Invasive Haemophilus influenzae *infection*

Background

Invasive *Haemophilus influenzae* (HI) type b (Hib) disease has become increasingly rare in Australia since Hib vaccines were included in the immunisation schedule in 1993 for children under five years of age. Case numbers of Hib disease under five years of age have declined from over 500 per year to 20 reported cases in 1999. As Hib disappears, it is important to monitor the occurrence of infection due to other serotypes (A to F) or non-typeable HI, as these may be seen more commonly, and to document changes in the age distribution and focus of infection in confirmed Hib cases. In addition, as an increasing proportion of the population at risk of Hib infection is immunised, more Hib cases are expected in immunised children. It is important to monitor both the proportion of cases that are vaccine failures and the particular vaccines used, including their batch number, to identify batch-related vaccine problems. Information about whether cases are at risk of poor response to Hib vaccines from underlying diseases which impair immunity is also important for interpreting vaccine failure.

Because children with invasive Hib disease usually come under the care of a paediatrician, the APSU reporting scheme was introduced in 1998 as a source of data additional to routine notifications to the National Notifiable Diseases Surveillance Scheme (NNDSS). Although invasive Hib disease is notifiable in all States and Territories, invasive disease due to other types of HI is notifiable only in South Australia.

Thus the APSU and, for Victoria, the Victorian Hospital Pathogen Surveillance Scheme (VHPSS) are the only other sources of data for non-Hib infections. The APSU also provides additional clinical information about risk factors for poor vaccine response.

As infection with Hib is now uncommon, many laboratories no longer have the kits to type HI or they may type incorrectly. Accordingly, confirmation of serotype by a reference laboratory (Centre for Infectious Diseases and Microbiology, Sydney or Microbiologic Diagnostic Unit, Melbourne) is strongly encouraged.

Objectives

- To provide an additional source of notification of cases of invasive *H. influenzae* disease in children.
- To determine the proportion of cases of invasive Hib disease which are vaccine failures.
- To identify risk factors for Hib vaccine failure.
- To determine whether *H. influenzae* isolates from cases which are due to vaccine failure differ from those which are not due to vaccine failure.

Case definition

Any child less than 15 years with:

1. *Isolation of* H. influenzae *(any type or non-typed) from a normally sterile site,* ***or***
2. *Identification of Hib antigen in cerebrospinal fluid, blood or joint fluid in association with clinical features compatible with invasive Hib disease,* ***or***
3. *A confident diagnosis of epiglottitis (by direct vision or laryngoscopy) with supporting evidence of Hib infection (positive urinary Hib antigen or Hib isolated from epiglottis swab)*

Results

A total of 19 reports of invasive *H. influenzae* (Hib) disease were received by the APSU in 2000, of which eleven were definite cases, five were duplicates and two were errors. Further information was not available on one case, giving a questionnaire response rate of 95% for 2000.

Between January 1998 and December 2000, a total of 87 reports of Hib were received, of which 51 were definite cases. Three additional cases known to the investigators were not reported to the APSU. Twenty-one of the 87 reports were duplicates and ten were errors- usually because the isolate was from a non-sterile site. For the remaining five cases, no information was available. The overall questionnaire return rate was 94%.

H influenzae non type b cases

In 2000, five HI non type b cases were reported, of whom four were neonates with non-typeable isolates and one was a nine month old child with Down syndrome who had meningitis due to HI type f. Five HI non type b cases were reported in 1999 and six in 1998. Overall, of the 16 HI non type b cases reported between 1998-2000, most (11) were due to non-encapsulated isolates, predominantly from neonates with early onset sepsis. The remaining five cases due to other capsular types of *Haemophilus* presented with meningitis. These included two cases of both HI type e and HI type f and one case where capsular typing was only available down to the level of either type a or type c.

