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2006

EPIDEMIOLOGY OF MENINGOCOCCAL DISEASE IN IRELAND



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Further information:

For further information on meningococcal disease in Ireland, please see:
<http://www.ndsc.ie/hpsc/A-Z/VaccinePreventable/BacterialMeningitis/>

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

Summary

In 2006, there was a very slight increase in the epidemiology of invasive meningococcal disease (IMD) in Ireland compared with recent years. Two hundred and ten cases of invasive meningococcal disease were notified in 2006 (5.0/100,000), while in 2005 and 2004, 203 and 198 cases, were notified, respectively.

The majority of the notifications in 2006 (82%) were classified as definite cases and 88% of notifications were laboratory confirmed. Detection of *N. meningitidis* nucleic acid by PCR was the diagnostic technique most commonly used in confirming these cases.

The incidence of IMD in 2006 was higher in males than in females, with a male to female ratio of 1.6:1.0. Incidence of IMD was highest in infants (86.8/100,000) and young children aged 1-2 years (46.2/100,000) and lowest in adults, 25 years of age and older (0.8/100,000).

Serogroup B accounted for the majority (80%) of the 2006 IMD notifications, 169 cases were notified. There were just four cases of serogroup C IMD and one of these cases was a MenC vaccine failure.

In 2006, there were five IMD related deaths giving a case fatality ratio (CFR) of 2.4%. There were six deaths in 2005 (CFR, 3.0%) and 10 deaths in 2004 (CFR, 5.1%). The five deaths in 2006 were all due to serogroup B disease and four of these deaths occurred in children <3 years of age.

Introduction

Disease caused by *Neisseria meningitidis* is a global problem. The incidence of the disease varies with age, season and geographical location. Invasive meningococcal disease (IMD) incidence is highest in young children and disease occurrence tends to peak during the winter months. Annual incidence rates of IMD vary from <1 per 100,000 in many developed countries to as high as 1,000 per 100,000 during epidemics in areas of sub Saharan Africa.¹ Serogroup distribution also varies according to geographical location. IMD infection in Africa is most commonly associated with serogroups A and W135, in Europe with serogroups B and C and in USA serogroup Y accounts for approximately one third of the cases.

The epidemiology of IMD has evolved in Ireland over the last 10 years. In the late 1990s, the disease was hyperendemic in this country, with annual incidence rates of almost 15 cases per 100,000 population occurring, the highest in Europe.² At that time serogroup B accounted for almost two thirds of the cases and serogroup C one third. The introduction of the meningococcal C conjugate (MenC) vaccine in October 2000 to the routine childhood immunisation schedule and a catch-up programme for under 23 year olds saw a 75% reduction in serogroup C disease within one year.³ By the end of 2003 the incidence of serogroup C disease had declined by 96% compared with the pre MenC vaccine era. As a result of this huge decline and coupled with a steady decrease in serogroup B cases over recent years, the overall incidence of IMD in Ireland has declined to approximately 5 cases per 100,000 population annually.³ Ireland has thus emerged from the hyperendemic period and IMD is presently at endemic levels.

Despite the relative reduction in the occurrence of IMD in recent times, IMD is still a serious, life-threatening illness that can progress rapidly. Prompt recognition and aggressive early treatment are the only effective measures against IMD once it occurs.⁴ Due to its rapid onset, high case fatality, and the occurrence of complications in a high proportion of survivors, IMD continues to remain high priority on the public health agenda both in Ireland and elsewhere.

The epidemiology of IMD in Ireland, 2006 is presented in this report.

Case Definitions⁵

For surveillance purposes, cases of invasive meningococcal disease are classified as definite, presumed or possible. Definitions for these classifications are provided below.

A **Definite** case of meningococcal infection includes children or adults who have:

- *N. meningitidis* isolated from blood, cerebrospinal fluid or other normally sterile body site (e.g. synovial fluid, pleural or pericardial fluid) or from a petechial or purpuric lesion
- A positive PCR test for meningococcus obtained on blood, cerebrospinal fluid or specimen from another sterile site.

A **Presumed** case of meningococcal infection includes children or adults who have:

- Gram negative intracellular diplococcus detected in cerebrospinal fluid on microscopy
- *N. meningitidis* isolated from an eye, throat or nasal swab, together with characteristic purpuric rash
- *N. meningitidis* isolated from an eye, throat or nasal swab and who have clinical and laboratory features of bacterial meningitis (cerebrospinal fluid pleocytosis) in whom no other cause of meningitis is identified
- A clinically compatible illness and who have gram negative intracellular diplococci detected in skin scrapings taken from the characteristic haemorrhagic rash
- A clinically compatible illness with a serological response which is reported by a reference laboratory as consistent with recent acute infection.

