

Articles

TRENDS IN INVASIVE *HAEMOPHILUS INFLUENZAE* TYPE B DISEASE IN AUSTRALIA, 1995–2005

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Abstract

The epidemiology of invasive *Haemophilus influenzae* type b (Hib) disease and its prevention by vaccination is reviewed for the period 1995 to 2005, comparing surveillance data for 1995–2000, when both PRP-OMP and HbOC vaccines were used, with 2000–2005, when only PRP-OMP vaccine was used. Over the whole time period, notifications of invasive Hib disease have declined dramatically. In the second time period, a greater decline in Hib cases was seen. This could be due to either the different vaccines being used, differences in vaccine coverage or both. Although disease incidence has decreased markedly in both Indigenous and non-Indigenous populations, Indigenous people are still at significantly greater risk. It is also concerning that almost 60% of invasive Hib cases in children are preventable, in that they are occurring in unimmunised or incompletely immunised children among whom the incidence of Hib disease is estimated to be about 15 times that of fully immunised children. Australia is now in the third era of Hib vaccine use, during which both PRP-T and PRP-OMP vaccines are used, depending on ethnicity or jurisdiction of residence. Continued enhanced surveillance for invasive Hib disease is important for optimal monitoring of trends into the future. *Commun Dis Intell* 2008;32:316–325.

Keywords: disease surveillance, disease control, *Haemophilus influenzae* type b, immunisation, vaccination, Indigenous

Introduction

Invasive *Haemophilus influenzae* type b disease in Australia

Haemophilus influenzae type b (Hib) is a bacterium that causes a broad spectrum of illnesses ranging from local respiratory infection to serious invasive disease, including meningitis, epiglottitis, septic arthritis and septicemia.¹ Among the six encapsulated strains that have been identified (designated as types a to f), Hib is the most virulent.^{1–3} Non-encapsulated strains, classified as non-typeable, have also been identified and are usually associated with non-invasive infections, however they are capable of causing invasive disease, including neonatal sepsis.^{2–4} Invasive Hib disease has been notifiable

in Australia in most jurisdictions since 1990 and in all by 1993; non-type b invasive *H. influenzae* is reportable only in South Australia and the Northern Territory.

Hib is predominantly a disease of childhood with over 80% of cases worldwide occurring in children aged less than 5 years.⁵ Prior to the introduction of immunisation, Hib was the most common cause of bacterial meningitis in Australian children.^{6,7} However, since the introduction of Hib capsular polysaccharide-protein conjugate vaccines, the incidence of invasive Hib disease has declined dramatically.⁸ Indigenous children are known to be at increased risk,^{9–13} and have remained at increased risk despite vaccination programs.¹⁴ Non-Indigenous children in central Australia also had a relatively high incidence in the pre-vaccine era.¹⁵

The first comprehensive review of the impact of Hib vaccines in Australia between July 1993 and June 2000 reported that in the four years 1996–97 to 1999–00, the average annual incidence of invasive Hib disease in children aged less than five years was 1.7 cases per 100,000 population,¹⁴ a reduction of 87%–95%. Although the reduction was most marked in the target population, reduced incidence was seen in older age groups not eligible for immunisation, consistent with a herd immunity effect.¹⁴ In July 2000, the recommended Hib vaccine for non-Indigenous children changed from one conjugated to mutant diphtheria toxin (HbOC) to one conjugated to the outer membrane protein of *Neisseria meningitidis* (PRP-OMP). Universal use of PRP-OMP ceased at the end of 2005, with some jurisdictions continuing with PRP-OMP and others adopting combination vaccines with the Hib component conjugated to tetanus protein (PRP-T). This article documents invasive Hib disease and vaccine coverage during the period January 1995 to December 2005, with particular emphasis on the period of universal PRP-OMP use from 2000 to 2005.

Haemophilus influenzae type b vaccine in Australia

A number of conjugated Hib vaccines have been used in Australia (Table 1). Vaccines using the polyribosylribitol phosphate (PRP) polysaccharide of the Hib capsule were first developed in the 1970s

Table 1. Conjugated Haemophilus influenzae type b vaccines previously and currently registered for use in Australia

Generic name	Trade name	Hib antigen	Conjugating protein	Currently available
PRP-D	ProHIBit*	Hib capsular polysaccharide	Diphtheria toxoid protein	No
PRP-T	ActHib*	Hib capsular polysaccharide	Tetanus toxoid protein	No
HbOC	HibTITER†	Hib capsular oligosaccharide	Mutant diphtheria toxoid protein (CRM 197)	No
PRP-OMP	Liquid PedvaxHIB‡	Hib capsular polysaccharide	Outer membrane protein of group B meningococcus	Yes
Hib (PRP-OMP)-hepatitis B	COMVAX‡	Hib capsular polysaccharide	Outer membrane protein of group B meningococcus, hepatitis B surface antigen	Yes
PRP-T	Infanrix hexa,§ Hiberix§	Hib capsular polysaccharide	Tetanus toxoid protein	Yes

* Manufactured by Aventis Pasteur.

