A prolonged outbreak of invasive meningococcal disease in an extended Irish Traveller family across three Health Service Executive (HSE) areas in Ireland, 2010 to 2013

L O'Connor (lois_oconnor@hotmail.com)[1], M Ward[1], D Bennett[2], R Mulhall[2], P O'Lorcain[3], R Cunney[2,3], R McDermott[1], E Neville[4], J Heslin[4], R FitzGerald[5], K Meyler[2], M Conlon[1], A Clarke[1], B Corcoran[6], G Fitzpatrick[1], B O'Connor[4], P Flanagan[3], D O'Flanagan[3], S Cotter[3]

1. Department of Public Health, HSE East, Dr Steevens' Hospital, Dublin, Ireland
2. Epidemiology and Molecular Biology Unit, Temple Street Children's University Hospital, Dublin, Ireland
3. Health Protection Surveillance Centre, Dublin, Ireland
4. Department of Public Health, HSE South-East, Kilkenny, Ireland
5. Department of Public Health, HSE Midwest, Limerick, Ireland
6. National Immunisation Office, Dublin, Ireland

Citation style for this article:
O'Connor L, Ward M, Bennett D, Mulhall R, O'Lorcain P, Cunney R, McDermott R, Neville E, Heslin J, FitzGerald R, Meyler K, Conlon M, Clarke A, Corcoran B, Fitzpatrick G, O'Connor B, Flanagan P, O'Flanagan D, Cotter S. A prolonged outbreak of invasive meningococcal disease in an extended Irish Traveller family across three Health Service Executive (HSE) areas in Ireland, 2010 to 2013. Euro Surveill. 2015;20(21):pii=21139. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21139

Article submitted on 09 July 2014 / published on 28 May 2015

Between March 2010 and November 2013 eight laboratory-confirmed cases of serogroup B, invasive meningococcal disease (IMD) were identified in an extended Irish Traveller family across three Health Service Executive (HSE) areas of Ireland. Cases were aged between 5 and 46 months, and were either a cousin or sibling of another case. All eight cases survived. Chemoprophylaxis was given to relevant nuclear family members and close contacts on each occasion, but failed to prevent further cases. *Neisseria meningitidis* isolates from six cases were highly related, belonging to the ST-41/44 clonal complex, and shared the *porA* designation 7–2,4. In November 2013, the outbreak control team recommended that directly observed ciprofloxacin chemoprophylaxis be administered simultaneously to the extended family, and that the four component meningococcal B (4CMenB) vaccine be administered to family members aged 2 months to 23 years inclusive and relevant close contacts of the eighth case. Subsequently these recommendations were implemented at three regional clinics. Additionally pharyngeal swabs (n=112) were collected to assess carriage rates of *N. meningitidis* in this extended family. Pharyngeal carriage of *N. meningitidis* was detected in 15 (13%) family members. From the epidemiological investigation and carriage study overcrowding was the most likely risk factor identified in this outbreak. To date, the combination of directly observed ciprofloxacin chemoprophylaxis and use of 4CMenB vaccine have controlled the outbreak with no further cases diagnosed.

Introduction

nvasive meningococcal disease (IMD) is a life-threatening infection caused by *Neisseria meningitidis*. Risk factors for IMD include close contact with a known case, crowded environments, recent upper respiratory tract infection or influenza, cigarette smoking and immunological susceptibility [1].

Under Irish law, clinicians and clinical directors of laboratories must immediately notify suspected cases of IMD to the Medical Officer of Health (MOH) at the local Department of Public Health. Laboratories must also immediately notify IMD cases which meet the laboratory criteria for confirmed or probable disease in accordance with the case definition [2].

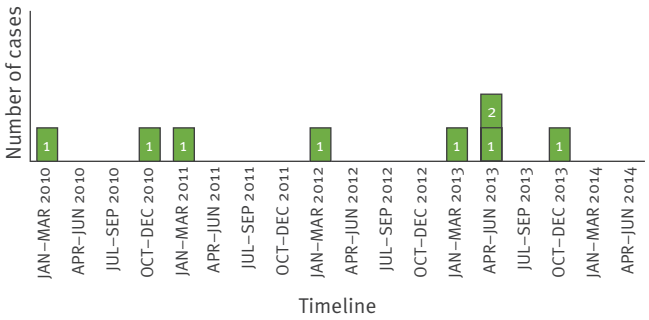
All notified cases of IMD are entered on to the Computerised Infectious Disease Reporting (CIDR) database which is hosted by the Health Protection Surveillance Centre (HPSC), Ireland's specialist agency for the surveillance of communicable diseases. CIDR is a shared national information system, developed to manage the surveillance and control of infectious diseases in Ireland [3].

In 2011, Ireland had the highest incidence of meningococcal disease in the European Union at 1.99 per 100,000 population [4]. However, this figure represents a decrease of 86% from 14.8 per 100,000 population reported in 1999. Irish Travellers are an indigenous minority in Ireland. Their lifestyle and culture, which may include a nomadic lifestyle, distinguishes them from the general population [5]. Irish Travellers experience social and cultural marginalisation in a similar manner to other indigenous minorities globally [6].

