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EPIDEMIOLOGY OF *HAEMOPHILUS INFLUENZAE* DISEASE (INVASIVE) IN IRELAND

cidr

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Authorship:
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Further information:
For further information on meningococcal disease in Ireland, please see:
http://www.ndsc.ie/hpsc/A-Z/VaccinePreventable/Haemophilusinfluenzae/Publications/

For details on the surveillance and epidemiology of meningococcal disease in Europe, please see http://www.euibis.org/

Summary

In 2006, 38 cases of invasive *Haemophilus influenzae* disease were notified in Ireland (0.9/100,000 total population). This was similar to previous years when 34 and 38 cases were notified in 2005 and 2004, respectively.

Non-capsular strains accounted for the majority of the invasive *H. influenzae* cases in 2006 (53%, n=20/38). The remaining cases were due to *H. influenzae* type b (Hib) (n=14, 37%), type e (n=2, 5%) and not typed (n=2, 5%). Incidence rates of invasive *H. influenzae* were highest in infants (8.2/100,000) and in elderly adults 65 years of age and older (2.6/100,000). Two invasive *H. influenzae* related deaths were reported in 2006, both due to non-capsular strains, one occurred in a child and the other in an adult.

The number of Hib cases notified in 2006 (n=14) declined compared with 2005 (n=18). The most notable decline in Hib disease in 2006 was seen in the 1-4 years old age group with just one case occurring compared to 12 such cases occurring in this age group in 2005. A dramatic decline in the number of true Hib vaccine failures was also seen, decreasing from 14 in 2005 to four in 2006. These data highlight the positive impact the Hib booster catch-up campaign introduced in November 2005 for children aged less than 4 years, has had in 2006 in reducing the incidence of Hib disease and the number of Hib vaccine failures seen in Ireland.

Introduction

Strains of *Haemophilus influenzae* are defined under two major categories, encapsulated strains and unencapsulated strains. Encapsulated strains are characterised on the basis of differences in their capsular polysaccharides, six serotypes known to cause disease are recognised (types a-f). Of these six serotypes, *H. influenzae* type b (Hib) is the most common cause of invasive disease. Unencapsulated / non capsular strains can also cause disease and in countries where the Hib conjugate vaccine is used, non capsular strains can now account for a substantial proportion of invasive cases (European Union Invasive Bacterial Infections Surveillance Network, see http://www.euibis.org).

Hib disease was once the leading cause of bacterial meningitis and a major cause of other serious invasive diseases particularly among children aged <5 years. After the Hib conjugate vaccine was introduced in Ireland in October 1992, the overall incidence of invasive disease declined considerably, from approximately 100 cases (2.9/100,000) per year in the late 1980s to around 10 cases (0.2/100,000) annually by 2000.

However, towards the end of 2004 an increase in the number of Hib infections was observed, but most worrying was that infection was occurring predominantly in fully vaccinated children. This trend continued into early 2005. In the six month period between October 2004 and March 2005 nine Hib vaccine failures had occurred compared with between one and four annually over the previous six years, 1996-2003.

The increase in the number of Hib cases in fully vaccinated children led to concerns that a three dose schedule was no longer sufficient to maintain long term protection. Based on the advice of the National Immunisation Advisory Committee, the Health Service Executive (HSE) launched a catch up campaign in November 2005 offering a Hib booster dose to children <4 years of age in order to further protect this age group from Hib disease. This campaign ran until May 2006 and defaulters were followed up over the summer months. Since September 2006 a routine Hib booster dose has been included in the primary childhood immunisation schedule at 12 months of age. This is in addition to the three doses of Hib vaccine given at 2, 4 and 6 months of age.

This report presents the epidemiology of invasive *H. influenzae* disease in Ireland, 2006, including Hib disease and the impact of the Hib catch up booster campaign is assessed.

Case Definitions

Clinical description
A clinical picture compatible with invasive disease, i.e. bacteraemia, meningitis, arthritis, epiglottitis, osteomyelitis or cellulitis.

Case classification
Confirmed: A clinically compatible case that is laboratory confirmed by one of the following:

- Isolation of *H. influenzae* from a normally sterile site
- Detection of *H. influenzae* nucleic acid from a normally sterile site

Probable: A clinically compatible case with detection of *H. influenzae* antigen from a normally sterile site.

Possible: A case with clinical epiglottitis without any laboratory confirmation or with identification only from a non-sterile site.

