Invasive *Haemophilus* influenzae in Ireland, 1996-2002

Key Points

- **Incidence of Hib disease increased in 2002, particularly in <5 year olds**
- **No increase due to non-b *H. influenzae* strains observed**
- **Number of true Hib vaccine failures ranged from 2-4 per year**
- **Surveillance of invasive *H. influenzae* in Ireland requires strengthening**

Introduction

Diseases of early childhood associated with *Haemophilus influenzae* type b (Hib) can now be prevented by vaccination. Hib was a leading cause of serious invasive infections such as meningitis, epiglottitis, pneumonia and septicaemia, prior to the licensing of the Hib conjugate vaccines. It was the most common cause of bacterial meningitis and occurred primarily among children under five years of age. The Hib vaccine was introduced in Ireland in October 1992 as part of the primary childhood immunisation schedule. A catch-up programme was also initiated at that time offering the vaccine to those under five years of age. The vaccine is specific for the diseases caused by Hib but does not protect against infections caused by other Haemophilus strains. Despite the fact that the incidence of Hib disease has dramatically declined since the introduction of the vaccine, it is essential that the incidence of all invasive *H. influenzae* infections continue to be closely monitored in Ireland. This will ensure that any changes in the epidemiology of the disease are detected promptly, that reasons for these changes are identified and that the necessary public health interventions are taken.

Materials and Methods

National data on invasive *H. influenzae* for 1996-1998 was collated by Dr Jerry Fogarty, Department of Public Health, WHB, while from 1999 onwards data have been collated by NDSC. NDSC obtains these data from three main sources:

1. Enhanced bacterial meningitis surveillance system (on an ongoing basis)

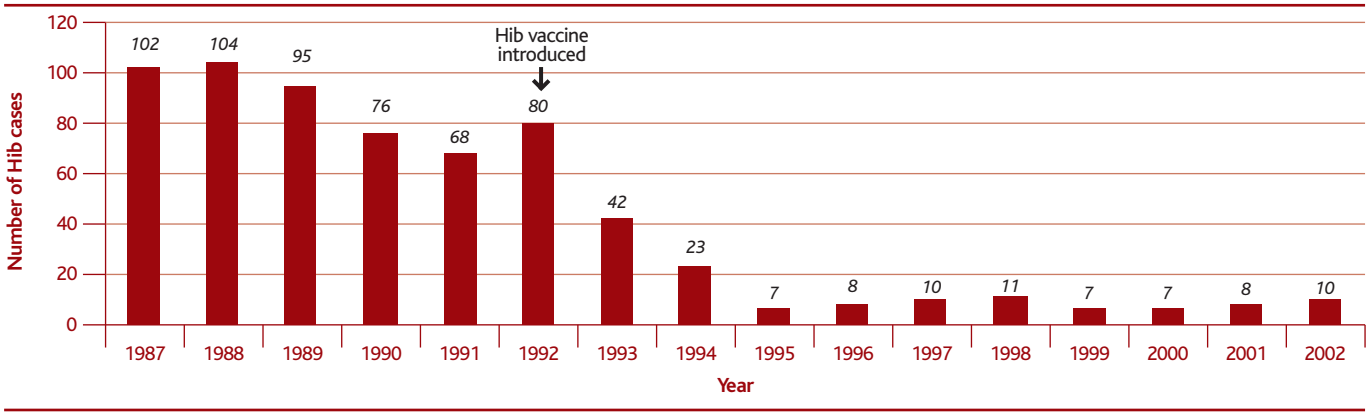

Figure 1. Invasive H. influenzae type b infections in Ireland, 1987-2002. Updated from J. Fogarty forum 1996.

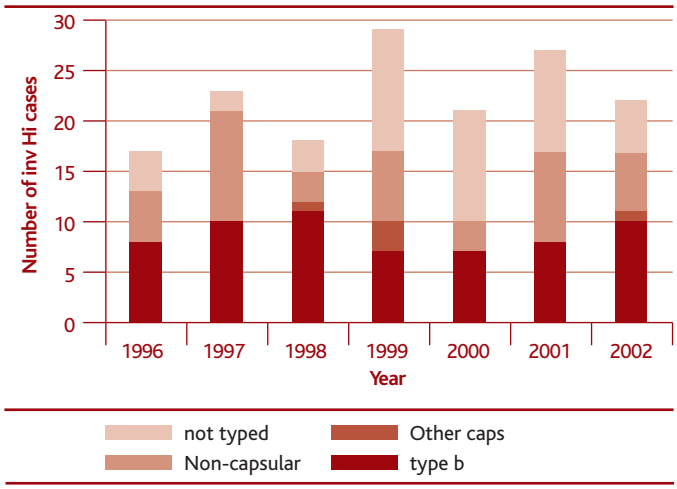

Figure 2. Number of invasive H. influenzae infections by serogroup (1996-2002)