A **Possible** case of meningococcal infection includes children and adults who have:

- Evidence of acute sepsis, with or without meningitis, together with characteristic haemorrhagic purpura
- Clinical evidence of sepsis without a purpuric rash, in whom no other cause of sepsis is identified, and in whom meningococcus is isolated from an eye, throat or nasal swab
- Received pre-admission antibiotics, have laboratory evidence of bacterial meningitis but are culture negative.

Materials and Methods

Invasive meningococcal disease (IMD) is notifiable in Ireland. From 1982-2003, it was notifiable under the disease bacterial meningitis (including meningococcal septicaemia). With the introduction of the Infectious Diseases (Amendment) (No.3) Regulations 2003 (SI No. 707 of 2003) on 1st January 2004, meningococcal disease became a notifiable disease in its own right.

An enhanced surveillance system for IMD has been in place in Ireland since 1997. Case based data from this surveillance system are available nationally since 1999 and all these notifications are now on the Computerised Infectious Disease Reporting (CIDR) system.

The case definition outlined in the previous page is used.

In 2006, for laboratories and/or Departments of Public Health using CIDR, IMD 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 it was entered on CIDR. The IMD notification data on CIDR were reconciled monthly by HPSC with the Irish Meningococcal and Meningitis Reference Laboratory (IMMRL) national database on laboratory confirmed cases. Quarterly validation and cleaning of IMD notification 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. Censuses of Population used as denominator data in the calculation of IMD incidence rates were applied as follows; Census 2006 for 2004-2006 data, Census 2002 for 2000-2003 data and Census 1996 for 1999 data. The Irish population from Census 2006 was used as the standard population in the direct age standardisation of the 2006 IMD data. Age standardisation was undertaken to control for the confounding effect of age to enable comparison of incidence rates between HSE areas.

The IMD figures presented in this report are based on data extracted from the CIDR system on 1st August 2007. These figures may differ from those published previously due to ongoing updating of notification data on CIDR.

Results

IMD notifications

In 2006, 210 cases of IMD (5.0/100,000) were notified in Ireland, which is a very slight increase from the previous two years when 203 cases (4.8/100,000) and 198 cases (4.7/100,000) were notified in 2005 and 2004, respectively (figure 1). Overall, the epidemiology of IMD has been largely unchanging over the last four years with less than 250 cases notified per annum contrasting with 1999 and 2000 when greater than 500 cases were occurring per annum (figure 1).