Taken from Case Definitions for Notifiable Diseases. Infectious Diseases (Amendment No. 3) Regulations 2003 (SI No. 707 of 2003). Available at http://www.hpsc.ie

Materials and Methods

Invasive *H. influenzae* disease is a notifiable disease in Ireland since the Infectious Disease (Amendment) (No. 3) Regulations (SI No. 707 of 2003) came into effect on 1st January 2004. Both laboratories and clinicians are legally obliged to notify.

Prior to this date, data on invasive H. influenzae disease cases were obtained through regular laboratory surveys, bacterial meningitis notifications and reports from the Health Protection Agency (HPA) reference laboratory in the UK. In 1999 an enhanced surveillance system for invasive *H. influenzae* commenced.

Records relating to cases prior to 2004 are stored on an MS Access database. *H. influenzae* notifications from 2004 onwards are collated on the Computerised Infectious Disease Reporting (CIDR) system. In 2006, for laboratories and/or Departments of Public Health using CIDR, *H. influenzae* notifications were entered locally; events created and enhanced information updated. For areas not yet using CIDR, notifications including enhanced data were sent to HPSC, from where they were entered on CIDR. Approximately once per quarter data on CIDR were reconciled by HPSC with reports from the HPA Reference Laboratory in the UK on Irish *H. influenzae* isolates typed there. Quarterly validation and cleaning of data was undertaken between Departments of Public Health and HPSC and final validation and data checks were completed following year end.

Data analysis for this report was performed using Business Objects Reporting in CIDR and MS Excel. Census of Population 2006 figures were used as denominator data in the calculation of incidence rates.
The invasive *H. influenzae* figures presented in this report are based on data extracted from the CIDR system on 16th July 2007. These figures may differ from those published previously due to ongoing updating of notification data on CIDR.

Results

Haemophilus influenzae notifications

In 2006, 38 cases of invasive *H. influenzae* disease were notified in Ireland (0.9/100,000 total population). This was similar to previous years when 34 and 38 cases were notified in 2005 and 2004, respectively (figure 1).

Non-capsular strains accounted for the majority of the invasive *H. influenzae* cases in 2006 (53%, n=20/38). The remaining cases were due to *H. influenzae* type b (Hib) (n=14, 37%), type e (n=2, 5%) and not typed (n=2, 5%). The number of Hib cases declined by a quarter in 2006 when compared with the previous two years and the number of cases due to non-capsular strains doubled (figure 1).

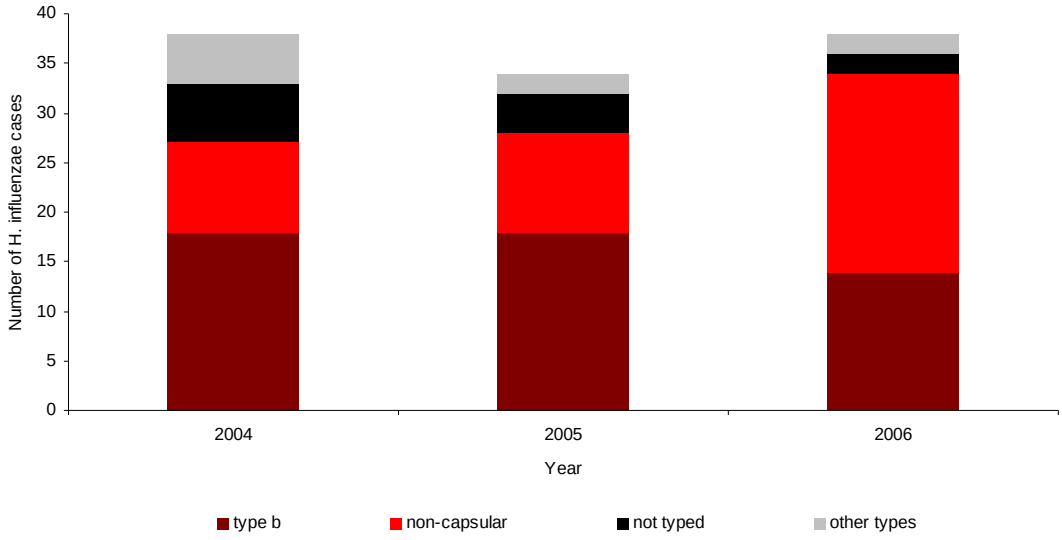


Figure 1. *Annual number of invasive Haemophilus influenzae cases notified in Ireland by serotype, 2004-2006*

The cases ranged in age from 2 weeks to 83 years. The incidence rates were highest in infants <1 year of age (8.2/100,000) and elderly adults 65 years of age and older (2.6/100,000), followed by 5-9 year old age group (2.1/100,000) (table 1). Cases in the young and the old accounted for 71% of the invasive *H. influenzae* notifications with 15 cases occurring in children under 10 years of age and 12 cases in elderly adults >65 years of age (table 1).