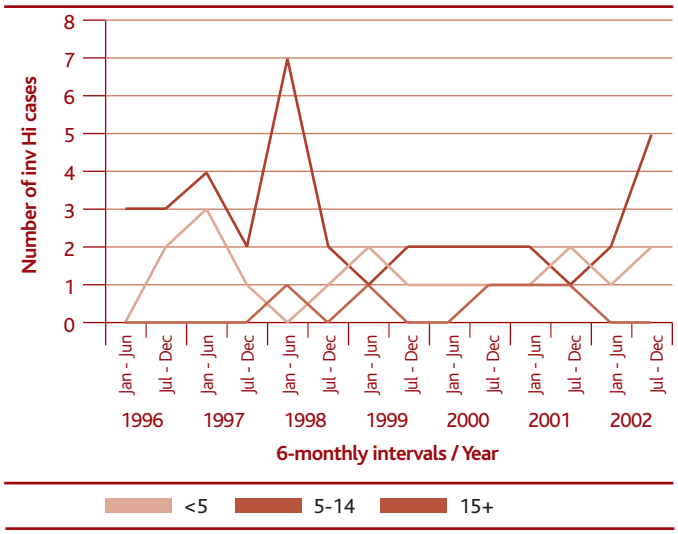

Figure 3. Number of invasive Hib cases in Ireland by age group

2. Directly from the laboratories/microbiologists (approximately once a year)

3. PHLS Haemophilus Reference Unit, Oxford, UK (occasionally)

Details of all invasive cases are inputted in an MS Access database. Vaccination details of cases are sought by Departments of Public Health if (i) the case was born after 1986 and (ii) the isolate is type b or has not been typed. In the event of a vaccine failure details on vaccination dates, vaccine brand and batch numbers are obtained.

A case is defined as invasive *H. influenzae* disease in a person with an isolate from a normally sterile site.

Hib vaccine failures are defined as:

True vaccine failure (TVF): Invasive Hib disease occurring (i) greater than two weeks after one dose of Hib vaccine given at age greater than one year, or (ii) greater than one week after three doses given at age less than one year.
Apparent vaccine failure (AVF): Invasive Hib disease occurring where the case was incompletely immunised or insufficient time had elapsed to be considered a TVF.

Possible vaccine failure (PVF): Invasive *H. influenzae* in a vaccinated child but where the isolate was not serotyped. Such a failure may be a possible true vaccine failure (PTVF) or a possible apparent vaccine failure (PAVF).

Results

Epidemiology of invasive H. influenzae

Since the Hib vaccine was introduced in 1992, the number of invasive *Haemophilus influenzae* type b (Hib) infections has declined from approximately 100 cases per year in the late 1980s to approximately 10 cases per year from the mid-1990s onwards (Figure 1).

Between 1996 and 2002, 156 cases of invasive *H. influenzae* were reported in Ireland, which is an average of 22 cases per year (0.61/100,000 total population; denominator data from 1996 census) (Figure 2). Over that period, 40% of the invasive cases were confirmed as Hib. However, the proportion of Hib cases may be higher since the serotype had not been determined (not typed) for 29% of the cases reported.

An increase in Hib infections was observed in 2002 (n=10; 0.26/100,000 total population, denominator data from 2002 census) when compared with the previous three years; this gives a mean of seven cases per year (Figure 2). This increase in 2002 was most pronounced in the latter half of the year and was predominantly in the less than five year olds (Figure 3). A similar increase due to other *H. influenzae* serotypes has not been observed in this age group (Figure 4).

The numbers of invasive *H. influenzae* and invasive *H. influenzae* type b (Hib) cases reported between 1996-2002 by age group are presented in Table 1a & 1b, respectively. Thirty five percent of the invasive *H. influenzae* cases occurred in under 5 year olds, while 31% occurred in over 65 year olds.