† Manufactured by Wyeth.

‡ Manufactured by CSL Biotherapies/Merck & Co Inc.

§ Manufactured by GlaxoSmithKline.

but these vaccines produced a T-cell independent immune response that was not effective in protecting aged children less than 18 months.¹⁶ Linking the PRP polysaccharide to a protein (i.e. conjugation) enhanced the immunogenicity of the vaccine by enabling T-cell stimulation. Conjugate Hib vaccines were first introduced in Australia in May 1992 for children over 18 months of age. Vaccines licensed for use in children aged more than 6 weeks became available in January 1993.¹⁴

There have been several key milestones in Hib immunisation practice in Australia since vaccine introduction, highlighted in Table 2. Between July 1993 and June 2000, a different Hib schedule was recommended for Indigenous and non-Indigenous children due to the increased risk of disease in Indigenous children and an earlier mean age of

onset (Table 3). Serological evidence suggested that in young infants a single dose of the PRP-OMP vaccine elicited a better immune response than a single dose of the HbOC vaccine.^{7,17} Therefore PRP-OMP vaccine (at 2 and 4 months and a booster dose at 12 months) was provided for all Indigenous children and all children in the Northern Territory, while HbOC at 2, 4 and 6 months of age with a booster at 18 months was provided for non-Indigenous children in other jurisdictions. In July 2000, the Hib vaccine provided for the funded program changed with PRP-OMP used for all infants commencing vaccination from this date. A final change occurred relatively recently. From November 2005 onwards, Queensland, Victoria, South Australia, the Northern Territory and Indigenous children in Western Australia continue to use PRP-OMP in a combined vaccine with Hepatitis B (PRP-OMP-

Table 2. Significant events in Haemophilus influenzae type b immunisation practice in Australia, 1992 to 2005

Year	Month	Event
1992	May	PRP-D (ProHIBit) approved for vaccination of infants aged at least 18 months.
1993	January	HbOC (HibTITER) and PRP-OMP (PedvaxHIB) marketed for use in children aged at least 2 months.
1993	April	PRP-T (ActHib) marketed for use in children aged at least 2 months.
1993	May	Reimbursement of vaccine cost for children born after February 1993.
1993	July	Fully funded national infant immunisation programme.
1993	August	Fully funded one dose catch up campaign for children aged less than 5 years.
2000	February	Combined Hib (PRP-OMP)-hepatitis B vaccine approved.
2000	May	PRP-OMP recommended for all infants (administered separately or in combination with hepatitis B vaccine).
2005	November	PRP-OMP recommended for all infants in Northern Territory, South Australia, Queensland, Victoria and Indigenous children in Western Australian PRP-T recommended for all infants in New South Wales, Australian Capital Territory, Tasmania and non-Indigenous children in Western Australian

HepB, COMVAX), in their funded programs. A PRP-T containing combination (Infanrix hexa) is being used for non-Indigenous children in Western Australia and all children in New South Wales, the Australian Capital Territory and Tasmania, using a 2, 4 and 6 month primary series with a booster dose at 12 months. Therefore, for non-Indigenous children in Australia there have been 3 vaccine eras (Table 3).

Methods

Study period

The two relevant time periods or vaccine eras covered by this article are between July 1993 and June 2000, when both HbOC vaccine and PRP-OMP were used depending on Indigenous status and residence in the Northern Territory (era 1) and July 2000 to November 2005 when PRP-OMP was used universally (era 2, see Table 3). To account for transition issues and to ensure relatively equal time periods, the two time periods examined for the purposes of this article are January 1995 to June 2000 and July 2000 to December 2005.

Data sources

Surveillance systems

Invasive Hib disease has been part of the National Notifiable Diseases Surveillance System (NNDSS) since its inception in 1990. The national invasive Hib disease case definition changed in 2004, during the period under surveillance.^{18,19} As of 1 January 2004 only confirmed cases of invasive Hib disease were reported (Table 4). Information collected through the NNDSS includes date of diagnosis, age, gender, postcode, state or territory, and Indigenous status. Data on notified cases of invasive Hib disease were obtained from the NNDSS as of March 2007.

The Hib Case Surveillance Scheme (HCSS) is an enhanced surveillance system designed to collect supplementary information not routinely available from the NNDSS on cases of laboratory-confirmed invasive Hib disease. The HCSS was established in January 1994 with data collected retrospectively to 1 July 1993. Designated state and territory health department staff complete an enhanced surveillance form for each case of invasive Hib disease. Data on cases with an onset during the period under surveillance were obtained from the HCSS as of January 2007. Data collected include detailed information on immunisation status and disease, including some information on past medical history of the case, outcome of the case and laboratory confirmation method. Although immunisation status is a data field in NNDSS, it is rarely completed and therefore the enhanced system is needed for reliable analysis of this variable.