Regarding the 15 children with invasive *H. influenzae* in 2006, the clinical manifestations of the disease were as follows: septicaemia (n=4), meningitis (n=3), meningitis and septicaemia (n=1), epiglottitis (n=3), cellulitis (n=2) and clinical diagnosis not reported (n=2).

Two deaths associated with invasive *H. influenzae* disease occurred in 2006. One death was in an adult who presented with pneumonia and the other in a young child with meningitis. Both deaths were due to non-capsular strains of *H. influenzae*.

Table 1. *Haemophilus influenzae cases and Hib vaccine failures by serotype and age group, 2006*

	Type b	Type e	Non capsular	Not typed	Total	ASIR of Hib	ASIR of all *H. influenzae*	TVFs
<1	4	0	1	0	5	6.5	8.2	0
1-4	1	0	3	0	4	0.4	1.7	1
5-9	3	0	3	0	6	1.0	2.1	3
10-19	0	0	0	0	0	0.0	0.0	0
20-54	5	0	1	0	6	0.2	0.3	0
55-64	1	1	3	0	5	0.2	1.2	0
65+	0	1	9	2	12	0.0	2.6	0
All ages	**14**	**2**	**20**	**2**	**38**	**0.3**	**0.9**	**4**
CIR	0.3	0.05	0.5	0.05	0.9	-	-	-

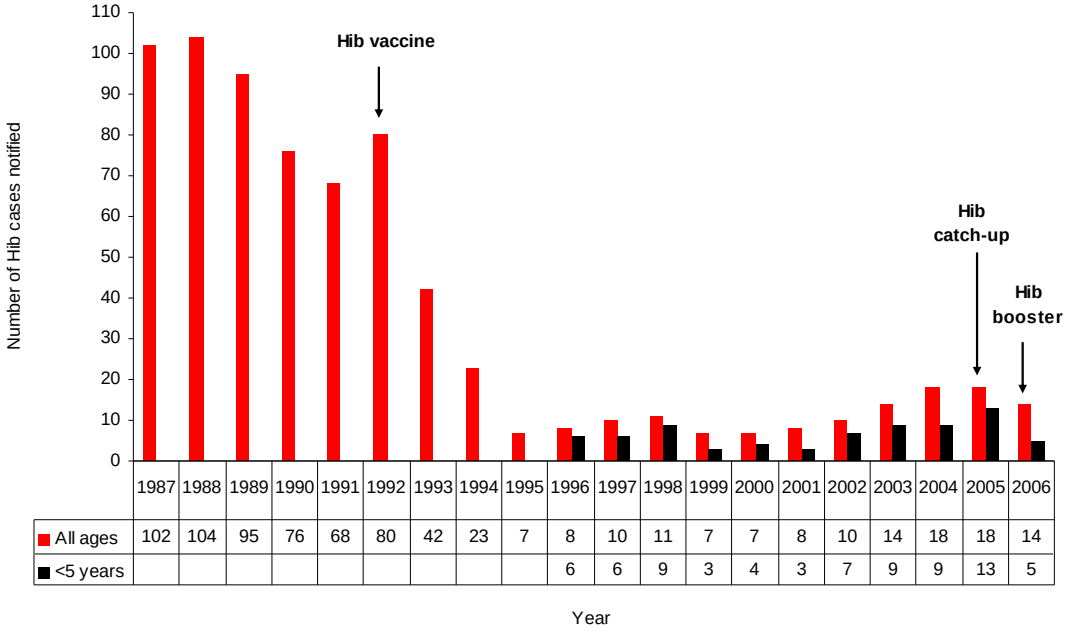
CIR, crude incidence rate per 100,000 total population
ASIR, age specific incidence rate per 100,000 population
TVFs, true Hib vaccine failures
A true Hib vaccine failure is defined as the occurrence of invasive Hib disease in an individual, despite being fully and age appropriately vaccinated in the past.