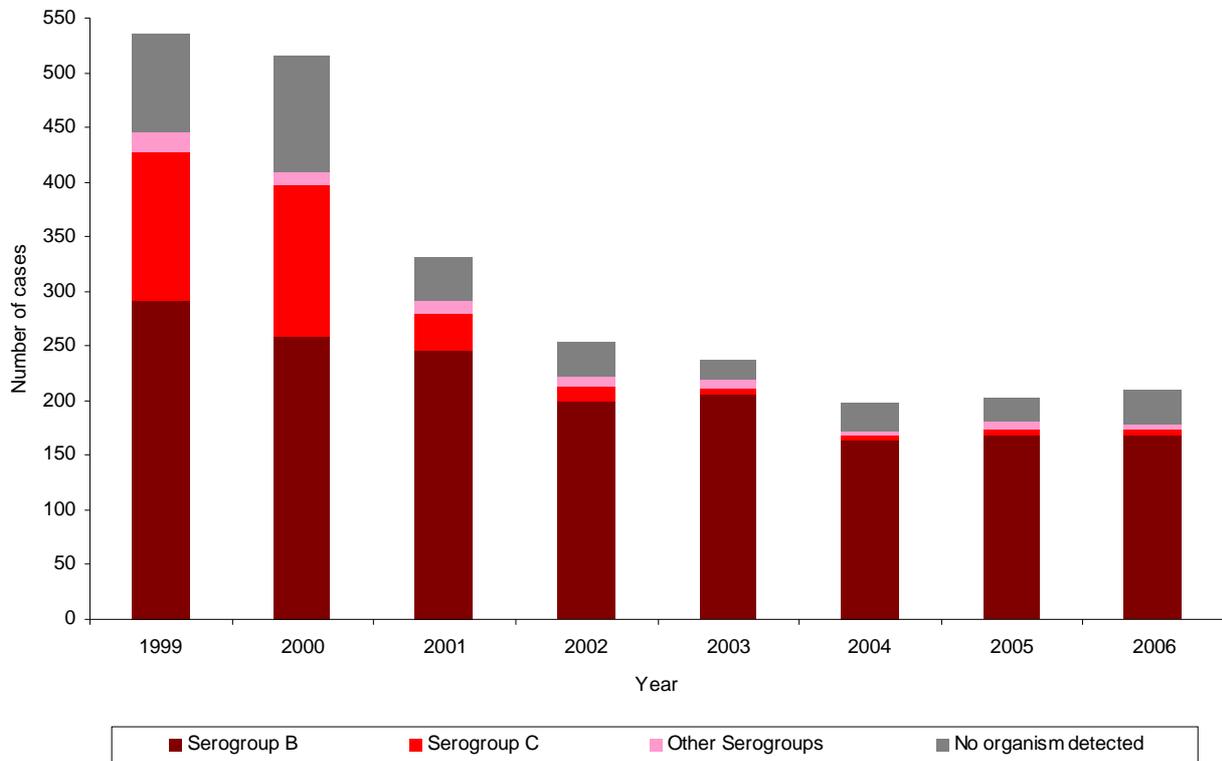


Figure 1. Annual number of invasive meningococcal disease notifications in Ireland by serogroup, 1999-2006

One hundred and seventy three of the notifications were classified as definite (82%), seven as presumed (3.3%) and 30 as possible (14%) in 2006 (table 1). Eighty-eight percent of cases were laboratory confirmed (184/210). The majority were confirmed by PCR alone (57%, n=105). Confirmation of the remaining cases was by culture alone (n=17), PCR and culture (n=52), serology (n=5) and microscopy (n=5).

Table 1. *Number of invasive meningococcal disease notifications in Ireland by serogroup and case classification, 2006*

	Definite	Presumed	Possible	Total
Serogroup B	163	5	1	169
Serogroup C	4	0	0	4
Serogroup W135	1	0	0	1
Serogroup Y	4	0	0	4
Non-groupable (NG)	1	0	0	1
No organism detected	0	2	29	31
Total	173	7	30	210

IMD by age and gender

In 2006, male cases (n=128) exceeded female cases (n=82), resulting in a male to female ratio for IMD of 1.6:1.0. Cases ranged in age from 2 weeks to 84 years, with a median age of two years. The incidence of IMD was highest in infants and young children (figure 2). Infants <1 year of age had an age specific rate of 86.8 per 100,000, followed by the 1-2 year olds (46.2/100,000) and then the 15-19 year olds (10.3/100,000). Thereafter, the incidence declined considerably in the older age groups (figure 2). There was a decrease in the incidence of IMD in 3-4 years age group (9.2/100,000) in 2006 when compared with recent years, when 19.2 cases per 100,000 occurred in this age group in 2004 and 15.4 cases per 100,000 in 2005. On the other hand an increase in the incidence of the disease in the 15-19 years age group was seen in 2006, with 10.3 cases per 100,000 population occurring, the highest incidence seen in this age group since 2001.

Since 2004, the distribution of cases by age-group has been very similar and incidence has declined considerably in infants, children and teenagers when compared with 2000 (figure 2).

