

The decline of *Haemophilus influenzae* type b disease in Australia

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Abstract

Between July 1993 and June 1996, there were 412 cases of invasive *Haemophilus influenzae* type b (Hib) disease reported to the Hib Case Surveillance Scheme, 71% in children under the age of five years. Meningitis was the most frequent illness reported, followed by epiglottitis, septicaemia and pneumonia. There were 18 deaths. Thirty-four cases were classified as vaccine failures. The number of vaccine failures increased over time and the total number of cases of Hib disease fell, consistent with an increase in Hib vaccine coverage. Based on an estimated vaccine coverage of 50% in April 1995, the vaccine efficacy for all vaccines in the period was estimated to be 89%. Invasive Hib is a serious illness of childhood which is being significantly reduced by the use of Hib vaccines, and has the potential to be eliminated from this country. Vaccination providers should aim to immunise all children against Hib disease on time and according to the National Health and Medical Research Council Standard Vaccination Schedule. *Comm Dis Intell* 1997;21:173-176.

Introduction

Haemophilus influenzae type b (Hib) has been a major cause of morbidity and mortality in children in Australia. Before the introduction of conjugate Hib vaccines, invasive Hib disease occurred at a rate of between 39 and 63 cases per 100,000 Australian children under the age of five years, with much higher rates being reported in the Northern Territory^{1,2,3}. Around 500 cases occurred annually and there were 10 to 15 deaths per year⁴.

Conjugate Hib vaccines first became available in Australia in 1992, with the introduction of the conjugate PRP-D vaccine, recommended for use in children aged 18 months or older. In 1993 another three conjugate vaccines, PRP-OMP, HbOC and PRP-T, became available for use in children under 18 months of age. Hib vaccines became free to all children under the age of five years from April 1993.

Since the introduction of conjugate Hib vaccines, the incidence of invasive Hib disease has dropped

dramatically. There was a 94% reduction in cases in children under the age of five years between 1992 and 1996⁵. The total number of cases declined from 549 in 1992 to 53 in 1996.

The Hib Case Surveillance Scheme (HCSS) was used to document the decline of Hib disease for a three year period between 1993 and 1996, and to estimate Hib vaccine efficacy.

Methods

The Hib Case Surveillance Scheme was created to obtain information on cases of invasive

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Hib disease which was not available in the National Notifiable Diseases Surveillance System (NNDSS). Additional information, including type of illness, method of diagnosis, vaccination status (including date of vaccination and type of vaccine used) and outcome, was obtained by State and Territory health authorities on cases notified under their public health legislations. The HCSS commenced in January 1994, with reports backdated to 1 July 1993. Because of differences in case definitions between the NNDSS and the HCSS, and a small amount of under-reporting to the HCSS, the numbers of cases reported to each system were not identical.

All cases of invasive Hib disease reported to the Hib Case Surveillance Scheme with onset dates between 1 July 1993 and 30 June 1996 were examined to describe the decline in the disease, clinical illness and outcome, and to estimate Hib vaccine efficacy.

A case of invasive Hib disease was defined as:

- Isolation of *Haemophilus influenzae* type b from any normally sterile site,

and/or

- Identification of Hib antigen in cerebrospinal fluid, urine or joint fluid with clinical features compatible with invasive Hib disease,

and/or

- A confident diagnosis of epiglottitis by direct vision, laryngoscopy or X-ray.

The definition of a Hib vaccine failure was based on the National Health and Medical Research Council (NHMRC) Standard Vaccination Schedule⁴. A Hib vaccine failure was defined as a case of invasive Hib disease more than 21 days after administration of the most recent Hib vaccine in:

1. An infant aged less than 12 months who had received
 - a. three doses of HbOC or PRP-T, or
 - b. two doses of PRP-OMP, or
 - c. two doses of HbOC or PRP-T where the first dose was given between 7 and 9 months of age.
2. A child aged 12 to 18 months who had received
 - a. three doses of HbOC or PRP-T, or
 - b. two doses of PRP-OMP where the first dose was given at 3 months or older, or
 - c. two doses of HbOC or PRP-T where the first dose was given between 7 and 11 months of age, or
 - d. a single dose of HbOC or PRP-T or PRP-OMP where the first dose was given at 12 months of age or older.

3. A child who had received three doses of PRP-OMP where the first dose was given at 2 months and the third dose at 12 months or older.
4. A child who received a single dose of HbOC or PRP-T or PRP-OMP at the age of 15 months or older.
5. A child who received a single dose of PRP-D at the age of 18 months or older.

All analyses were performed in Epi Info version 6⁶.