Table 1a. Number of invasive H. influenzae cases by age group

Year	<1	1-4	5-9	10-14	15-24	25-34	35-44	45-54	55-64	>65	Total
1996	3	5	0	0	0	0	1	2	2	4	17
1997	7	4	0	2	2	2	0	1	1	4	23
1998	4	7	1	0	1	1	0	1	0	3	18
1999	2	2	2	0	2	1	1	6	2	11	29
2000	5	5	1	0	1	0	1	1	0	7	21
2001	2	2	2	2	4	1	2	1	2	9	27
2002	0	7	0	0	1	1	0	2	1	9	21
Total	**23**	**32**	**6**	**4**	**11**	**6**	**5**	**14**	**8**	**47**	**156**

Table 1b. Number of invasive H. influenzae type b cases by age group

Year	<1	1-4	5-9	10-14	15-24	25-34	35-44	45-54	55-64	>65	Total
1996	1	5	0	0	0	0	0	1	1	0	8
1997	3	3	0	0	0	1	0	0	1	2	10
1998	3	6	1	0	0	0	0	1	0	0	11
1999	1	2	1	0	0	0	0	1	1	1	7
2000	2	2	1	0	0	0	0	0	0	2	7
2001	1	2	2	0	0	0	1	0	0	2	8
2002	0	7	0	0	0	0	0	0	0	3	10
Total	**11**	**27**	**5**	**0**	**0**	**1**	**1**	**3**	**3**	**10**	**61**

Sixty two percent of Hib cases reported between 1996 and 2002 occurred in under 5 year olds (38/61). Seven cases of Hib infection occurred in this age group in 2002, which is an age specific incidence rate of 2.5 per 100,000 in 2002 (denominator data from 2002 census).

Between 1996 and 2002, 55 cases of invasive *H. influenzae* in children under 5 years of age have been reported. The disease presentations in these children were as follows: meningitis (n=18); septicaemia (n=14); meningitis & septicaemia (n=4); epiglottitis (n=7); osteomyelitis/septic arthritis (n=4); pneumonia (n=4); cellulitis (n=1); other (n=1) and unknown/not reported (n=2).

Hib vaccine failures

Since 1996, 28 Hib vaccine failures have been reported in Ireland (19 TVF, 7 AVF, 1 PTVF, 1 PAVF). The vaccination status is unknown for an additional five cases and therefore these potentially could be vaccine failures also. The number of TVF tends to vary between 2 and 4 per year (Figure 5). Eighty nine percent (17/19) of the TVF occurred in the 1-4 years age group. The two exceptions were both between 5-9 years of age. Four AVF occurred in children less than one year of age and three in 1-4 years old children. The PTVF was in a 1-4 year old and the PAVF was in a child less than one year of age. One third (13/38, 34%) of the Hib cases that occurred in under 5 year olds between 1996 and 2002 had not been vaccinated (Figure 6).

Discussion

In England & Wales, an increase in Hib infections been observed particularly in the under 5 year olds. A similar increase has not been seen with other *H. influenzae* serotypes. The incidence rate of Hib disease in this age group increased from 1.0 in 1999, to 1.86 in 2000, to 2.7 in 2001 to 4.17 in 2002.[1] The majority of these Hib cases (approx 90%) occurred in vaccinated children, thereby leading to concerns in the UK regarding the efficacy of the Hib vaccine.

Possible reasons for the increase in Hib disease in the UK include[2]

1. Random variation in Hib disease occurrence

2. Decreasing herd immunity

3. Rapid infant vaccination schedule in the UK of 3 doses at 2, 3 and 4 months with no booster dose and also subsequent waning of the initial impact of the catch-up campaign

4. A reduced immune response to Hib vaccines in part of the vaccinated population may be occurring, which could be related to the use of a combination acellular pertussis, diphtheria, tetanus and Hib vaccine during 2000-2001, which produces lower Hib antibody levels, compared with whole-cell pertussis and Hib combinations. A similar increase in invasive Hib has not been seen in other countries using acellular pertussis vaccines; these countries mostly use a routine booster at 12-15 months.

Although the number of cases of invasive *H. influenzae* reported in Ireland did not change greatly between 1996 and 2002, an increase in Hib infections was observed in 2002. This increase was most marked in the under 5 year olds, seven

