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# Botulism in Injecting Drug Users, Dublin, Ireland, 2008.

On Monday, 24 November 2008, public health authorities in Dublin were notified that an injecting drug user (IDU) had been admitted to a Dublin hospital with neurological signs suggestive of botulism. Serum was sent to the Botulism Reference Laboratory, Colindale. The patient required treatment with botulism anti-toxin and supportive measures. This patient was subsequently confirmed as suffering from botulism; *Clostridium botulinum* toxin type B was identified as the causative toxin. By Friday, 28th November three additional suspected cases of botulism were reported, all of whom received anti-toxin. Two further suspect case were reported to the Department of Public Health Service Executive (HSE) Eastern region on December 9<sup>th</sup> and 10<sup>th</sup>. Both received anti-toxin. The latter patient died shortly after admission. These six patients were admitted to four different hospitals. All patients were injection drug users, four of whom reported injection of heroin subcutaneously ("skin popping"). There were no obvious linkages or clustering of the six patients, in terms of their areas of residence or in terms of their drug supply.

For the purpose of this investigation a *possible* case of wound botulism was defined as a person, in the Republic of Ireland, with acute onset of symmetrical cranial nerve palsy or difficulty in swallowing or speech, unexplained stridor or difficulty breathing or descending flaccid paralysis without any obvious cause since November 1, 2008. A *probable* case was defined as having the clinical features of a possible case and occurring in a person with a history of injecting drug use. A *confirmed* case was defined a having the features of a probable case in whom a diagnosis of botulism was laboratory confirmed. (detection of botulinum toxin in serum or isolation of *Clostridium botulinum* from a wound or abscess site).

A summary of selected demographic, clinical, and drug use for each case is presented in table 1.

Case (no)	Sex	Age (years)	Onset symptoms	Date of admission	Ventilatory support required	Anti toxin given	Heroin use	Outcome
1	М	33	20.11.2008	20.11.2008	no	yes	yes	Alive
2	М	23	21.11.2008	27.11.2008	yes	yes	yes	Alive
3	F	34	17.11.2008	19.11.2008	yes	yes	yes	Alive
4	Μ	39	unclear	21.11.2008	yes	yes	yes	Alive
5	М	38	unclear	08/12/2008	no	yes	yes	Alive
6	F	42	unclear	9 or 10/12/2008*	no	unknown	yes	Died

\*patient admitted during night - exact time unknown at time of report writing

# Meningitis in Ireland, 2007/2008

#### Introduction

Meningitis is an infection of the meninges which is the thin lining that surrounds the brain and the spinal cord. The most common form of bacterial meningitis is caused by Neisseria meningitidis. Invasive Meningococcal Disease (IMD) only infects humans and may occur at any age, but is most common in infancy and early childhood, with a second smaller peak of incidence in adolescents and young adults. In Ireland serogroup B and C strains accounted for over 99% of all IMD prior to the introduction of the serogroup C conjugate vaccine (Men C) to the routine infant immunisation schedule in October 2000 [2]. Since July 2008 infants in Ireland have received the MenC vaccine at 4, 6 and 13 months, rather than at 2, 4 and 6 months which was previously the case. In contrast to IMD and other bacterial meningitis infections, viral meningitis causes mild or inapparent disease, but severe cases may be hospitalised. There is no specific drug treatment for viral meningitis, but those infected usually make a full recovery. [3].

#### **Materials and Methods**

Data analysis for this report was performed using both Business Objects Reporting<sup>TM</sup> in CIDR and MS Excel. Incidence rates were calculated using the 1996, 2002 and 2006 census population data as the denominator for the epidemiological years' data 1999/2000 to 2007/2008. The figures presented in this report are based on data from CIDR as of 27<sup>th</sup> November 2008. The 2007/2008 figures are provisional.

#### Results

## IMD cases by epidemiological year, serogroup and case classification

Between July 2007 and June 2008, 164 cases of IMD were notified in Ireland, an incidence rate of 3.9 per 100,000 total population. This result is part of a continuous decline since 1999/2000 when the comparable rate was 15.2 per 100,000 (Figure 1).

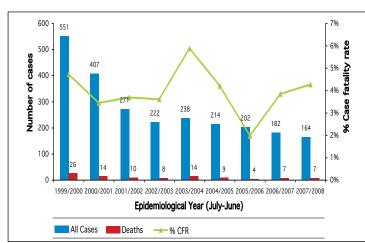


Figure 1 Number of IMD cases, deaths and case fatality rates in Ireland by epidemiological year, 1999/2000 - 2007/2008

Figure 2 shows the number of cases by serogroup per epidemiological year. The latest figures show that serogroup B accounted for 89% of the notifications with serogroups C and W135 accounting for 2% and 1% cases, respectively. No organism was detected for 13 (8%) of the cases. Ninety-two percent (n=151/164) of the notified cases were classified as definite, none as presumed and 8% as possible (n=13).