In Ireland, ethnic identification is not routinely collected on all individuals with notifiable infectious diseases. Consequently, assessing national rates of disease by ethnicity is not possible. However since 2004, when the CIDR system became operational, limited data on ethnicity is available. Based on such data, it is evident that while the incidence of IMD has decreased in the

Figure

Cases of invasive meningococcal disease in an outbreak affecting an extended Irish Traveller family, Ireland, 2010–2013 (n=8)



general population, a similar reduction has not been seen in the Irish Traveller population. In contrast, since 2004 there has been an increase in reported cases of IMD in this population group [7].

In 2013, 84% of meningococcal disease in Ireland was caused by *N. meningitidis* serogroup B [8]. While most cases of IMD occur sporadically, occasionally an unusual cluster or outbreak is reported. The National Guidelines on the Clinical and Public Health Management of Bacterial Meningitis defines an outbreak of meningococcal disease as *'a minimum of four cases of definite meningococcal disease within a three-month interval, or 40/100,000 in any age group in a three month period, in a geographical area that makes epidemiological sense AND where available microbiological characterisation of the organism is the same'* [9].

We describe the identification of eight cases of IMD due to *N. meningitidis* serogroup B in an extended Irish Traveller family over a three and a half year period across three of eight public health areas of the Health Service Executive (HSE) in Ireland. All eight cases occurred in young children (≤46 months) who were siblings or first cousins of identified cases in the outbreak. The measures to prevent further cases are described. Although the cluster formed by the eight cases does not fulfil the criteria for the above outbreak definition, the term 'outbreak' is used in this report to reflect the high endemicity within this extended family.

Methods

Case definitions

In Ireland, case definitions are specified for the purpose of reporting of selected infectious diseases. Clinical symptoms and signs suggestive of IMD include meningeal signs, haemorrhagic (petechial or purpuric) rash and septic shock [10].

A confirmed case requires one of the following laboratory criteria:

- Isolation of *N. meningitidis* from a normally sterile site or from a haemorrhagic skin lesion.
- Detection of *N. meningitidis* nucleic acid from a normally sterile site or from a haemorrhagic skin lesion.
- Detection of *N. meningitidis* antigen in cerebrospinal fluid (CSF).
-

The case definition used in this outbreak was 'A laboratory-confirmed case of IMD caused by *N. meningitidis* serogroup B in a person who is a member of this extended Irish Traveller family'.

Strain characterisation and antimicrobial susceptibility testing

Laboratories refer all confirmed meningococcal samples to the Irish Meningococcal and Meningitis Reference Laboratory (IMMRL) for further characterisation. Specimens from all eight cases reported here were processed in the IMMRL by polymerase chain reaction (PCR) testing [11,12]. Characterisation of *N. meningitidis* isolates using multilocus sequence typing (MLST) [13], porA [14] and fetA [15] variable region fine-typing was also undertaken at the Epidemiology and Molecular Biology Unit (EMBU), which is linked to the IMMRL.

Antimicrobial susceptibility testing to cefotaxime, ciprofloxacin, penicillin, rifampicin and sulfadiazine was performed using Etest methodology according to the manufacturer's instructions (BioMérieux).

Control measures for cases of meningococcal disease

When a case of suspected or confirmed meningococcal disease is reported to the MOH by a clinician or laboratory the following public health actions are carried out in order to prevent secondary cases; contact is made by public health doctors with the clinician responsible for the care of the case to discuss the clinical situation, contact is made with the case or next of kin to provide information on the illness and to identify close contacts, as defined in detail in the national guidelines [9], who require prompt chemoprophylaxis and possibly vaccination. Evidence-based information is also disseminated to local general practitioners (GPs), family members and, where relevant, schools and pre-schools.

Carriage study

A carriage study was conducted to estimate the prevalence of *N. meningitidis* carriage in the extended Irish Traveller family in which outbreak cases had been identified. The objective was to see if this family had a higher rate of carriage than that seen in the general population which may have contributed to increased transmission to and increased disease in the young children. A posterior pharyngeal swab was collected from all family members who attended special outbreak control clinics. These swabs were anonymised but selected demographic data was collected including;

Table 1

Description of cases of invasive meningococcal disease in an outbreak affecting an extended Irish Traveller family, Ireland, 2010–2013 (n = 8)