Data from the Australian Childhood Immunisation Register (ACIR), which contains information on the vaccination status of all Australian children born since 1996 and registered with Medicare, was used to assess Hib coverage for the time period of interest. A second or third dose assumption was used when estimating coverage. If the second PRP-OMP or third HbOC was recorded as having been given, it was assumed that the preceding doses had also been given. If a child was recorded as having received either a second or third dose of Hib-containing vaccine the child was categorised as being fully immunised at 12 months of age. If a child was recorded as having received either a third or fourth dose of Hib-containing vaccine, the child was categorised as being fully immunised at 24 months of age.¹⁴

In this article Indigenous status consists of two categories, 'Indigenous' which measures whether a person is identified as being of Aboriginal or Torres

Table 3. Recommended Haemophilus influenzae type b for Indigenous and non-Indigenous Australian children, July 1993 to December 2005 – 'The 3 eras of Haemophilus influenzae type b vaccination in Australia'

Time period	Haemophilus influenzae type b recommended	
Era 1 July 1993–June 2000	PRP-OMP* All Indigenous children and non-Indigenous children in the Northern Territory	HbOC† Non-Indigenous children outside the Northern Territory
Era 2 July 2000–November 2005	PRP-OMP All children	PRP-OMP All children
Era 3 From November 2005	PRP-OMP All children in the Northern Territory, Queensland, Victoria, South Australia and Indigenous children in Western Australia	PRP-T‡ All children in New South Wales, the Australian Capital Territory, Tasmania and non-Indigenous children in Western Australia

* PRP-OMP (COMVAX, Liquid PedvaxHIB): 2 doses at 2 and 4 months, booster dose at 12 months.

† HbOC (HibTITER): 3 doses at 2, 4 and 6 months, booster dose at 18 months.

‡ PRP-T (Hiberix, Infanrix hexa): 3 doses at 2, 4 and 6 months, booster dose at 12 months.

Table 4. Case definition for notification of invasive *Haemophilus influenzae* type b disease to the National Notifiable Diseases Surveillance System

Time period	Case definition*
Prior to 2004 ¹⁸	<p>a) A clinically compatible illness (meningitis, epiglottitis, cellulitis, septic arthritis, osteomyelitis, pneumonia, pericarditis or septicaemia) <i>and</i> either:</p> <ul style="list-style-type: none"> • the isolation of <i>Haemophilus influenzae</i> type b (Hib) from blood <i>or</i> • detection of Hib antigen in a clinical case <i>or</i> • detection of Gram negative coccobacilli where the organism fails to grow in a clinical case <p><i>or</i></p> <p>b) A confident diagnosis of epiglottitis by direct vision, laryngoscopy or x-ray.</p>
January 2004 onwards ¹⁹	<p>a) Isolation of <i>Haemophilus influenzae</i> type b (Hib) from a normally sterile site where typing has been confirmed at an approved reference laboratory</p> <p><i>or</i></p> <p>b) Detection of Hib antigen in cerebrospinal fluid when other laboratory parameters are consistent with meningitis.</p>

* Only confirmed cases should be notified from January 2004 onwards (by laboratory definitive evidence).

Strait Islander origin and a composite category, 'other' which includes those recorded as non-Indigenous and those listed as 'not stated/inadequately described'. The latter group will be described as 'non-Indigenous' throughout this report. Coverage by Indigenous status has been accurately recorded on the ACIR since 2002.²⁰

Population denominators and death data

For the years 1991 to 2005 resident populations were derived from both the Australian Bureau of Statistics (ABS) and the Australian Institute of Health and Welfare (AIHW). Death data for cases were cross matched between NNDSS and HCSS databases.

Estimating per cent reduction between the two vaccine eras

The formula used for estimating per cent reduction between the two eras was:

$$\text{Percentage reduction} = ((R1-R2)/R1) \times 100 = (1-R2/R1) \times 100$$

where R1 and R2 are the January 1995–June 2000 and July 2000–December 2005 Hib incidence rate, respectively. The 95% confidence interval (CI) of reduction was calculated using the Taylor Series for Rate Ratio.²¹

Definitions of vaccine eligibility and vaccination status

A number of definitions were applied to identify eligibility for vaccination and vaccination status of cases (Table 5). Doses of vaccine given less than 15 days prior to disease onset were not considered to count towards the immunisation status of the case.

