.6/100 000 children aged less than 5 years, giving a cumulative risk of 1:850 children by their 5th birthday.

One child had sickle cell disease, and another had non-syndromic dysmorphic features, otherwise

there were no recognised predisposing factors. No secondary cases involving siblings or close contacts were documented in this series.

Ampicillin resistance was found in 11.3% of *H influenzae* type b isolates: all the resistant strains produced β -lactamase. Of the non-typable isolates, 15.8% produced β -lactamase and one of these was also chloramphenicol resistant.

There were 10 recorded deaths, eight of which were due to meningitis, one due to epiglottitis, and one to bacteraemia. The age range of those who died was from 3 months to 5 years (median=1 year 2½ months). Five of these cases were diagnosed at postmortem examination after sudden unexpected deaths. The mortality rate for all systemic *H influenzae* type b disease was 5.0%. *H influenzae* type b meningitis carried a 5.6% mortality, while other clinical presentations combined had a mortality of 3.4%.

Of the 35 survivors of meningitis in 1985, three have bilateral sensorineural hearing loss requiring amplification and a fourth has global development delay with severe learning difficulties. Thus over 11% of survivors have major neurodevelopmental sequelae. Information regarding lesser disabilities was not sought.

Discussion

The epidemiological patterns we observed are in keeping with comparable data from the United Kingdom,^{6,8} United States,^{11,12} and Australia¹³ except for a lower incidence of septic arthritis. If there is any bias in our figures it is likely to be in underdetection of the less common manifestations of systemic *H influenzae* type b disease as appropriate cultures may not have been sent. Prior antibiotic treatment may have resulted in some missed cases if all cultures were negative.

Our mortality rates concur with recently published series.^{8,13-15} As a number of these deaths occur before arrival in hospital, therapeutic refinements for systemic *H influenzae* type b disease are unlikely to substantially reduce mortality.

We acknowledge the limitations of uncontrolled follow up data in the assessment of morbidity after *H influenzae* type b meningitis: well controlled long term studies are lacking in the United Kingdom. Studies from the United States report a wide range of significant sequelae in 8%¹⁶ to 37%¹⁷ of survivors, although a recent 10 to 12 year follow up in Pittsburgh showed comparable academic achievements with sibling controls, despite a 21% frequency of neurological sequelae.¹⁸ Our findings of over 11% with significant sequelae tend to confirm that there is an accumulating register of children with

Table Clinical presentations by age of 200 cases of systemic *H influenzae* type b disease in children in the Oxford region January 1985-June 1988

	Age (years, months)				Total No (%)
	<1-0	1-0-1-11	2-0-4-11	>5-0	
Meningitis	60	45	33	4	142 (71)
Epiglottitis	1	6	15	1	23 (12)
Cellulitis	11	0	1	0	12 (6)
Bone/joint infection	4	3	5	0	12 (6)
Pneumonia	3	1	2	0	6 (3)
Bacteraemia	3	1	1	0	5 (2)

impairments after *H influenzae* type b meningitis despite modern methods of management.

The total live birth rate in the United Kingdom is 790 000/annum with an upward trend predicted over the next decade. Extrapolating from our data to a population of 3.95 million children aged under 5 years, about 1300 cases of systemic *H influenzae* type b disease, over 900 cases of *H influenzae* type b meningitis, and 65 deaths would be predicted annually in the United Kingdom.

The Communicable Disease Surveillance Centre (CDSC) at Colindale received reports of 787 cases of *H influenzae* type b meningitis or bacteraemia from participating laboratories in England and Wales for 1987. Not all microbiology departments send data to CDSC so this is acknowledged as incomplete surveillance. There were an additional 83 cases reported to the Communicable Diseases (Scotland) Unit. Other national data collection systems such as statutory notification and hospital activities analysis have even greater limitations.

There is an urgent need for prospective studies to be set up in other regions to assess accurately the incidence of systemic *H influenzae* type b disease. Such baseline data will be essential to determine the effect of intervention such as active immunisation with one of the conjugate *H influenzae* type b vaccines.

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