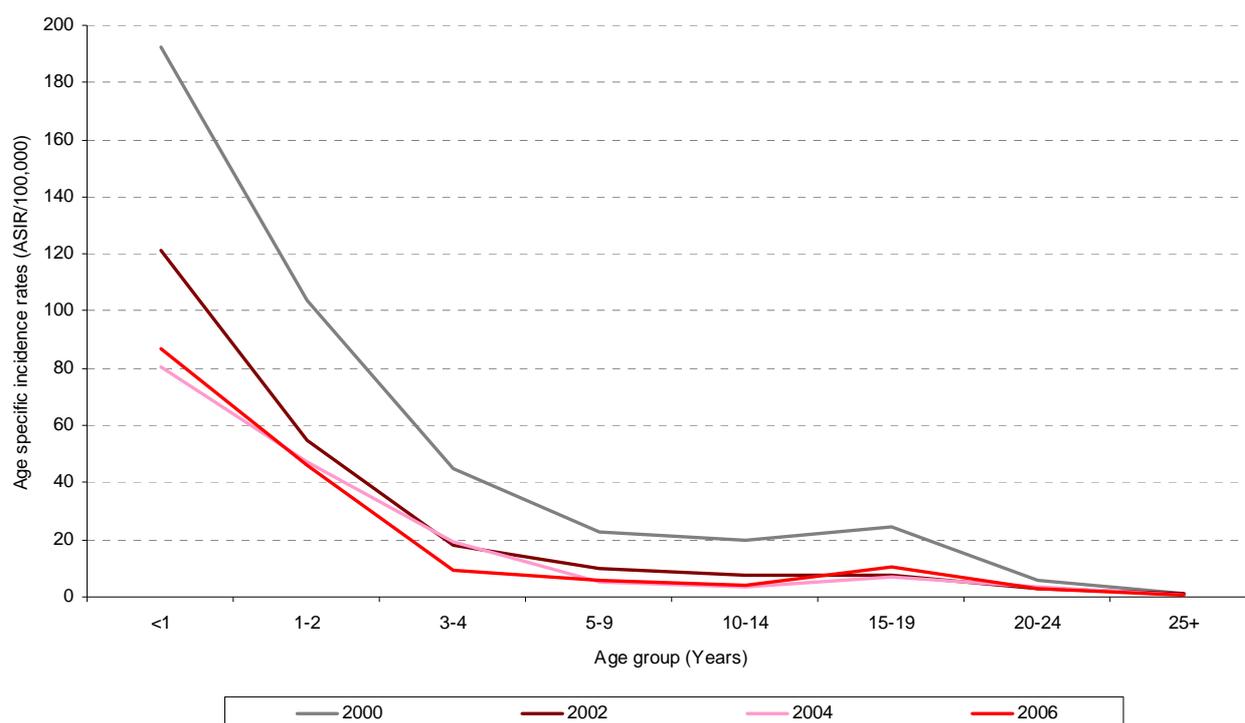


Figure 2. Age specific incidence rates of invasive meningococcal disease in Ireland in 2000, 2002, 2004 and 2006.

IMD by serogroup

Neisseria meningitidis serogroup B was the pathogen most commonly associated with IMD, in 2006 and accounted for 80% (n=169) of the notifications (figure 1 and table 1). Each year since 2003 serogroup B has accounted for 80% or more of the IMD notifications (figure 1). Over half of the serogroup B cases in 2006 occurred in young children aged <5 years (57%, 96/169).

IMD due to serogroup C has remained at very low levels over the last four years with no more than five cases occurring annually. In 2006, just four (0.09/100,000) serogroup C cases arose (figure 1). One case occurred in a young child, while the remaining three were in adults (age range 22-84 years). Serogroup C disease has declined in all age groups when compared with 2000. Overall, there has been a 97% decline in serogroup C cases (table 2). In 2006, there were no serogroup C cases in <1 year olds and in the age groups between 3-19 years (100% decline).

IMD due to non B/non C serogroups continued to remain low, with just one serogroup W135, four serogroup Y and one non-groupable cases being reported in 2006 (table 1).

Table 2. Number of serogroup C cases of invasive meningococcal disease notified in 2006 compared with 2000 and percentage decline

	2000	2006	% Decline
<1	20	0	100
1-2	24	1	96
3-4	13	0	100
5-9	15	0	100
10-14	20	0	100
15-19	31	0	100
20-24	8	1	86
25+	8	2	75
Total	139	4	97

MenC vaccine failures

A MenC vaccine failure is serogroup C disease occurring in an individual despite having been fully vaccinated against this form of IMD in the past. There was one MenC vaccine failure in 2006, which was in a child aged between 1-2 years having received three doses of MenC as an infant (figure 3). The remaining three serogroup C cases notified in 2006 had not been vaccinated, although one was in a young adult who was eligible for vaccination at the time of the MenC catch-up campaign. One MenC vaccine failure also occurred in 2005, this too was in a fully vaccinated child aged 1-2 years. There were no MenC vaccine failures in either 2004 or 2003 (figure 3). All cases of serogroup C disease associated with MenC vaccine failures survived the illness.