Results

National Notifiable Diseases Surveillance System

Between 1993 and 2005 a total of 1,046 invasive Hib cases were reported to the NNDSS (Table 6). The number of Hib notifications per quarter between is shown in Figure 1. For the 30-month pre-vaccination period between January 1991 and June 1993, the average number of overall Hib notifications to NNDSS per quarter was 120 (range 81–142). This can be compared with notifications during the two vaccine periods between January 1995 and June 2000, and July 2000 to December 2005, where the average reported notifications per quarter was 14 (range 3–33) and 6 (range 1–12), respectively. These figures reveal that since the introduction of vaccination in mid-1993, there has been a dramatic decrease in the number of invasive Hib cases, both in the overall population and among those eligible for vaccine.

Table 6 shows the rate of invasive Hib disease by Indigenous status and the rate ratio between Indigenous and non-Indigenous Australians. It can be seen that despite universal vaccination and large decreases in overall incidence in both populations, Indigenous people continue to remain at significantly higher risk of invasive Hib disease compared to non-Indigenous Australians, with rate ratios ranging from 2.7 in 1993–94 to 17.6 in 2002–03. These ratios exceeded unity for all time periods under surveillance.

There were 309 notifications of invasive Hib diseases with onset between January 1995 and June 2000 and 120 notifications between July 2000 and

Table 5. Definitions of vaccine eligibility and vaccination status

Eligible for vaccination	<ul style="list-style-type: none"> • Children born after 31st July 1988.
Eligible for routine infant immunisation	<ul style="list-style-type: none"> • Children born from 1 March 1993 onwards.
Fully immunised for age	<ul style="list-style-type: none"> • Two doses of PRP-OMP before the age of one year and > 14 days before disease onset among children 4 to 12 months of age (i.e. eligible to have completed the primary series) • Three doses of HbOC before the age of one year and > 14 days before disease onset among children 6 to 12 months of age (i.e. eligible to have completed the primary series) • Two doses of PRP-OMP before the age of one year AND a booster dose at 12 months of age and > 14 days before disease onset among children at least 12 months of age (i.e. eligible to have completed the primary series and booster) • Three doses of HbOC before the age of one year AND a booster dose at 12 months of age and > 14 days before disease onset among children at least 12 months of age (i.e. eligible to have completed the primary series and booster) • One dose of any Hib vaccine given at 15–59 months of age and > 14 days before disease onset • One dose of any Hib vaccine given at 12–14 months of age AND a booster dose given at least 2 months after and > 14 days before disease onset
Partially immunised for age	<ul style="list-style-type: none"> • One or more doses of any Hib vaccine but not fully immunised for age (see above). • Fully immunised for age but with disease onset within 14 days of receipt of last dose
Unimmunised	<ul style="list-style-type: none"> • No Hib immunisations • First dose of primary series Hib vaccine given within 14 days of disease onset

Table 6. Invasive Haemophilus influenzae type b disease incidence in Indigenous and non-Indigenous Australians and incidence rate ratios, 1993 to 2005

Date of diagnosis	Australia		Indigenous		Non-Indigenous		Indigenous: non-Indigenous	
	n	Rate per 100,000	n	Rate per 100,000	n	Rate per 100,000	Rate ratio	95%CI
Jan 93–Dec 94	617	1.74	35	4.48	582	1.68	2.67	(1.84, 3.76)
Jan 95–Dec 96	167	0.46	11	1.34	156	0.44	3.06	(1.50, 5.63)
Jan 97–Dec 98	92	0.25	11	1.29	81	0.22	5.77	(2.77, 10.89)
Jan 99–Jun 00	50	0.18	9	1.35	41	0.15	9.17	(3.92, 19.16)
Jul 00–Dec 01	38	0.13	4	0.59	34	0.12	4.87	(1.26, 13.66)
Jan 02–Dec 03	50	0.13	15	1.59	35	0.09	17.54	(8.90, 32.96)
Jan 04–Dec 05	32	0.08	5	0.51	27	0.07	7.48	(2.25, 19.70)

December 2005. Figure 2 compares the Hib incidence rates by jurisdiction during the two Hib vaccine eras described previously. Both Indigenous and non-Indigenous cases have been included in these calculations. Disease rates have decreased in all jurisdictions, with the Northern Territory continuing to have the highest incidence of Hib disease. The overall rate of disease has declined between the two time periods by 63.6% from 0.30 to 0.11 cases per year per 100,000 population. The decrease ranged from 23% in the Northern Territory to 100% in the Australian Capital Territory. The decline in invasive disease has been greatest among children under 5 years of age; from 2.12 to 0.55 per 100,000 in children aged 1 to 4 years, and from 5.32 to 1.52 cases per 100,000 in infants aged under 1 year (Figure 3).

Deaths

There were 16 deaths recorded in NNDSS due to invasive Hib disease between January 1995 and June 2000 with an overall case fatality rate (CFR) of 5.2%, and 7 deaths between July 2000 and December 2005 with a CFR of 5.8%. For the first time since surveillance began, no deaths from invasive Hib disease were reported in 2005. The CFR did not differ by Indigenous status.