Case	A	B	C	D	E	F	G	H
HSE area	East	East	East	Mid-west	East	East	South-east	East
Date of diagnosis	09/03/2010	20/11/2010	08/03/2011	01/01/2012	20/03/2013	29/04/2013	12/06/2013	28/11/2013
Clinical symptoms, signs	Fever, purpuric rash, cough, vomiting	Fever, purpuric rash, listlessness	Bulging fontanel, cough, fever, lethargy, poor feeding, purpuric rash	Fever, non-blanching rash, vomiting	Disseminated intravascular coagulation (DIC), fever, non-blanching rash	Anorexia, fever, irritability, lethargy, non-blanching rash	Fever, irritability, non-blanching rash	Eye swelling, lethargy, limb swelling, not drinking
Pre-hospital antibiotics	Not known	Benzylpenicillin	Benzylpenicillin	Not known	Benzylpenicillin	No	No	No
Length of hospital stay	13 days	10 days	8 days	8 days	14 days	12 days	8 days	23 days
Number of close contacts	18	7	19	16	8	26	33	18
Chemoprophylaxis (number of close contacts)								
Rifampicin	17	7	18	16	8	25	31	18
Ceftriaxone	1	0	1	0	0	1	2	0

HSE: Health Service Executive.

Fever is defined as body temperature ≥37.5°C.

In some of cases, a previous case was a close contact. For example, case A was a close contact in case C. Case B was a close contact in case H, case F was a close contact in case E.

age, sex, housing type and size, number of people living in household, pregnancy, contact with a previous case and previous chemoprophylaxis.

Pharyngeal swabs were cultured for *N. meningitidis* and processed for analysis using a *ctrA;porA* duplex real-time *N. meningitidis*-specific PCR assay (data not shown) [12]. Characterisation of *N. meningitidis* isolates using serotyping, genogrouping, *porA/fetA* fine-typing, multilocus restriction typing (MLRT) and MLST was also undertaken [13-18]. Antimicrobial susceptibility testing was performed on isolates as above.

Results

Description of the outbreak

Between March 2010 and November 2013 eight cases met the case definition (Figure).

Cases are described from A to H in chronological order (Table 1). At the time of the third case's illness (case C), it was confirmed that this case's sibling (case A) and first cousin (case B) had been reported as having IMD the previous year (2010). In April 2013, following the identification of two additional family cases, one in March 2013 and the other in April 2013 an outbreak was reported based on the recognition of a cluster of cases over a prolonged period of time. This led to the further identification of affected individuals including the retrospective finding of a case in 2012 (Figure). All cases were less than four years-old (median age: 7.5 months; range: 5–46 months). Male to female ratio was 5:3 (Table 1). Seven cases made a complete recovery. In spring 2014, the eighth case (case H) continued to receive outpatient medical care.

On average 18 close contacts were identified per case (range: 7–33). According to the Irish guidelines [9], relevant close contacts received rifampicin chemoprophylaxis. Pregnant contacts received prophylaxis with intramuscular (IM) ceftriaxone. Among the total number of close contacts identified for all cases, 36 family members were identified as close contacts to more than one case. These family members therefore received chemoprophylaxis repeatedly during the outbreak period. Delay between rounds of chemoprophylaxis in these close contacts varied. For some (close contacts in case A and C), the gap was one year. For others (close contacts in case B and H), the gap was three years.

Laboratory results

All eight cases were diagnosed by detection of *N. meningitidis* serogroup B DNA in extracts of clinical specimens by PCR. Two of the eight cases yielded a *N. meningitidis* isolate from a normally sterile site. Case B had *N. meningitidis* diplococci identified and cultured from CSF on lumbar puncture and case H had *N. meningitidis* isolated from blood culture. Both isolates were identified as B:4:NT/P1.4/NT with the *porA* genotype 7–2,4 (B:4;P1.7–2,4), and were sequence type (ST)-6697 of the ST-41/44 clonal complex by MLST (ST-6697(cc41/44)). Both were sensitive to cefotaxime, ciprofloxacin, penicillin, rifampicin, and sulfadiazine.

Table 2

Summary of control measures for an outbreak of invasive meningococcal disease in an extended Irish Traveller family, Ireland, 2010–2013

At risk population identified (N = 123)	Clinic X	Clinic Y	Clinic Z	Total
Number invited to attend clinics	31	61	31	123
Number that attended	32[a]	53	27	112
Number that received chemoprophylaxis	32	53	27	112
Ciprofloxacin	32	52	27	111
Rifampicin	0	1[b]	0	1
Total number eligible for 4CMenB vaccine	29	43	21	93
Total number that received 4CMenB vaccine	29	36[c]	20[d]	86
Number that reported side effects	7	0	0	7
Facial swelling, nausea, vomiting	1	0	0	1
Sore arm at injection site	6	0	0	6

4CMenB: four component meningococcal B vaccine.

[a] An additional child, who lives permanently with relatives in this region, attended this clinic as opposed to another clinic site with the rest of their immediate family. Consequently, this child was given chemoprophylaxis and vaccination.

[b] Ciprofloxacin contra-indicated.

[c] Six family members declined to attend for vaccination; one other family member did not attend and was not followed up as they were almost 24 years-old.

[d] One child was unwell at the clinic and did not receive the vaccine.