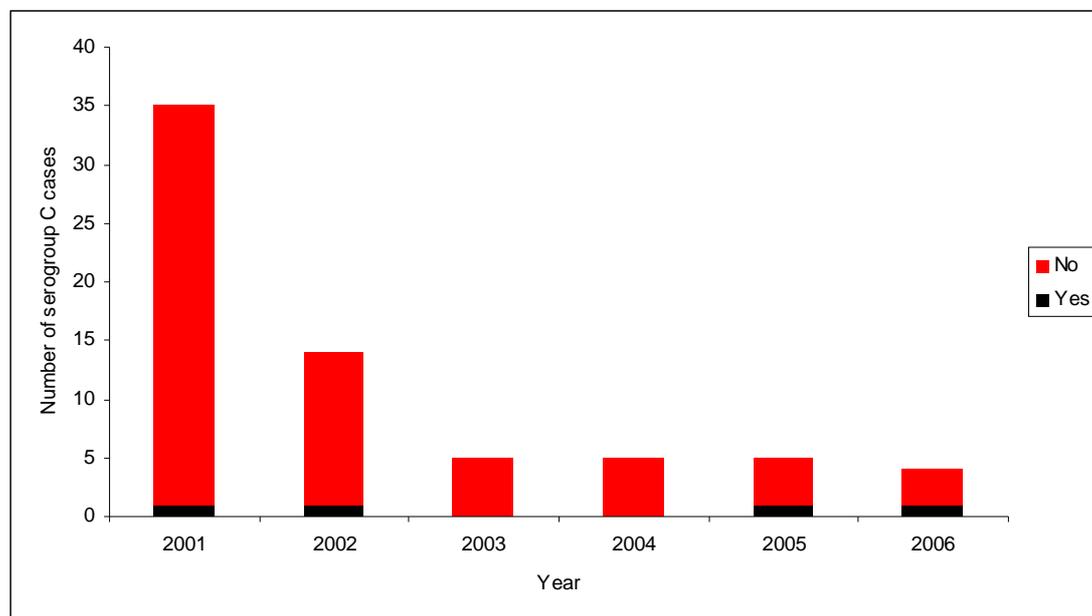


Figure 3. Number serogroup C cases notified 2001-2006 and whether associated with a vaccine failure (yes) or not (no)

IMD by HSE area

In 2006, the national crude incidence rate was 5.0 cases per 100,000 total population. Incidence ranged from 3.1 per 100,000 population in HSE-W to 5.8 per 100,000 in HSE-MW (figure 4). Five of eight HSE areas had crude incidence rates within 0.2 of the national rate i.e. between 4.8 and 5.2 cases per 100,000. To adjust for the confounding effect of age across HSE areas, direct age standardisation of the 2006 IMD data was undertaken. The trends were the same as for the crude incidence rates with HSE-W having the lowest rate (3.2/100,000; 95% CI 1.4-4.9/100,000) and HSE-MW the highest (5.9/100,000; 95% CI 3-4-8.4/100,000) (figure 4). None of the rates in the HSE area were considered statistically different from the national rate of 5.0 per 100,000 (95% CI 4.3-5.6/100,000) since the confidence intervals overlapped (figure 4).

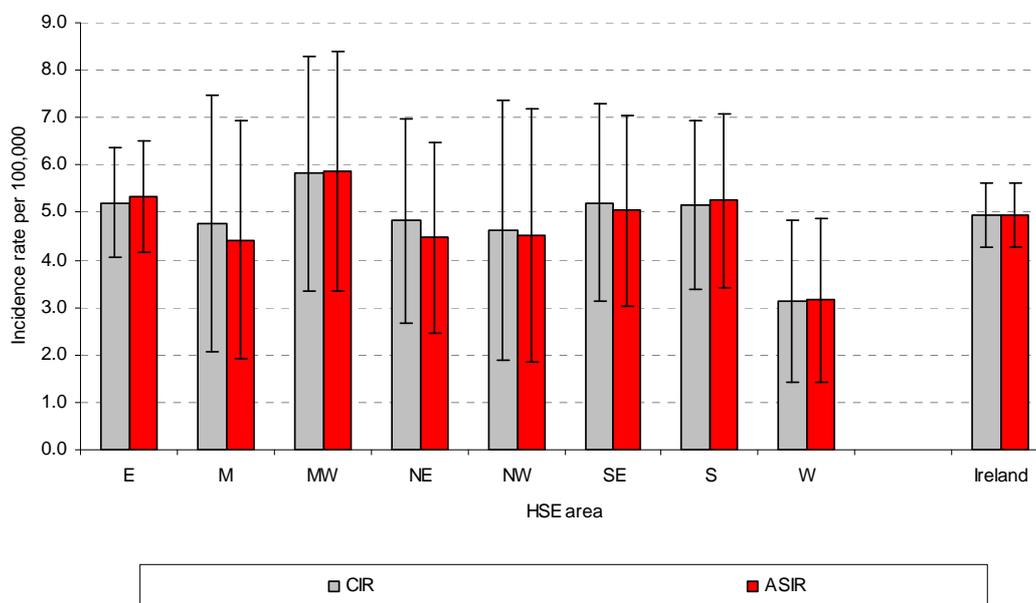


Figure 4. Crude incidence rates (CIR) and age standardised incidence rates (ASIR) with 95% confidence intervals for invasive meningococcal disease by HSE area, in 2006

The crude incidence of serogroup B disease per 100,000 population ranged from 2.4 per 100,000 in HSE-W to 5.3 per 100,000 in HSE-MW, with a national incidence rate of 4.0 per 100,000 (figure 5). For other serogroups which included serogroups C, W135, Y and non-groupable (NG) the national incidence rate was very low at 0.2 per 100,000 population with three of the eight HSE areas having no cases attributable to these serogroups (figure 5).