When limiting the analysis to the vaccine-eligible population, 6 cases died between January 1995 and June 2000 with an overall CFR of 3.2% and 2 cases died between July 2000 and December 2005 with a CFR of 2.8%. Of note, both of the deaths in the

Figure 1. Number of Haemophilus influenzae type b notifications per quarter and publicly funded immunisation, Australia, 1992 to 2005

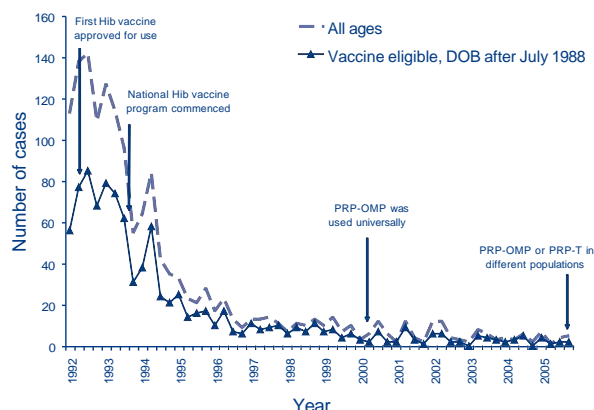


Figure 2. Incidence of invasive Haemophilus influenzae type b disease per 100,000 population, by state or territory and percentage reduction in illness between the two vaccines eras

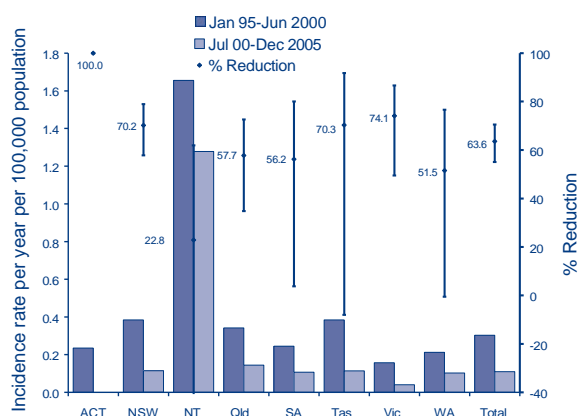
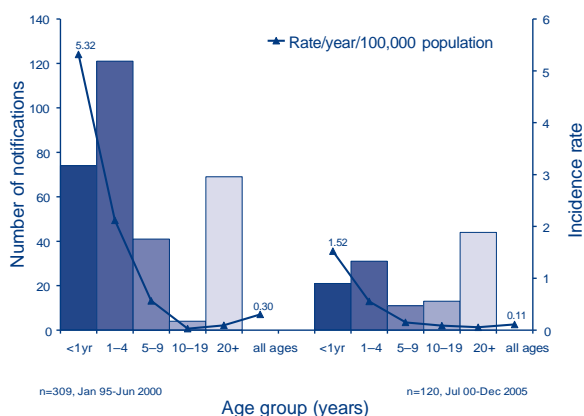


Figure 3. Number of Haemophilus influenzae type b cases, Australia, by age and age-specific incidence rates during the two vaccine eras

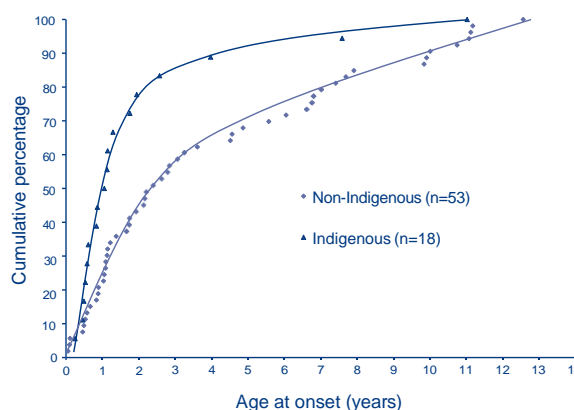


second time period were among infants with septicæmia aged under 12 months, one of whom was too young to receive vaccine, the other of whom had only received one dose of their primary series.

Haemophilus influenzae type b Case Surveillance Scheme

All Hib cases reported to HCSS with onset dates between July 1993 and December 2005 were examined by age to determine eligibility for vaccine according to birth date (definitions are outlined in Table 5). A total of 643 cases were identified in the HCSS; 491 were vaccine-eligible as they were born after July 1988. This included 60 Indigenous or Northern Territory residents for whom PRP-OMP was recommended in all time periods, with 20 having disease onset between July 2000 and December 2005 (i.e. era 2). Of the remaining 431, 163 had disease onset between January 1995 and June 2000 and 51 had disease onset between July 2000 and December 2005. Therefore during era 2 a total of 71 cases were reported. Indigenous children had a significantly earlier age of illness onset compared to non-Indigenous children (log-rank test $p=0.02$) (Figure 4). The median age of Indigenous cases was 14 months compared with a median age of 30 months among non-Indigenous cases (non-parametric test for median $p=0.02$).