Characterisation of *N. meningitidis* DNA extracted from the remaining six non-culture diagnosed cases determined two of them to be also ST-6697 (cc41/44) with the *porA* genotype 7–2,4 (cases C and E). Analysis of clinical extracts from two additional non-culture confirmed cases (cases A and F) did not yield a complete MLST profile, so it was not possible to officially assign a clonal complex to these. However, based on their partial MLST profiles (case A: 5 alleles, case F: 4 alleles) and consultation with www.pubmlst.org/neisseria, they are very likely to be ST-41/44 complex meningococci and we have putatively assigned them as so. Also, it was not possible to assign a clonal complex to the isolates from the remaining two cases (cases D and G) due to insufficient MLST data.

Antimicrobial susceptibility results from the EMBU confirmed that the predominant outbreak strain was sensitive to cefotaxime, ciprofloxacin, penicillin, rifampicin, and sulfadiazine.

Control measures for the outbreak

Following the notification of each case, control measures were promptly carried out as per national guidance. These included dissemination of information and administration of appropriate chemoprophylaxis to close contacts. As the outbreak was first recognised in one HSE area (HSE East), information was initially disseminated to local GPs and the Traveller Health Network facilitated by Pavee Point, the Traveller education and development group. Further investigations were initiated to determine whether all cases were caused by the same strain and whether specific risk factors could be identified to account for this cluster. A local outbreak control team (OCT) reviewed the cases. When additional cases in other HSE areas were identified a national OCT was convened.

The national OCT reviewed all cases linked to the outbreak, ascertained the epidemiological links and risk factors for infection, assessed control measures already implemented and considered what further measures were required. Representatives from Departments of Public Health covering the affected HSE areas, the HPSC, the EMBU and the National Immunisation Office (NIO) participated. Expert opinion was also obtained from a consultant in paediatric infectious diseases.

In June 2013, after the initial national OCT meeting, the following actions were undertaken: (i) an alert was sent to all departments of public health informing them of the outbreak and advising increased awareness of possible further cases; (ii) further characterisation of the outbreak strain/s of *N. meningitidis* was carried out by the EMBU; (iii) communication with the manufacturers of a new four-component protein-based meningococcal serogroup B (4CMenB) vaccine was established to determine availability of this vaccine in Ireland and (iv) immunological testing of cases was requested to determine if there was any underlying susceptibility to infectious diseases. Tests to identify immunological susceptibility to IMD were subsequently carried out on four of the cases. No immunological deficit was detected.

In November 2013, after the eighth case of IMD (case H) was notified it was agreed to offer all members of the extended Irish Traveller family, regardless of whether they had been a contact of an actual case or not, additional simultaneous chemoprophylaxis with ciprofloxacin. Ciprofloxacin is recommended as first line chemoprophylaxis for close contacts of cases of

IMD in the United Kingdom (UK) [19]. As this medication is a single dose treatment compliance can be directly observed. Following recommendations from the independent national expert group (the National Immunisation Advisory Committee (NIAC)), it was also agreed that all members of the extended family aged two months to 23 years inclusive and relevant close contacts of case H would be offered the 4CMenB vaccine, in accordance with manufacturer's immunisation schedule [20].

On 18 December 2013, three clinics were organised to implement these actions. In addition a posterior pharyngeal swab was taken from all family members who attended. In total, 123 family members were invited to attend, of which 112 (91%) attended (Table 2). Of the 11 who did not attend, eight did not attend on the day but subsequently received rifampicin. Three other family members did not attend and did not receive chemoprophylaxis. Of those who did attend, one family member attended an alternative clinic to the one this person was invited to. In December, vaccine was administered at only one clinic site. Children less than two years of age received antipyretic medication on site, in accordance with NIAC recommendations, due to the reported increased risk of post-vaccination fever in this age group. Due to logistical difficulties, the administration of vaccine to eligible family members who attended the remaining two clinics was deferred until January 2014. In total 86 family members, 92% of the 93 who were eligible, received their first dose 4CMenB vaccine by end January 2014.

Arrangements were made with local GPs to complete the vaccination course for the extended family members who required further vaccinations. Public health doctors provided vaccination for the remaining relevant extended family members. Two cases and a number of accompanying family members had relocated to England. Consequently, colleagues at Public Health England agreed to follow up those households.

One family member reported nausea, vomiting and facial swelling after receiving ciprofloxacin and 4CMenB vaccine simultaneously. However, these symptoms resolved spontaneously without additional treatment. When followed up by telephone interview, six family members reported sore arms at the injection site on the day after vaccination. All reported symptoms resolved within three days of onset.

Carriage study results

Posterior pharyngeal swabs were obtained from 112 family members of whom 62 were male (Table 3).