H influenzae type b cases

Five HI type b cases were reported in 2000. In one case, the isolate from blood culture (obtained before antibiotic treatment) was typed as HI type b but the CSF isolate (obtained 24 hours later) appeared to be non-encapsulated, even after evaluation by polymerase chain reaction. The foci of infection, age group and aboriginality of the 33 HI type b cases reported between 1998–2000 are shown in Table 12. Of the five meningitis cases under six months of age, one was a neonate and one had both epiglottitis and meningitis.

Table 12 Age, Focus and Aboriginality of HI type b cases

Focus	Age				
	≤6 mths	**>6 mths ≤ 24 mths**	**>2 yrs ≤5 years**	**> 5 years**	**Total**
Meningitis	5(2)	8(1)	2(1)	2	17(4)
Epiglottitis	0	1	2	2	5
Pneumonia	3(1)	2(1)	1	1	7(2)
Bone/joint*	0	1	0	0	1
Other	2†	1‡	0	0	3
Total	**10(3)**	**13(2)**	**5(1)**	**5**	**33(6)**

Cases in parentheses are Aboriginal children.
* Age of one case not available
† Septicaemia
‡ Uvulitis

Vaccination status

Of the 33 HI type b cases reported between 1998-2000, eight had received no doses of Hib vaccine. Five of these children were too young or too old to be eligible for immunisation and in two children, parents objected to immunisation. One case was overdue for the first dose (four months). There were 16 vaccine failures reported, of whom nine had received booster doses. Apart from one case of Down syndrome, none of the vaccine failures had any illnesses likely to compromise immune function (Table 13). Overall, ten cases were not age-appropriately immunised, and therefore were potentially preventable.

Table 13 Number of cases by vaccination status

Vaccination status	Total (Aboriginal)	Age appropriate*
No doses	8(3)	5
Partial immunisation †	9 (1)	4
Full immunisation‡	7(1)	5
Full + booster§	9(1)	9
Total	**33(6)**	**23**

* Age appropriate = All doses scheduled for ag
† Partial immunisation = 1 dose PRP-OMP, 1 or 2 doses of HbOC
‡ Full immunisation = 2 doses PRP-OMP, 3 doses HbOC
§ Full + booster = 3 doses PRP-OMP, 4 doses HbOC

Comparison with other data sources

Two sources of Hib cases are available other than the APSU (Table 14). These are the National Notifiable Diseases Scheme (NNDSS) and an enhanced subset of this scheme, which also documents immunisation status for all cases notified to States and Territories. The National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases (NCIRS) now coordinates reporting of the notifications to these two schemes.

Table 14 Sources of information about invasive Haemophilus disease

Information	NNDSS*	APSU
Age distribution	√	√
Non type b isolates	X	√
Vaccine failure investigations	X	√

* National Notifiable Diseases Surveillance Scheme.

In 1998–2000, there were 59 children less than five years of age with HI notified to NNDSS. Twenty- four of these were also notified to the APSU. Five additional children were notified to the APSU alone, of whom three were notified to the enhanced scheme but not to the NNDSS. Thus the sensitivity of APSU ascertainment for *H. influenzae* type b for children less than five years is 41%. It was encouraging that none of the children with invasive *H. influenzae* disease due to non type b serotypes had been notified to the NNDSS.

Conclusion

Reporting of *Haemophilus influenzae* invasive disease through the APSU was completed in December 2000. Although only 41% of the total Hib cases reported by mandatory laboratory notification were notified to the APSU, this surveillance has provided detailed clinical information not available from laboratory notification. In particular, the APSU data has shown that underlying conditions likely to compromise the immune response to Hib are unlikely to be a significant contributor to vaccine failure. The APSU also identified cases of *Haemophilus influenzae* meningitis occurring outside the neonatal period and due to other serotypes. In total, these cases were less than a third as numerous as HI type b cases. This APSU surveillance has demonstrated that in Australia, as in other developed countries, there is little evidence of a significant shift to other HI serotypes, almost ten years following the introduction of Hib vaccines into the Australian standard immunisation schedule.

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