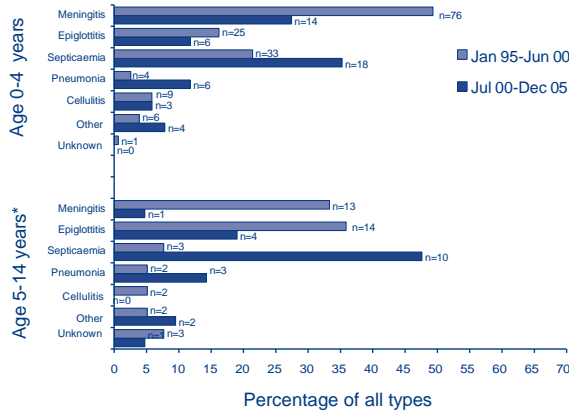
Figure 4. Age at onset of Haemophilus influenzae type b cases occurring between July 2000 to December 2005 among vaccine-eligible Indigenous and non-Indigenous children (n=71)



Clinical presentation of Hib disease varied with age and between the two time periods (Figure 5). While overall disease was less common during the second time period, the relative frequency of clinical presentations varied. Hib meningitis and epiglottitis among children under 5 years of age decreased between the two time periods by 81.6% and 76%,

respectively, whereas the proportion coded as septicæmia and pneumonia increased among older children.

Figure 5. Clinical presentation of Haemophilus influenzae type b cases, by age group and time period

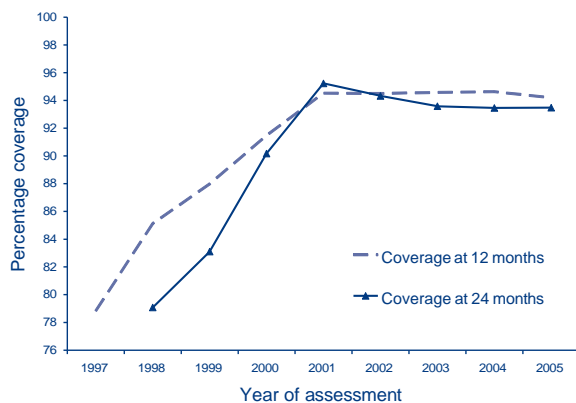


* Included children born before July 1988.

Estimating vaccine coverage

Since 2000, every state and territory in Australia has achieved Hib vaccine coverage rates above 90% for the primary series, as recorded by ACIR and assessed at 12 months of age (Figure 6). Vaccine coverage for the primary series and booster, assessed at 24 months of age is slightly lower, but above 90%. Since 2002, when ACIR Indigenous data quality has been acceptable, coverage in Indigenous children has been slightly lower than that of non-Indigenous children (by about 1%), but has also been above 90% for both the primary series and primary series

Figure 6. Haemophilus influenzae type b vaccine coverage at 12 and 24 months of age, Australia, 1997 to 2005

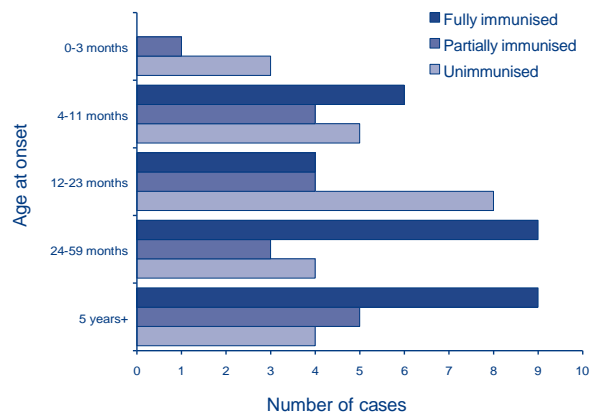


with booster. Vaccine coverage varied minimally by state and territory. Given the high coverage, a large proportion of cases occurring among vaccinated individuals would be expected even with a highly effective vaccine.

Preventable cases between July 2000 and December 2005

Of the 71 invasive Hib disease cases occurring among vaccine-eligible children during era 2 when PRP-OMP was used throughout Australia, 2 did not have completed information on vaccination status and 4 occurred in children too young to have completed the primary series (i.e. less than 4 months of age). The latter 4 were not preventable by vaccination (Figure 7). Out of the remaining 65 cases (Figure 8), 15 (23%) occurred in children 4–11 months of age (eligible for primary series) and 50 (77%) occurred in children 12 months of age and older (eligible for primary and booster). There was a total of 28 Hib cases that were fully immunised according to their age and were therefore vaccine failures.