On PCR 15 (13%) swabs were positive for *N. meningitidis* and 14 of these were also culture positive. Thirteen (12%) swabs were PCR positive for serogroup B. Eight of the serogroup B positive isolates were identified as B:4:NT/p1.4/NT:ST6697(cc41/44), seven were found to have por A genotype 7–2.4 on whole genome sequencing. Five of the 15 positive swabs were from people aged less than 24 years, nine were from those aged between 25 and 39; one positive swab was from a person whose age was unknown. Ten family members with a positive swab result for *N. meningitidis* lived in a trailer/caravan and ten lived in households of eight people or more. All eight family members with B:4:NT/p1.4/NT:ST6697(cc41/44) isolates had previously received chemoprophylaxis. Antimicrobial sensitivity testing indicated that the eight B:4:NT/p1.4/NT:ST6697(cc41/44) isolates were sensitive to cefotaxime, ciprofloxacin, penicillin, rifampicin, and sulfadiazine.

Discussion

This report describes an outbreak of *N. meningitidis* serogroup B in an extended Irish Traveller family over a three and a half year period. While outbreaks of IMD are more commonly associated with serogroup C disease [5,21], prolonged community based and institutional outbreaks of serogroup B disease have been described [22,23]. Control measures in these outbreaks differed. In a prolonged serogroup B outbreak in northern France (2003–2005), an unlicensed monovalent outer membrane vesicle vaccine from Norway was thought to be affective and was administered initially to high risk groups and subsequently to all the population [22]. In contrast, in a prolonged university outbreak in the United States (2008–2010), health promotion and ciprofloxacin chemoprophylaxis were the control measures used. Vaccination was not used as a control measure because a serogroup B vaccine was not licenced in the United States at that time [23]. Family clusters have also been described in the literature but their time duration is considerably shorter than our outbreak [24].

Transmission of *N. meningitidis* occurs through droplet spread of respiratory secretions or saliva [25]. On average 10 to 15% of the population are colonised with *N. meningitidis* at any given time and the duration of carriage can vary from days to months [26,27]. When cases continue to occur, despite appropriate management of contacts, possible reasons for ongoing transmission of *N. meningitidis* include; immunological susceptibility, poor compliance with chemoprophylaxis, resistance to chemoprophylaxis, unidentified close contacts and overcrowding. We considered each of these as a possible cause of this outbreak continuing.

The association between immunological factors, host genetics and IMD is well recognised [28,29]. However, in this outbreak the four cases who underwent comprehensive immunological tests had normal immunological results; therefore immunological susceptibility was not thought a likely cause of increased incidence or ongoing transmission.

Compliance of contacts with the recommended four dose schedule of rifampicin chemoprophylaxis could not be independently verified. Consequently, in order

to ensure compliance, directly observed treatment with ciprofloxacin was provided at the clinics. Antimicrobial susceptibility results from the EMBU confirmed that the predominant outbreak strain was sensitive to cefotaxime, ciprofloxacin, penicillin, rifampicin, and sulfadiazine. These results are in line with previous findings that IMD-associated strains of *N. meningitidis* which exhibit decreased susceptibility to cefotaxime, ciprofloxacin, penicillin, rifampicin and sulfadiazine are currently very rare in Ireland (data not shown).

There were on average 18 close contacts identified per case. This number is high when compared with an average of 7.6 contacts per case reported from a 2012 series of 38 IMD events in four regions in Ireland (data not shown). As this is a larger number of contacts than usually identified, it remains possible that not all close contacts were identified. Despite multiple interviews with the family to ensure identification of as many true close contacts as possible, it was recognised that recolonisation from a wider network remained a possibility.

A carriage rate of *N. meningitidis* of 13% was identified. This rate may have been affected by the large number of family members who had received chemoprophylaxis previously (n = 68), especially those who received it in the preceding month, n = 18. In the general population highest carriage rates of *N. meningitidis* are seen in the 15 to 24 years-old age group [27]. The 2011 Irish census identified 22.4 years as the average age of an Irish Traveller compared with 36.1 years for the general Irish population [30]. In this outbreak associated cohort, 83 (74%) of the participants in the carriage study were less than 25 years of age and 22 (20%) were aged between 15 and 24. It is conceivable that cases in this outbreak had many opportunities to mix with young adult relatives. However, results from the carriage study reveal that only three (14%) of the 22 participants aged between 15 and 24 years demonstrated *N. meningitidis* carriage, compared with nine (45%) of the 20 participants aged between 25 and 40 years. The higher rate of carriage in the older age group is higher than expected when compared with previously undertaken carriage studies which revealed carriage rates of 8.8% in individuals aged 25 and older (data not shown).

Traditionally Irish Traveller family size is larger than that of the general population of Ireland. In 2011, 26.9% of Traveller women reported to have five or more children compared with 2.6% of the general population [30]. Irish Travellers often live in houses or caravans in crowded conditions [30]. Household crowding and attendance at crowded venues such as clubs and parties are recognised as risk factors for carriage of *N. meningitidis* and IMD [31,32]. Irish Travellers also frequently attend large family gatherings where there are large groups of people in close proximity for a prolonged period of time. This is supported by the large number of close contacts identified in the outbreak cases. From the carriage study two thirds (n = 10, 67%) of the identified *N. meningitidis* carriers lived in a trailer or caravan. Census information documents from 2011 identify that 12.3% of Irish Travellers live in trailers or caravans overall [30]. Therefore a larger proportion than expected of *N. meningitidis* carriers lived in a trailer or caravan which is likely to consist of one or two rooms in total. As the carriage study also identified that two thirds (n = 10, 67%) of positive carriers live in households of eight or more, in contrast to 8.32% of the total Irish Traveller population [30], an element of household crowding is likely to be present.