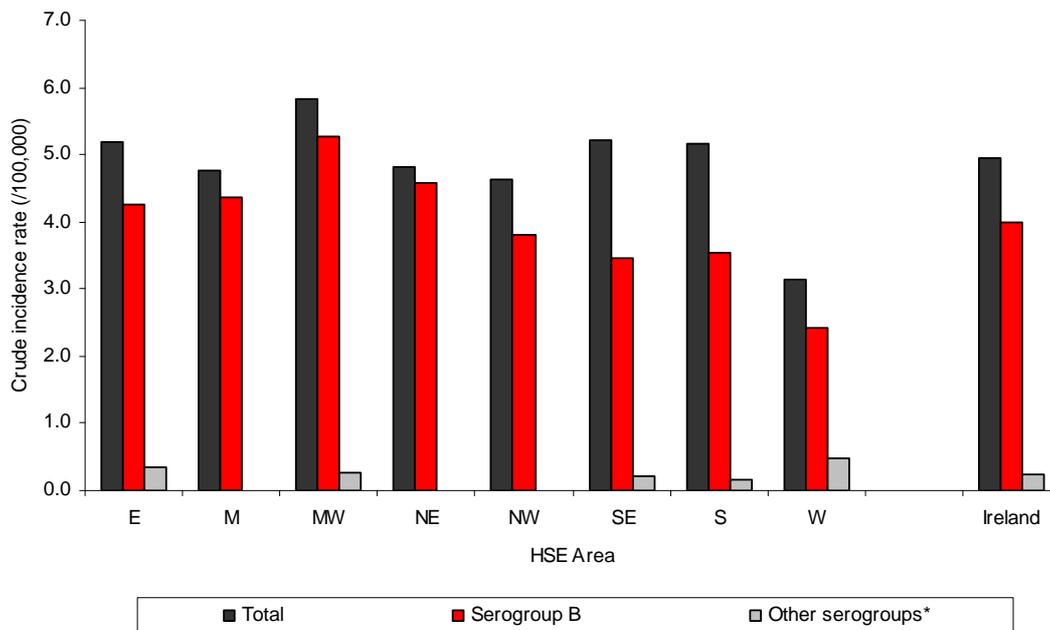


Figure 5. Crude incidence rates of total, serogroup B and other serogroups of invasive meningococcal disease by HSE area in 2006

*Other serogroups include C, W135, Y and non-groupable (NG)

Note: Total = serogroup B + other serogroups + cases where no organism detected

IMD deaths

In 2006, five IMD associated deaths occurred in Ireland, giving a case fatality ratio of 2.4%. There were six IMD related deaths in 2005 and 10 in 2004. The five deaths in 2006 were all due to serogroup B disease with four of these deaths occurring in children <3 years of age. The other death was in an adult.

No serogroup C deaths occurred in either 2005 or 2006 while one each occurred in 2003 and 2004, both in middle aged adults. Thus, no young person has died from serogroup C disease in Ireland since 2001.

Other forms of bacterial meningitis

Streptococcus pneumoniae

In 2006, 23 cases of pneumococcal meningitis were notified, compared to 19 in 2005 and 22 in 2004 (table 3). Cases ranged in age from 1 month to 80 years in 2006. There were three pneumococcal meningitis related deaths reported, all were in adults. However, it should be noted that the pneumococcal meningitis figures presented here may be an underestimate of the true burden of this disease because in 2006 of the 293 cases of invasive pneumococcal disease notified, clinical diagnosis was reported for just 55 of these (23 of which were due to meningitis). Therefore, clinical diagnosis was not reported for 238 of these notifications.

Haemophilus influenzae

In 2006, four cases of meningitis due to *H. influenzae* were notified (table 3). Three cases were in young infants, age <6 months and all were due to *H. influenzae* type b. The fourth case caused by *H. influenzae* non-capsular was in a 2 year old child. This patient died.

Group B Streptococci

Four cases of meningitis due to *Streptococcus agalactiae* were notified in 2006. All were neonatal cases. No deaths were reported.