Estimates of vaccination coverage were based on the Australian Bureau of Statistics 1995 immunisation survey⁷. Vaccine efficacy (VE) was estimated in Epi Info using the relationship between the percentage of cases vaccinated (PCV) and the percentage of the population vaccinated (PPV) which has been described by Orenstein *et al*⁸:

$$VE = \frac{PPV-PCV}{PPV(1-PCV)}$$

Results

There were 412 cases of invasive Hib disease reported to the Hib Case Surveillance Scheme with onset dates in the period 1 July 1993 to 30 June 1996. Of these, 292 cases (71%) occurred in children under the age of five years. There was a marked decline in case numbers over the period (Figure 1). There were 419 cases of Hib disease reported to the National Notifiable Disease

Figure 1. Cases of invasive Hib disease, July 1993 to June 1996, by month and age group

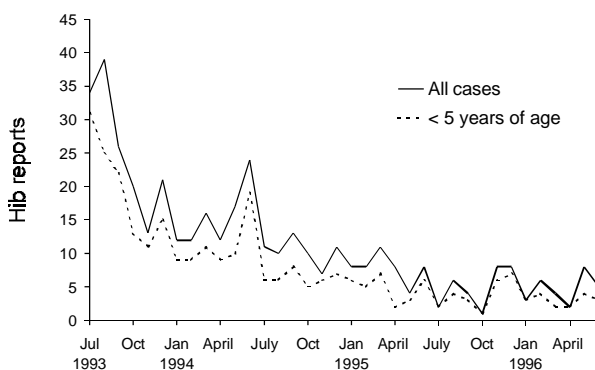


Figure 2. Cases of invasive Hib disease, July 1993 to June 1996, by type of illness

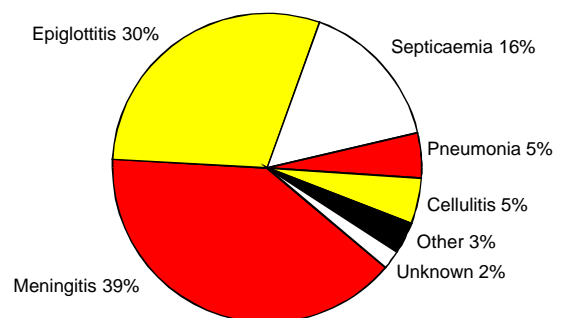


Table. Hib cases and vaccine failures in children under the age of 6 years

	Year				Total
	1993 (July to December)	1994	1995	1996 (January to June)	
Cases aged less than 6 years	126	114	63	21	324
Vaccine failures aged less than 6 years (%)	2 (2)	10 (9)	15 (24)	7 (33)	34 (10)

Surveillance System for the same period.

More males than females were reported; the male:female ratio was 1.3:1. Twenty-five cases (6%) were reported to be Aboriginal or Torres Strait Islanders. For 10% of cases Aboriginality was not reported.

Meningitis was the most frequent manifestation of invasive Hib disease, followed by epiglottitis, septicaemia and pneumonia (Figure 2). Ninety-one per cent of meningitis cases occurred in children under the age of five years.

There were 18 deaths (4%), and outcome was not reported for 21 cases (5%). Deaths occurred in 10 males and eight females; their ages ranged from four months to 97 years. Eight deaths occurred in children under the age of five years, with two in Aboriginal or Torres Strait Islander children. In those who died there were nine cases of septicaemia, six of meningitis, two of epiglottitis and one of pneumonia. Deaths in children under the age of five years declined from five in the last six months of 1993 to one in each subsequent year.

Information on vaccination status was available for all but 14 cases (3%). Ninety-three cases (23%) were reported to have received one or more doses of Hib vaccines; all were less than six years of age. Thirty-four cases were classified as vaccine failures. Vaccine failures were associated with HbOC (17 cases, 50%), PRP-OMP (5, 15%) and PRP-D (6, 18%). For six vaccine failures the type of vaccine received was not reported.

Vaccine failures occurred in more males than females; the male:female ratio was 2.4:1. Four vaccine failures occurred in Aboriginal or Torres Strait Islander children. All had been vaccinated with PRP-OMP. There were no deaths among those classified as vaccine failures.

The number of vaccine failures increased over time, while the total number of cases of Hib disease fell (Table). Based on an estimated vaccine coverage of 50% in April 1995, the vaccine efficacy for all vaccines in the period was estimated to be 89%.

Of the 59 cases who had received one or more doses of Hib vaccine but were not classified as vaccine failures, 31 had received a single dose of vaccine, 19 two doses and 6 three doses of vaccine (dose information was not reported for three cases). Forty cases were not old enough to have completed their course of vaccines, and 16 were old enough but had not completed their vaccination schedule according to the NHMRC recommendations.