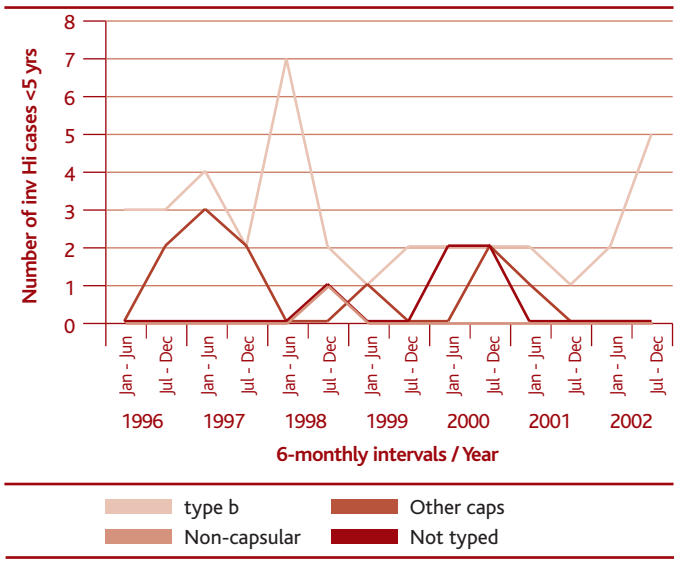

Figure 4. Number of invasive H. influenzae infections by serogroup in under-5 year olds

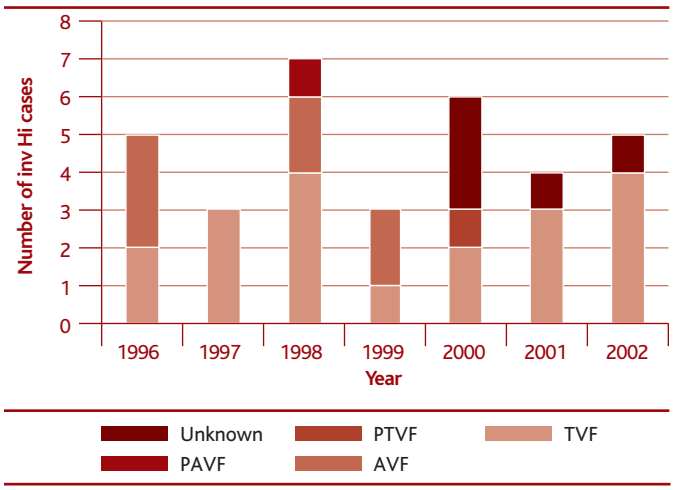

Figure 5. Number of Hib vaccine failures in Ireland, 1996-2002

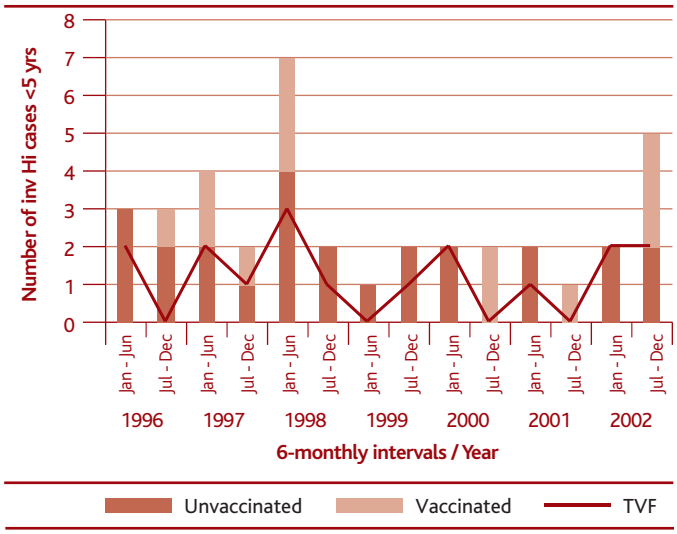

Figure 6. Number of H. influenzae type b cases and true vaccine failures (TVF) in <5 year olds.
Note: The difference between the number vaccinated and TVF is due to Apparent Vaccine Failures or where failure type not known

cases (2.5/100,000) were reported with five of these seen in the latter half of 2002. The increase in this age group continued into the first half of 2003 with six cases being reported to the end of June. Although the incidence of Hib infections in the under five year olds in Ireland in 2002 was similar to that reported in England and Wales in 2001, a far greater proportion of the cases in England & Wales were in vaccinated individuals (90%) when compared with Ireland (57%). Hib vaccine uptake at 24 months in UK is 94% compared to 84% in Ireland. Based on these observations it would indicate poor uptake of the Hib vaccine in Ireland may be as much a contributory factor to the recent increase in Hib infections as to any particular issue regarding the efficacy of the vaccine.

It is vital that the surveillance of invasive *H. influenzae* is improved in Ireland. Such improvements would ensure that any changes in trends of the disease can be detected in a timely manner and assist in identifying the reasons for these changes. Such information in return would enable informed public health decisions and actions to be taken regarding improved prevention of the disease if so required.

Acknowledgements

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References

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2. Steinhoff M, Goldblatt D, Conjugate Hib vaccines *Lancet* 2003; **361**: 360-361.