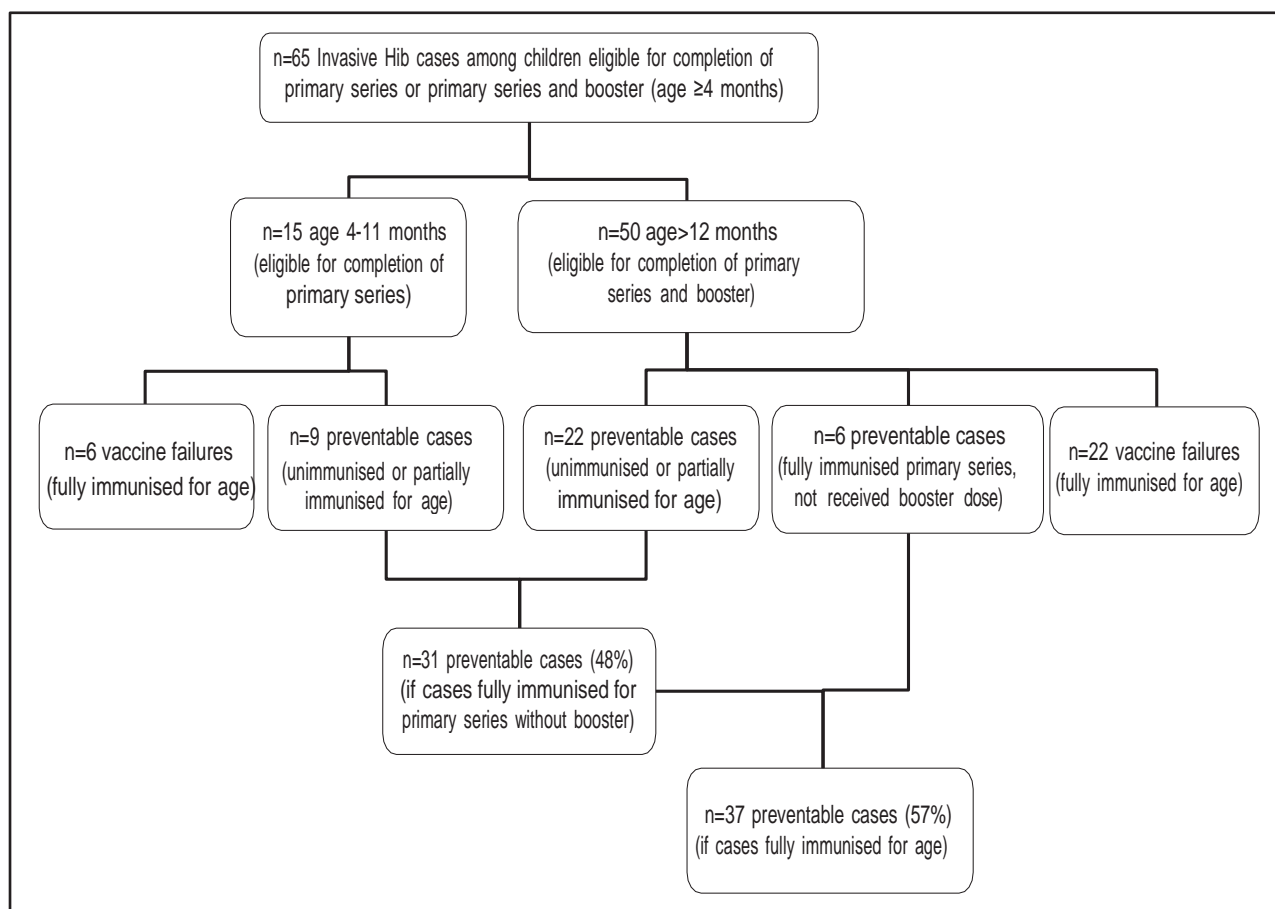
Figure 7. Vaccine status among vaccine-eligible Haemophilus influenzae type b cases (n=69*), July 2000 to December 2005, by age



* Two cases were removed as their vaccine status was unknown.

In children aged 4–11 months, 9 (60%) were either unimmunised or had only partially completed their primary series vaccination. Of the 50 cases in children aged 12 months or older, 28 (56%) were either unimmunised or had received only partial immunisation for age according to the definition in Table 5. Within this latter group, 6 cases were fully immunised for the primary series but had not received their booster dose. Therefore, 37 of 65 cases (57%) might have been prevented had they been fully immunised for age. The proportion of

Figure 8. Preventable cases of invasive *Haemophilus influenzae* type b disease in vaccine eligible children, July 2000 to December 2005



preventable cases would decrease to 48% if primary series alone (i.e. without booster) was considered. The proportion of cases identified as preventable, did not differ significantly between Indigenous and non-Indigenous Australians (59% versus 56%, respectively).