Table 3. Annual number of other forms of bacterial meningitis notified

Notified under	Causative Pathogen	2004	2005	2006
<i>Streptococcus pneumoniae</i> infection (invasive)	<i>Streptococcus pneumoniae</i>	22	19	23
<i>Haemophilus influenzae</i> disease (invasive)	<i>Haemophilus influenzae</i>	4	9	4
Listeriosis	<i>Listeria monocytogenes</i>	1	1	1
Streptococcus group A infection (invasive)	<i>Streptococcus pyogenes</i>	0	1	1
Tuberculosis	<i>Mycobacterium tuberculosis</i>	6	9	6*
Bacterial meningitis (not otherwise specified)	<i>Escherichia coli</i>	1	0	3
	<i>Klebsiella pneumoniae</i>	0	0	1
	<i>Pseudomonas aeruginosa</i>	1	1	0
	<i>Staphylococcus aureus</i>	0	1	1
	Staphylococcus Coagulase negative	0	0	1
	<i>Streptococcus agalactiae</i> (Group B haemolytic Streptococcus)	6	5	4
	Streptococcus Group C	0	1	0
	Unknown	28	22	36
	Total BacMen (nos)	36	30	46
Grand Total - Other forms of Bacterial Meningitis		69	69	81

* TB meningitis figure for 2006 is provisional

Escherichia coli

Three cases of *E. coli* meningitis were notified in 2006. Two were neonatal cases occurring in infants <1 month of age and one in an older infant <1 year of age.

Mycobacterium tuberculosis

In 2006, six *M. tuberculosis* meningitis cases were notified (provisional figure). Cases ranged in age from 1-74 years, involving four children and two adults. Four of the six *M. tuberculosis* meningitis cases were in individuals born in Ireland. No deaths were reported.

Other causative pathogens

Cases of bacterial meningitis due to other pathogens were notified in 2006. One meningitis notification each were received for the following: *Listeria monocytogenes* in a middle aged adult, *Klebsiella pneumoniae* in a 1 month old, *Staphylococcus aureus* in a 1 year old, coagulase negative staphylococcus in an infant <1 year and *Streptococcus pyogenes* (group A streptococcus) in a teenager.

Bacterial meningitis (not otherwise specified)

In total 46 cases of meningitis under the disease category bacterial meningitis (not otherwise specified) were notified in 2006. The causative pathogens were identified in 10 of these and are detailed above (see group B streptococci, *E. coli*, *K. pneumoniae*, *S. aureus* and coagulase negative staphylococcus). No causative pathogen was identified for 36 of the notifications, an increase compared to 2005 (n=22) and 2004 (n=28). The 36 cases in 2006 where a causative pathogen was not identified ranged in age from 2 weeks to 86 years. One third of these cases (n=12) were in infants <1 year of age.

A marked increase in viral meningitis activity was also seen in 2006, with 148 cases being notified compared to 35 cases in 2005 (see relevant chapter in HPSC annual report 2006 for further details). There is a possibility that some of the bacterial meningitis cases of unknown aetiology reported in 2006 may in fact be viral meningitis cases but could not be distinguished clinically, hence explaining the increase in the former.

Discussion

The epidemiology of IMD in Ireland has remained largely unchanged in recent years, with incidence rates now almost one third of what they were in 1999 and 2000. The greatest reduction has been in serogroup C disease with incidence rates declining from 3.7 per 100,000 in 1999 to 0.09 in 2006, a reduction of 97%. This is a reflection of the hugely positive impact the introduction of the MenC vaccine had on reducing the incidence of serogroup C disease in Ireland. The attack rate due to serogroup B disease has halved in recent years, from incidence rates of 8.1 per 100,000 in 1999 to 4.0 per 100,000 in both 2005 and 2006. Serogroup B now accounts for 80% of cases of IMD with well over half of these occurring in young children.

In 2006, 120 of the 210 IMD cases notified (57%) occurred in children <5 years of age and 80% of cases in this age group were due to serogroup B disease. The highest incidence rate by far was seen in infants <1 year of age. The five IMD related deaths in 2006 were all due to serogroup B and four of the five deaths were in young children. Therefore, morbidity and mortality due to IMD in Ireland remains highest in infants and young children and continues to be treated as a serious public health concern.

Effective vaccination is necessary for the comprehensive prevention and control of IMD. However, the meningococcal vaccines available are only effective against serogroups A, C, W135 and Y. The development of a serogroup B vaccine that is effective in infants has proven problematic. For several reasons conventional methods of vaccine development have failed to produce a vaccine with a broad range of protection against circulating serogroup B strains. Safe and effective serogroup B vaccines that are suitable for use in infants and young children are needed to fully achieve prevention and control of IMD in Ireland.