Haemophilus influenzae type b (Hib) notifications

H. influenzae type b (Hib) accounted for 37% of the invasive *H. influenzae* notifications in 2006. Fourteen cases were notified (0.3/100,000 total population) which is a slight decrease from the 18 cases notified in each of the previous two years (figure 2). The majority of the Hib cases in 2006 were in children (n=8, 57%); four cases occurring in infants <1year, one in 1-4 years age group and three cases in 5-9 years age group. These Hib cases presented as meningitis and/or septicaemia (n=4), epiglottitis (n=3) and cellulitis (n=1).

The number of Hib cases in <5 year olds (n=5) in 2006 was the lowest it had been since 2001 (figure 2). In particular in 2006, the greatest decline in Hib cases was seen in the 1-4 years old age group, with just one case occurring compared to 12 such cases in 2005.

There were no Hib related deaths reported in 2006.



	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
All ages	102	104	95	76	68	80	42	23	7	8	10	11	7	7	8	10	14	18	18	14
<5 years										6	6	9	3	4	3	7	9	9	13	5

Figure 2. *Number of Haemophilus influenzae tybe b (Hib) cases notified, in all age groups and in < 5 year olds, 1987-2006.*
Note data by age group available nationally since 1996 only.

Hib vaccine failures

A true Hib vaccine failure is defined as the occurrence of invasive Hib disease despite having being fully and age appropriately vaccinated in the past. An apparent Hib vaccine failure is defined as the occurrence of invasive Hib disease in an incompletely vaccinated individual.

In 2006, four true Hib vaccine failures occurred. This was a dramatic decrease from 2005, when 14 true vaccine failures arose (figure 3). The Hib vaccine failures in 2006 arose in children aged between 2 and 7 years, each had received three doses of Hib vaccine when they were less than one year of age. Three of the vaccine failures were in slightly older children, aged 5-7 years, which is in contrast with previous years when failures occurred predominantly in the 1-4 years age group (figure 3). Particularly in 2005, 12 of the 14 vaccine failures occurred in children <5 years of age. Of these 12 failures, 11 actually occurred in children aged <4 years.

In 2006, there were three apparent Hib vaccine failures compared to one in 2005. These failures occurred in children who had been incompletely immunised, all were <1 year of age and each had received only one dose of Hib vaccine.

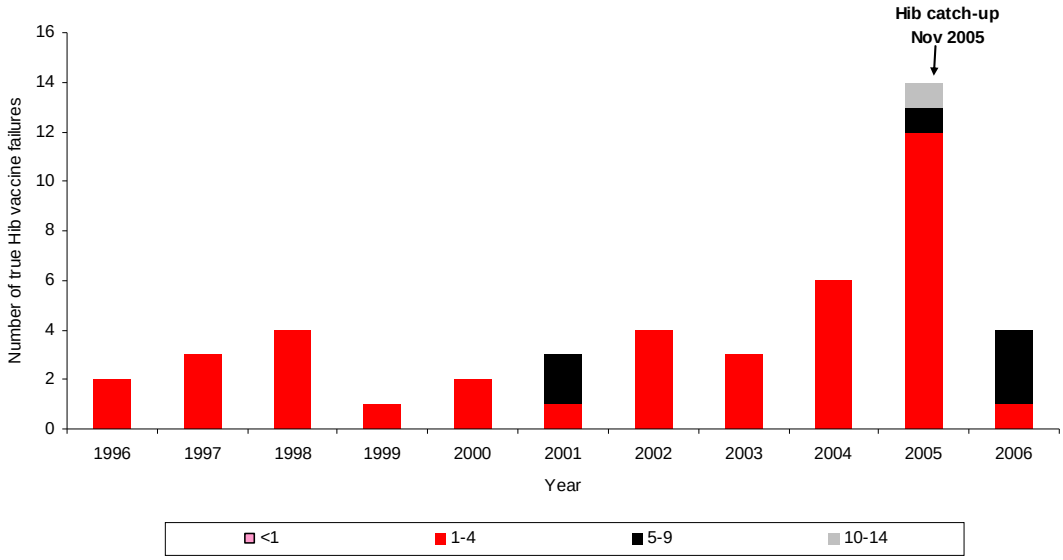


Figure 3. *Number of true Hib vaccine failures by age group, 1996-2006*

H. influenzae non-capsular notifications

In 2006 the number of invasive *H. influenzae* cases due non-capsular strains (n=20) doubled compared with previous years (figure 4). Increases were seen in all age groups, but in particular in elderly adults aged 65 years of age and older (figure 4). It is not clear whether this rise in non-capsular cases was due to true increase in invasive infection caused by this strain of *H. influenzae* or improved reporting by laboratories of invasive cases of the *H. influenzae* disease. Of the 20 non-capsular cases notified in 2006, cases ranged in age from 2 weeks to 83 years, with a median age of 58 years. Sixty five percent of cases (13/20) occurred in those aged 15 years of age and greater, elderly adults in particular accounted for almost half of the total cases (9/20) (figure 4) Two deaths attributed to invasive infection due *H. influenzae* non-capsular strains were notified, one in a young child and the other in a middle aged adult.