There has been a large increase in the proportion of IMD cases due to serogroup B from 50% in 1999/2000 to 89% in 2007/2008, while serogroup C has decreased from 30% to 2% in the same

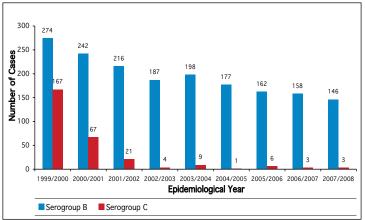


Figure 2 IMD cases in Ireland caused by serogroups B and C and epidemiological year, 1999/2000 - 2007/2008

period. These proportional changes are due to the introduction of the MenC vaccine against serogroup C in 2000. The actual number of cases of serogroup B has decreased by 47% during this time from 274 cases in 1999/2000 to 146 cases in 2007/2008.

The proportion of cases due to other serogroups (including nongroupable) has also fallen during this period from 2% (13/551 cases) to 1% (2/164 cases). The number of cases with no organism detected fell from 18%, (n=97) to 8% (n=13).

#### IMD by age and HSE area

The latest overall age specific incidence rate (ASIR) was highest in those aged less than one year (67.1/100,000) and in the 1-4 year old age group (20.7/100,000). This pattern was repeated in IMD associated with serogroup B. The ASIR for those under one year of age was 57.3/100,000 and 19.5/100,000 for the 1-4 year old age group. Overall there were 146 serogroup B cases in 2007/2008. One of those cases (a young adult aged 20-24 years) was imported and brings the total of IMD imported since 1999/2000 to 19, of which 80% (15 cases) were serogroup B.

There were no serogroup C cases in children under five years of age in 2007/2008. Three cases occurred in people aged less than 25. One of these had not been vaccinated while the vaccination status for the other two cases was not known. This compares with 65 cases in children under five and nine cases in the under 25s in 1999/2000, before the introduction of the MenC vaccine in October 2000. Overall there were 167 serogroup C cases in that epidemiological year.

In 2007/2008 the national crude incidence rate of IMD was 3.8 per 100,000 population, excluding imported cases. This compares with 15.1 per 100,000 population in 1999/2000. The latest figures show that incidence of the disease ranged from a low of 1.9 per 100,000 in HSE-W to a high of 6.6 in HSE-NE.

#### IMD deaths

Seven deaths were notified in 2007/2008 - a case fatality rate (CFR) of 4.3%. There has been little change in the CFR between 1999/2000 and the latest figures and overall there is an epidemiological yearly average of 4% (Figure 1). Over the nine year period, the CFR for serogroup B fell from 5.5% (15 deaths/274 cases) to 3.4% (5 deaths/146 cases) and for serogroup C increased from 6.6% (11 deaths/167 cases) to 33.3% (1 death/3 cases).

In 2007/2008, two of the five serogroup B deaths were reported in HSE-E, two in HSE-NE and one in HSE-S. Three of the five serogroup B deaths occurred in patients under 25 years of age while the

Table 1. Meningitis notifications in Ireland b	y epidemiological year, 2004/2005 - 2007/2008
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Table 1. Meningitis notifications in reland by e					
Notified under	Causative Pathogen	2004-05	2005-06	2006-07	2007-08†
Meningococcal disease	Neisseria meningitidis	214	202	182	164
Streptococcus pneumoniae infection (invasive)	Streptococcus pneumoniae	24	22	28	31
Tuberculosis	Mycobacterium tuberculosis	8	9	5*	7
Haemophilus influenzae disease (invasive)	Haemophilus influenzae	9	6	3	1
Streptococcus group A infection (invasive)	Streptococcus pyogenes	0	2	0	2
Listeriosis	Listeria monocytogenes	2	1	1	1
Bacterial meningitis NOS	Escherichia coli	0	1	2	2
(not otherwise specified)	Gamella species	0	0	0	1
	Klebsiella pneumoniae	0	1	0	0
	Pseudomonas aeruginosa	1	0	0	0
	Proteus mirabilis	0	0	0	1
	Staphylococcus aureus	1	1	0	1
	Staphylococcus coagulase negative	0	0	1	0
	Streptococcus agalactiae (Group B Strep.)	4	8	4	8
	Streptococcus Group C	1	0	0	0
	Unknown	19	28	34	11
	Total Bacterial meningitis (NOS)	26	39	41	24
All forms of bacterial meningitis excl. meningococcal			79	78	66
Viral meningitis			34	150	50
ALL FORMS OF MENINGITIS			315	410	280

**†** Figures for 2007/2008 are provisional

\* TB meningitis figures for 2006/2007 are provisional

remaining two occurred in adults under 60 years of age. The one serogroup C death reported in 2007/2008 occurred in HSE-E in an adult aged 45-49 years. An additional serogroup W135 death was reported in 2007/2008 in a 5-9 year old in HSE-S.

In the nine year period from 1999/2000 serogroup B disease in children under five years of age accounted for 60.7% of all cases with an average CFR of 4.8%. During this same period the annual average percentage in adults over 20 years of age was 12% with an average CFR of 5.2%.