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Appendix 1: Annual Number of Meningococcal Disease Notifications by HSE Area

Total Meningococcal Disease Notifications

	1999	2000	2001	2002	2003	2004	2005	2006
HSE-E	232	192	122	89	74	62	64	78
HSE-M	28	33	22	18	23	10	21	12
HSE-MW	40	31	28	27	24	16	16	21
HSE-NE	50	50	20	25	21	20	18	19
HSE-NW	18	20	17	14	8	16	11	11
HSE-SE	49	71	43	24	30	28	19	24
HSE-S	91	86	51	41	46	34	36	32
HSE-W	28	32	27	15	11	12	18	13
Ireland	536	515	330	253	237	198	203	210
CIR*	14.8	13.1	8.4	6.5	3.1	4.7	4.8	5.0

* National crude incidence rate per 100,000 total population

Serogroup B Meningococcal Disease Notifications

	1999	2000	2001	2002	2003	2004	2005	2006
HSE-E	146	123	95	71	68	52	51	64
HSE-M	15	19	17	15	19	9	17	11
HSE-MW	19	15	24	19	23	15	15	19
HSE-NE	28	30	15	23	20	16	17	18
HSE-NW	11	10	14	10	7	14	10	9
HSE-SE	21	28	24	14	23	19	11	16
HSE-S	38	20	34	32	39	27	33	22
HSE-W	14	13	22	15	7	11	15	10
Ireland	292	258	245	199	206	163	169	169
CIR*	8.1	6.6	6.3	5.1	5.3	3.8	4.0	4.0

* National crude incidence rate per 100,000 total population

Appendix 2: Annual Number of Meningococcal Disease Deaths by HSE Area

Total Meningococcal Disease Deaths

	1999	2000	2001	2002	2003	2004	2005	2006
HSE-E	5	10	2	4	3	3	5	5
HSE-M	1	2	0	2	2	1	0	0
HSE-MW	2	1	2	0	3	0	0	0
HSE-NE	2	5	0	2	0	2	1	0
HSE-NW	2	2	1	0	0	1	0	0
HSE-SE	1	2	1	0	1	2	0	0
HSE-S	3	1	4	0	3	1	0	0
HSE-W	1	2	2	0	0	0	0	0
Ireland	17	25	12	8	12	10	6	5
CFR*	3.2	4.9	3.6	3.2	5.1	5.1	3.0	2.4

* Case fatality ratio, number of deaths/number of cases x 100%

Serogroup B Meningococcal Disease Deaths

	1999	2000	2001	2002	2003	2004	2005	2006
HSE-E	4	6	2	4	3	2	4	5
HSE-M	1	1	0	2	1	1	0	0
HSE-MW	1	1	1	0	3	0	0	0
HSE-NE	2	3	0	2	0	0	1	0
HSE-NW	1	0	0	0	0	1	0	0
HSE-SE	1	1	1	0	1	2	0	0
HSE-S	2	0	2	0	3	1	0	0
HSE-W	0	1	2	0	0	0	0	0
Ireland	12	13	8	8	11	7	5	5
CFR*	4.1	5.0	3.3	4.0	5.3	4.3	3.0	3.0

* Case fatality ratio, number of deaths/number of cases x 100%

Appendix 3: Annual Number of Meningococcal Disease Notifications and Deaths by Age Group

Meningococcal Disease Notifications

	1999	2000	2001	2002	2003	2004	2005	2006
<1	128	105	84	66	68	49	52	53
1-4	179	166	101	81	77	80	76	67
5-9	65	60	41	26	18	15	15	17
10-14	51	57	29	22	14	9	12	11
15-19	56	76	33	23	26	21	19	30
20-24	25	20	16	10	8	11	8	9
25-34	7	9	10	8	10	5	3	4
35-44	6	6	2	5	2	2	3	5
45-54	5	7	5	2	4	2	2	7
55-64	4	5	2	5	7	2	8	2
65+	9	4	7	5	3	2	4	5
Unknown	1	0	0	0	0	0	1	0
Total	536	515	330	253	237	198	203	210

Note: age-groups are age in years

Meningococcal Disease Deaths

	1999	2000	2001	2002	2003	2004	2005	2006
<1	2	6	6	5	5	2	3	2
1-4	6	5	1	3	1	6	2	2
5-9	2	0	0	0	0	0	0	0
10-14	0	3	1	0	2	0	0	0
15-19	1	7	1	0	1	0	0	0
20-24	3	3	1	0	0	0	1	1
25-34	0	0	0	0	0	1	0	0
35-44	0	0	0	0	0	0	0	0
45-54	1	0	0	0	0	0	0	0
55-64	1	0	1	0	2	0	0	0
65+	1	1	1	0	1	1	0	0
Total	17	25	12	8	12	10	6	5

Note: age-groups are age in years