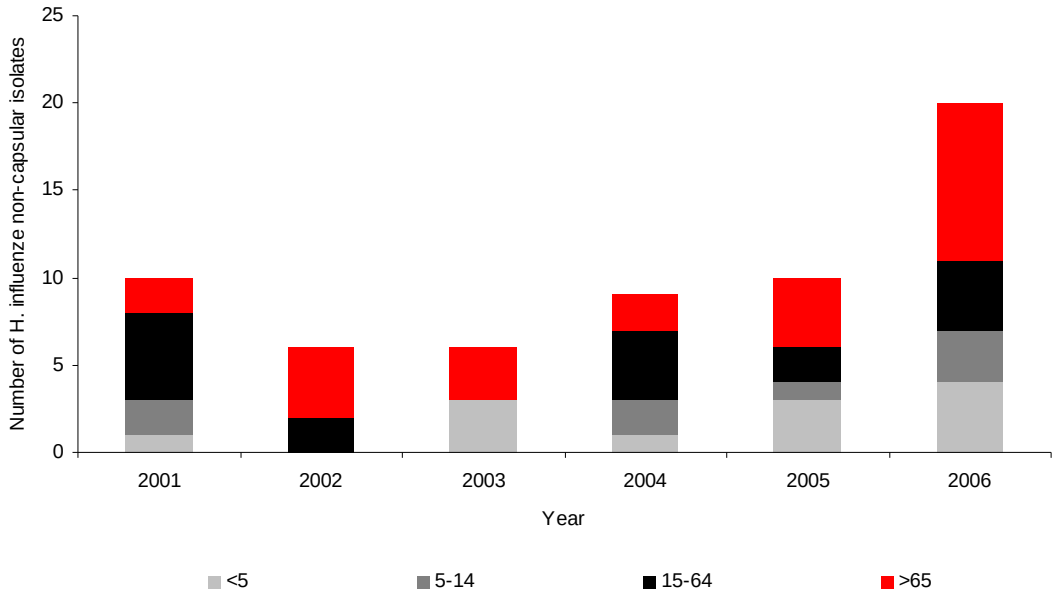


Figure 4. *Number of H. influenzae non-capsular notifications, 2001-2006*

Discussion

The latest trends regarding the epidemiology of invasive Hib disease in Ireland indicate the positive impact the Hib booster catch-up campaign has had in reducing Hib disease in children. In 2006, the lowest number of Hib cases in <5 year olds since 2001 was reported and in the age group targeted by the catch-up campaign (1-3 year olds) the number of Hib cases plummeted from eight and 12 cases in 2004 and 2005, respectively to just one case in this age group in 2006.

The number of Hib vaccine failures has also dropped dramatically from 14 in 2005 to four in 2006, which is back to levels seen in the years prior to the upsurge seen in late 2004, early 2005. Even more impressive has been the decline in the number of vaccine failures in children <5 years of age; six occurred in 2004, 12 in 2005 and just one in 2006. Unlike previous years, more Hib vaccine failures were seen in slightly older children in 2006, three failures occurred in the 5-14 years old age group. Two such failures occurred in this age group 2001 and 2005, whereas none arose in the intervening years.

Non capsular strains of *H. influenzae* accounted for the majority of the invasive cases of the disease in Ireland in 2006. These cases occurred predominantly (65%) in adults. The two *H. influenzae* related deaths reported in 2006 were also due to non capsular strains. Therefore, non capsular strains contribute substantially to the morbidity and mortality associated with invasive *H. influenzae* disease.

The decline in Hib disease and especially in cases associated with vaccine failures is encouraging and is an indication of the immensely valuable impact the Hib booster catch-up campaign is having in protecting children from this disease. However, Hib disease continues to pose a threat to Irish children due to the continued circulation of the bacteria in the population in general. To ensure Irish children are protected from this disease on an ongoing basis, it is important that parents ensure their children are fully vaccinated, that 95% Hib vaccine uptake levels are reached in the infant population and that children receive the Hib booster dose at 12-13 months of age.