Additional previously reported factors associated with carriage of *N. meningitidis* include personal and passive cigarette smoking and recent or concomitant respiratory tract infections or influenza [32-34]. Cigarette smoking rates are higher among Irish Travellers than in the general population (52.5% vs 29%) [6,35] and therefore it is possible that cigarette smoking could be associated with this outbreak. However, as information on cigarette smoking is not currently collected on enhanced surveillance for IMD the rate of cigarette smoking for the outbreak family could not be confirmed. Neither information on cigarette smoking nor exposure to cigarette smoking was requested during the carriage study undertaken in December 2013.

Table 3

Characteristics of individuals who were swabbed for a carriage study, outbreak of invasive meningococcal disease among an extended Irish Traveller family, Ireland, 2010–2013 (n=112)

Characteristics of family members swabbed	Swabs (N = 112) n (%)
Sex	
Male	62 (55)
Female	49 (44)
Not specified	1 (1)
Age groups in years	
0–9	44 (39)
10–19	35 (31)
20–29	13 (12)
≥ 30	19 (17)
Not specified	1 (1)
Household size[a]	
2–7 residents	48 (43)
≥ 8 residents	56 (50)
Accommodation type	
House	67 (60)
Trailer/caravan	45 (40)
Not specified	0 (0)
Self-reported previous contact of meningococcal case	
No	32 (29)
Yes	80 (71)
If yes, previous chemoprophylaxis?	
Yes	68 (85)
No	12 (15)

[a] Only numbers of persons with available information are shown.

Previously it has been difficult to control serogroup B IMD due to the absence of a vaccine. This has changed recently with the approval in 2014 by the Food and Drug Administration of a vaccine for the United States (Trumenba from Pfizer) [36]. Earlier, in January 2013, a four component Men B vaccine, referred to here as 4CMenB (Bexsero from Novartis), was licensed by the European Medicines Agency for use against serogroup B disease [37]. 4CMenB vaccine contains three antigens, factor H binding protein, neisserial adhesion A and *Neisseria* heparin binding agent. In addition, the vaccine contains PorA (serosubtype P1.4) from the outer membrane vesicle of the New Zealand strain 98/254. These antigens affect meningococcal survival, function and virulence [38]. As the outbreak strain was identified as B:4:P1.7–2,4:ST-6697 (cc41/44), we were confident that the use of the vaccine would be beneficial to this outbreak.

The Meningococcal Antigen Typing System (MATS) is an enzyme-linked immunosorbent assay (ELISA) designed to evaluate expression of 4CMenB target proteins and to evaluate their cross reactive potential. Strains are predicted to be covered by 4CMenB if they carry the porA p1.4 epitope or meet a minimum threshold of reactivity to *Neisseria* heparin-binding antigen (NHBA), factor H binding protein (fHbp) or *Neisseria* adhesin A (nadA) in the MATS ELISA, known as the positive bactericidal threshold (PBT) [39]. The case B isolate (which was identified as the outbreak strain) has undergone MATS testing and results predict this strain is covered by any of porA (p1.4), NHBA or fHbp peptides it carries.

The decision by two of the affected HSE regions to delay administration of the vaccine until January 2014 was not thought to have impacted on control measures. The affected family members received ciprofloxacin chemoprophylaxis and therefore short-term eradication of *N. meningitidis* was likely. The duration of eradication of *N. meningitidis* after receipt of chemoprophylaxis can vary from weeks to months [40]. Subsequently, the administration of 4CMenB in January was thought likely to provide longer-term immunity.

To our knowledge, this outbreak was the first time 4CMenB vaccine was used in an outbreak situation in Europe. In December 2013, this vaccine was used in an outbreak of serogroup B disease at Princeton University in the United States when in excess of 5,000 students and staff received this vaccine [41]. More recently in March 2014, the University of California, Santa Barbara vaccinated ca 9,000 students and staff in response to four confirmed cases of serogroup B disease in the university [41].

Conclusion

This is a unique outbreak of IMD caused by *N. meningitidis* serogroup B in an extended Irish Traveller family across three regions of Ireland over a period of three and a half years. This outbreak continued despite instigating all appropriate control measures on multiple occasions. From descriptive epidemiological data and the carriage study, the most likely risk factor identified for this ongoing outbreak was overcrowding. We hope that the combined use of directly observed ciprofloxacin chemoprophylaxis, in addition to vaccination with 4CMenB will be successful in halting this outbreak. We continue to monitor this family for new cases and strive to ensure that all relevant family members complete the recommended vaccine schedule. To date there have been no further cases of IMD in this family.