Discussion

Since the introduction of conjugate Hib vaccines in Australia, the decline in the number of cases of invasive Hib disease has been dramatic. The Hib Case Surveillance Scheme also shows a corresponding decline in deaths. While the HCSS provides no information on morbidity, significant morbidity following Hib meningitis has been demonstrated⁹, and will continue to occur until Hib disease is eliminated.

The Hib Case Surveillance Scheme has a number of limitations. It is likely that there is some under-reporting, as fewer cases were reported to the HCSS than to the NNDSS. Epiglottitis in particular may be under-reported because an organism is not always identified in these cases. Epiglottitis can however also be caused by other organisms and it is possible that as Hib disease becomes less common epiglottitis will be increasingly caused by other organisms. The use of epiglottitis in the case definition of invasive Hib disease should now be reviewed, and it may be necessary to verify Hib by laboratory means in

these cases. Finally, incomplete reporting of information on cases, for example the number of doses and timing of vaccines, could result in some misclassification of cases in the HCSS. In particular this could result in an underestimate of the number of vaccine failures.

The spectrum of illness caused by invasive Hib disease in this study is consistent with a previous report¹⁰, with meningitis and epiglottitis the most frequent illnesses reported. The proportion of deaths also remained constant, although the total number of deaths declined.

This study indicates that Aboriginal and Torres Strait Islander people may remain at increased risk of invasive Hib disease. Proportionally more deaths occurred in this population, and the proportion of vaccine failures was also higher than for the Australian population overall. While selective reporting of Aboriginality could have affected these results, elimination of invasive Hib disease from Aboriginal and Torres Strait Islander communities should remain a public health priority.

The decreasing number of invasive Hib cases, and the increasing number of Hib vaccine failures identified in Australia, is consistent with an increase in Hib vaccination coverage. Hib coverage has however been difficult to measure, and the best national estimate is 50% coverage in April 1995, from the Australian Bureau of Statistics⁷. A study in Sydney however showed Hib vaccine coverage to be 77% in August 1994¹¹. Coverage is also likely to vary with age, with those in the younger age groups having higher rates than those in older age groups. In addition no studies have identified the proportion each type of vaccine contributes to the overall coverage, and hence estimates of vaccine efficacy for individual vaccine types cannot be produced.

Varying estimates of vaccine coverage could significantly change the estimate of vaccine efficacy in this study, and more detailed research is required to provide an accurate estimate.

The rise in the proportion of vaccine failures in Australia is consistent with the Canadian experience¹². However, while 34 cases met the Australian case definition of a vaccine failure, a further 24 cases would meet the United Kingdom vaccine failure definition. In the United Kingdom, where PRP-T vaccine is recommended at two, three and four months of age, a vaccine failure is defined as a case occurring after at least two doses of vaccine given in the first year of life or after a single vaccination given to children at the age of 12 months or more¹³. Using this definition, Australia would have had 58 vaccine failures, or 18% of cases under the age of six years. This difference indicates that the PRP-T may be a more immunogenic vaccine than those used in Australia. All the doses of vaccine recommended by the NHMRC appear to be required to prevent a high vaccine failure rate.

The HCSS does not provide information on risk factors for vaccine failures. In Canada a number of vaccine failures have been associated with underlying medical problems¹². Immune system defects may also be associated with vaccine failures¹⁴. Clinicians should consider further immunological investigation of Hib vaccine failures if underlying medical conditions are not present. In addition

the NHMRC recommends an additional dose of PRP-OMP at six months for premature children who commence on this vaccine⁴.

The 16 cases of invasive Hib disease which occurred in children who had not completed their course of vaccinations according to the NHMRC schedule, and many cases in unvaccinated children, were potentially preventable. Vaccination providers and parents should remain aware of the need to vaccinate children appropriately and on time against Hib.

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Hepatitis A outbreak in New South Wales

A cluster of hepatitis A infection reported to the South-Eastern Sydney Public Health Unit and the New South Wales Health Department has been linked to a Sydney restaurant. There have been 17 cases reported in the last two weeks, and all had dined at the restaurant between 11 and 18 May. Epidemiological investigations have shown that it is likely the

infections were caused by frozen prawns from Burma. Of the reported cases, ten are female and seven are male, with ages ranging from seven to 48.

The prawns have not been on sale to the general public and the importer is conducting a voluntary recall. The Public Health Unit and the New South Wales Health Department staff are

tracing other wholesale and distribution outlets to prevent further stocks of the implicated batch of prawns from reaching the public.