#### Other forms of meningitis

In 2007/2008, there were 361 reported cases of invasive Streptococcus pneumoniae infection, 31 (8.6%) of which resulting in meningitis. Of these, 13 occurred in children under 4 years of age and 18 in adults ranging in age 19-85 years. Five of the overall cases died (16.1%), three of whom were under 2 years of age. In 2007/2008, only one case of meningitis due to Haemophilus influenzae was notified. The case occurred in an infant under 12 months and was due to *H. influenzae* type f. The other forms of bacterial meningitis reported in 2007/2008 included one case of Listeria monocytogenes (age range 20-24 years), two cases of Streptococcus pyogenes (age range 6-76 years) and seven cases of TB meningitis (age range 10-85+ years), one of which (aged 55-59 years) died from tuberculosis. In 2007/2008, 24 cases of bacterial meningitis due to pathogens not otherwise specified (NOS) were also notified. One death (causative agent unknown) was reported in a young adult (aged 15-19 years). In 13 of the 24 cases, the causative pathogens were identified, 12 of which were under two months of age (table 1). The 11 remaining cases, whose aetiology was unknown, ranged in age from one month to 66 years, five of whom were under five years of age. Fifty cases of viral meningitis notifications (age range: one month to 61 years) were reported in 2007/2008 (table 1), 35 (70%) of which had their causative organism identified: 23 enterovirus, five herpes simplex virus, five varicella zoster virus and one each of echovirus and parachovirus. One case resulted in death, the causative agent was unknown.

#### Discussion

IMD rates in Ireland between 1999/2000 and 2001/2002 showed a sharp decline, which was later followed by a more gradual decrease with current rates a quarter of what they were prior to the introduction of the MenC vaccine. The proportion of cases attributable to serogroup C also dropped sharply between 1999/2000 and 2007/2008. Clearly, the MenC vaccine continues to have a positive impact on the number of serogroup B cases seven years after its introduction.

Despite the decline in the number of cases, serogroup B disease remains a considerable cause of morbidity and mortality, with children under five years of age being most affected accounting for more than half of all cases on average between 1999/2000 and 2007/2008 with an average CFR of nearly 5%. The burden in adults over 20 years during this same period of time was, in contrast, much lower at over 10%, but with a similar average CFR. This highlights the importance of recognising symptoms and providing timely access to treatment, which are vital to survive this disease, regardless of the age at presentation. Currently, there is no suitable serogroup B invasive meningococcal vaccine available.

The introduction of a Hib vaccine has successfully led to the reduction in the incidence of this form of meningitis with no cases reported in 2007/2008. It is now hoped that the introduction of the pneumococcal vaccine (PCV) to the vaccination schedule for children born after July 1<sup>st</sup> 2008 will also be equally successful in reducing the numbers of *Streptococcus pneumoniae* meningitis.

The one reported death from viral meningitis in 2007/2008 occurred in an adult and was the first since 1997/1998. The fact that there have been 681 recorded cases of viral meningitis since that time indicates just how rare death from viral meningitis is in Ireland.

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# Botulism in Injecting Drug Users, Dublin, Ireland, 2008.

The outbreak has been managed by an outbreak control team which is led by the Department of Public Health, HSE-E and includes staff from the Health Protection Surveillance Centre (HPSC) and the HSE Drug Services. Information alerts were sent to drug services, emergency departments, neurological services, microbiology services and public health departments throughout the country. Internationally, the European Centre for Disease Control (ECDC) and the European Monitoring Centre for Drugs and Drug Addiction were informed. HPSC alerted other European countries using the Early Warning and Response System (EWRS) supported by the European Commission and run by the ECDC. Advice in relation to 'skin popping' using potentially contaminated heroin is distributed to the drug using community through the drug services and the network of 13 local drugs task forces in Dublin.

#### Discussion

Since 2000, there have been three outbreaks of clostridial infections in IDUs in Dublin. In 2000, an outbreak of *Clostridium novyi* Type A occurred, in which 22 patients were infected, of whom eight died.<sup>1.2.3</sup> A simultaneous outbreak occurred in Liverpool and Glasgow. In 2002 an outbreak of botulism involving three IDUs occurred.<sup>4,5</sup>

Wound botulism became a notifiable disease in Ireland on January 1<sup>st</sup>, 2004. Prior to this date, only food- borne botulism was notifiable under the disease category of *Acute Infectious Gastroenteritis*.

Wound botulism occurring among injecting drug users was first reported in the United States in 1982.<sup>6</sup> Since then, both sporadic botulism cases and outbreaks have been reported among this population, often associated with black tar heroin usage. Heroin users who inject either subcutaneously ("skin popping") or intramuscularly are at particular risk, as administration using this method is conducive to wound infection, abscess formation and subsequent release of botulism toxin if contaminated supply has been used.

Botulism is extremely rare in Ireland, unlike many European countries which routinely see cases each year. Maintaining high levels of awareness of the risk of botulism among the injecting drug using population is vital so that they are aware of the risk and seek urgent medical attention if they develop any of the signs or symptoms associated with the disease. Alerting clinicians to botulism increases the likelihood that clinicians will diagnosis and institute appropriate treatment with anti-toxin and other supportive treatment rapidly in these patients, thus decreasing mortality and complications. Delays in administration of anti-toxin treatment increase mortality, hospital stay and rehabilitation time.

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