This outbreak highlights the importance of recording ethnicity as part of the enhanced surveillance information collected on all cases of meningococcal disease. We recommend the gathering of ethnicity data for key notifiable diseases including IMD. We also recommend that consideration be given to the use of 4CMenB vaccine for vulnerable groups living in similar crowded conditions.

Acknowledgments

We wish to acknowledge the work of Alan Marsh who inputted and analysed the data on the carriage study as part of a Health Protection Surveillance Centre internship. We also wish to acknowledge the Health Service Executive staff who assisted us at the three HSE area clinics in HSE East, South-East and Mid-West.

Conflict of interest

None declared.

Authors' contributions

All authors contributed to the gathering and analysis of the information. Lois O'Connor and Mary Ward wrote the first draft of the manuscript in consultation with the outbreak control team. All authors read and critically revised the first as well as subsequent drafts to this manuscript and approved the final version.

References

1. Weiss D, Stern EJ, Zimmerman C, Bregman B, Yeung A, Das D, et al.; New York City Meningococcal Investigation Team. Epidemiologic investigation and targeted vaccination initiative in response to an outbreak of meningococcal disease among illicit drug users in Brooklyn, New York. Clin Infect Dis. 2009;48(7):894-901. http://dx.doi.org/10.1086/597257 PMID:19231975
2. Infectious Diseases Regulations 1981, Stat. S.I.No. 390 of 1981;1981.
3. Health Protection Surveillance Centre (HPSC). Computerised Infectious Disease Reporting (CIDR) 2011. Dublin: HPSC. [Accessed 28 May 2014]. Available from: http://www.hpsc.ie/CIDR/
4. European Centre for Disease Prevention and Control (ECDC). Annual Epidemiological Report Reporting on 2011 Surveillance Data and 2012 Epidemic Intelligence Data. Stockholm: ECDC, 2013.
5. All Ireland Traveller Health Study. Our Geels. Summary of Findings. Dublin: Minister for Health and Children Mary Harney; 2010.
6. Stephens C, Porter J, Nettleton C, Willis R. Disappearing, displaced, and undervalued: a call to action for Indigenous health worldwide. Lancet. 2006;367(9527):2019-28. http://dx.doi.org/10.1016/S0140-6736(06)68892-2 PMID:16782493