The data were further analysed to estimate the incidence of disease in children who had been fully immunised for age versus those who were not, including cases with disease onset between July 2000 and December 2005 who were older than 12 months (Figure 7). The denominators were obtained by selecting from the ACIR a cohort of children born between July 1995 and December 2004. The 'fully immunised' denominator was calculated using the ACIR criteria for fully immunised at 24 months, as the Hib booster is due at 12 months of age. The estimated incidence of invasive Hib disease in children aged over 12 months who were fully immunised for age was 0.9 per 100,000 (22/2,343,878), compared with an estimated incidence of 14.0 per 100,000 (28/199,697) in children who were not fully immunised.

Discussion

Immunisation with Hib vaccine has resulted in a dramatic and sustained reduction in the incidence of invasive Hib disease in Australia. The data demonstrate that the rate of the decline in disease was significantly greater between 2000 and 2005, in all jurisdictions excluding the Northern Territory, when the entire country was using the PRP-OMP vaccine, than during the earlier time period when HbOC was the primary vaccine in use. However it is important to note that some people with disease onset between 2000 and 2005 may have been immunised with HbOC if they were born when this vaccine was being used in their jurisdiction of residence, but their disease onset was during the latter time period. The increased rate of disease decline in the most recent 5-year period may therefore be related to differences in the vaccine, increasing vaccine coverage (though under-reporting to the ACIR would have to be taken into account especially prior to 2000) or a combination of factors.

Although disease incidence has decreased markedly in both Indigenous and non-Indigenous

populations, the continued disparity in incidence is concerning. This disparity is not unique to Australia, having been observed among Indigenous populations in both the United States of America and Canada.^{11,22,23} Studies in Alaskan populations suggest that continued low-level nasopharyngeal colonisation facilitates transmission to susceptible children.²⁴ Environmental and housing conditions, including overcrowding, are also potential contributing factors to these health disparities.^{25,26}

Higher rates of invasive Hib disease among Indigenous children have continued throughout the time period under surveillance despite high vaccine coverage among both Indigenous and non-Indigenous children in the latter vaccine era. ACIR data have shown that infant vaccination is more frequently delayed in Indigenous children, stressing the importance of continual emphasis on timely receipt of immunisation.^{27,28} Given the earlier onset of disease among Indigenous people, it is appropriate to continue the use of PRP-OMP in jurisdictions where there are a large proportion of Indigenous people.

It is concerning that almost 60% of invasive Hib cases are preventable, in that they are occurring among people who are either not immunised or not fully immunised for age. These children remain at risk for serious invasive disease, despite herd immunity effects. Until all children are immunised with Hib vaccine in a timely manner, preventable cases will continue. No vaccine is 100% effective and vaccine failures are expected. However, the total number of true vaccine failures among infants continues to be small. Despite some protection from herd immunity, the rate of disease among children who were not fully vaccinated for age was about 15 times higher than in fully immunised children, a potentially powerful incentive for continued Hib immunisation despite Hib disease having become rare.

A recent publication from Scheifele and colleagues has suggested that children with Hib vaccine failure are more likely to be immunosuppressed.¹³ Of the 28 Hib cases occurring among fully immunised children, 2 (7%) were known to have had immunocompromising conditions and 17 (61%) were reported to have no underlying illness. However, detailed information was not available on all children in order to assess this systematically.

Australia is now in the third era of Hib vaccine, during which both PRP-T and PRP-OMP are being used, depending on ethnicity or jurisdiction of residence. Continued surveillance will allow monitoring of the impact of this change but the small number of cases now occurring mean that any change, should it occur, will take many years to detect. The data presented in this report suggest that

the regional changes in recommended Hib vaccine are appropriate given current invasive Hib disease epidemiology in Australia. One needs to balance the benefits of improved compliance associated with giving multiple antigens in combination vaccines that use PRP-T with the benefits of earlier protection with PRP-OMP and this will vary depending on the setting.

Acknowledgements

We thank the state and territory Hib enhanced surveillance contacts: Anne Murphy from the Department of Human Services in Melbourne, Caroline Giele from the Health Department of Western Australia, Craig Davis from the Communicable Diseases Unit of Queensland Health, David Coleman from the Department of Community and Health Service in Tasmania, Lesley Scott from the Department of Health and Community Services in the Northern Territory, Robin Gilmour from the Communicable Diseases Branch of the New South Wales Health Department and Ros Holland from the Department of Human Services Communicable Disease Branch in Adelaide.

We also wish to acknowledge Brynley Hull for providing Australian Childhood Immunisation Register data and the data contributed by laboratories throughout Australia and the following organisations for provision of additional data for this article: the Surveillance Policy and Systems Section of the Office of Health Protection, Australian Government Department of Health and Ageing, for data from the National Notifiable Diseases Surveillance System; and the Australian Institute of Health and Welfare, Hospitals and Mental Health Services Unit and Population Health Unit, for data from the National Hospital Morbidity and Mortality Databases.

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