7. Cotter S, O'Connor L, O'Lorcain P, Flanagan P, O'Flanagan D. Meningococcal Disease in Ireland 2005-2013 - can determinants of increased risk be identified? Epi Insight. 2014;15(3).
8. Health Protection Surveillance Centre ((HPSC). Meningococcal disease: Annual Report 2013. Dublin: HPSC;. 2014. Available from: http://www.hpsc.ie/A-Z/VaccinePreventable/BacterialMeningitis/Publications/AnnualReports/File,15164,en.pdf
9. Bacterial Meningitis Sub-Committee of the Scientific Advisory Committee of the HPSC. Guidelines for the early clinical and public health management of bacterial meningitis (including meningococcal disease). Dublin: Health Protection and Surveillance Centre; 2012.
10. Health Surveillance Protection Agency. Case definitions for Notifiable Diseases. Dublin: Health Protection Surveillance Centre;2012. p. 58.
11. Drew RJ, Ó Maoldomhnaigh C, Gavin PJ, O' Sullivan N, Butler KM, Cafferkey M. The impact of meningococcal polymerase chain reaction testing on laboratory confirmation of invasive meningococcal disease. Pediatr Infect Dis J. 2012;31(3):316-8. http://dx.doi.org/10.1097/INF.0b013e318241f824 PMID:22173139
12. Guiver M, Borrow R, Marsh J, Gray SJ, Kaczmarski EB, Howells D, et al. Evaluation of the Applied Biosystems automated Taqman polymerase chain reaction system for the detection of meningococcal DNA. FEMS Immunol Med Microbiol. 2000;28(2):173-9. http://dx.doi.org/10.1111/j.1574-695X.2000.tb01473.x PMID:10799809
13. Maiden MC, Bygraves JA, Feil E, Morelli G, Russell JE, Urwin R, et al. Multilocus sequence typing: a portable approach to the identification of clones within populations of pathogenic microorganisms. Proc Natl Acad Sci USA. 1998;95(6):3140-5. http://dx.doi.org/10.1073/pnas.95.6.3140 PMID:9501229
14. Russell JE, Jolley KA, Feavers IM, Maiden MC, Suker J. PorA variable regions of Neisseria meningitidis. Emerg Infect Dis. 2004;10(4):674-8. http://dx.doi.org/10.3201/eid1004.030247 PMID:15200858
15. Thompson EA, Feavers IM, Maiden MC. Antigenic diversity of meningococcal enterobactin receptor FetA, a vaccine component. Microbiology. 2003;149(Pt 7):1849-58. http://dx.doi.org/10.1099/mic.0.26131-0 PMID:12855736
16. Wedege E, Høiby EA, Rosenqvist E, Frøholm LO. Serotyping and subtyping of Neisseria meningitidis isolates by co-agglutination, dot-blotting and ELISA. J Med Microbiol. 1990;31(3):195-201. http://dx.doi.org/10.1099/00222615-31-3-195 PMID:2107317
17. Bennett DE, Cafferkey MT. Multilocus restriction typing: a tool for Neisseria meningitidis strain discrimination. J Med Microbiol. 2003;52(Pt 9):781-7. http://dx.doi.org/10.1099/jmm.0.05225-0 PMID:12909655
18. Bennett DE, Cafferkey MT. Consecutive use of two multiplex PCR-based assays for simultaneous identification and determination of capsular status of nine common Neisseria meningitidis serogroups associated with invasive disease. J Clin Microbiol. 2006;44(3):1127-31. http://dx.doi.org/10.1128/JCM.44.3.1127-1131.2006 PMID:16517911
19. Health Protection Agency (HPA). Meningococcus and Haemophillus Forum. Guidance for public health management of meningococcal disease in the UK. London: HPA; 2011.
20. Novartis. Bexsero. Summary of product characteristics. 2013.
21. Brooks R, Woods CW, Benjamin DK Jr, Rosenstein NE. Increased case-fatality rate associated with outbreaks of Neisseria meningitidis infection, compared with sporadic meningococcal disease, in the United States, 1994-2002. Clin Infect Dis. 2006;43(1):49-54. http://dx.doi.org/10.1086/504804 PMID:16758417
22. Rouaud P, Perrocheau A, Taha MK, Sesboué C, Forgues AM, Parent du Châtelet I, et al. Prolonged outbreak of B meningococcal disease in the Seine-Maritime department, France, January 2003 to June 2005. Euro Surveill. 2006;11(7):178-81. PMID:16966800
23. Mandal S, Wu HM, MacNeil JR, Machesky K, Garcia J, Plikaytis BD, et al. Prolonged university outbreak of meningococcal disease associated with a serogroup B strain rarely seen in the United States. Clin Infect Dis. 2013;57(3):344-8. http://dx.doi.org/10.1093/cid/cit243 PMID:23595832
24. Acheson P, Barron R, Borrow R, Gray S, Marodi C, Ramsay M, et al. A cluster of four cases of meningococcal disease in a single nuclear family. Arch Dis Child. 2012;97(3):248-9. http://dx.doi.org/10.1136/archdischild-2011-301074 PMID:22247241
25. Stephens DS, Greenwood B, Brandtzaeg P. Epidemic meningitis, meningococcaemia, and Neisseria meningitidis. Lancet. 2007;369(9580):2196-210. http://dx.doi.org/10.1016/S0140-6736(07)61016-2 PMID:17604802
26. Kellerman SE, McCombs K, Ray M, Baughman W, Reeves MW, Popovic T, et al.; Georgia Emerging Infections Program. Genotype-specific carriage of Neisseria meningitidis in Georgia counties with hyper- and hyposporadic rates of meningococcal disease. J Infect Dis. 2002;186(1):40-8. http://dx.doi.org/10.1086/341067 PMID:12089660
27. Yazdankhah SP, Caugant DA. Neisseria meningitidis: an overview of the carriage state. J Med Microbiol. 2004;53(Pt 9):821-32. http://dx.doi.org/10.1099/jmm.0.45529-0 PMID:15314188
28. Brouwer MC, Read RC, van de Beek D. Host genetics and outcome in meningococcal disease: a systematic review and meta-analysis. Lancet Infect Dis. 2010;10(4):262-74. PMID:20334849
29. Fijen CAP, Kuijper EJ, te Bulte MT, Daha MR, Dankert J. Assessment of complement deficiency in patients with meningococcal disease in The Netherlands. Clin Infect Dis. 1999;28(1):98-105. http://dx.doi.org/10.1086/515075 PMID:10028078
30. Central Statistics Office. Census 2011 Profile 7 Religion, Ethnicity and Irish Travellers. Dublin: Central Statistics Office; 2012.
31. Simmons G, Martin D, Stewart J, Jones N, Calder L, Bremner D. Carriage of Neisseria meningitidis among household contacts of patients with meningococcal disease in New Zealand. Eur J Clin Microbiol Infect Dis. 2001;20(4):237-42. http://dx.doi.org/10.1007/PL00011260 PMID:11399012
32. Baker M, McNicholas A, Garrett N, Jones N, Stewart J, Koberstein V, et al. Household crowding a major risk factor for epidemic meningococcal disease in Auckland children. Pediatr Infect Dis J. 2000;19(10):983-90. http://dx.doi.org/10.1097/00006454-200010000-00009 PMID:11055601
33. Block C, Gdalevich M, Buber R, Ashkenazi I, Ashkenazi S, Keller N. Factors associated with pharyngeal carriage of Neisseria meningitidis among Israel Defense Force personnel at the end of their compulsory service. Epidemiol Infect. 1999;122(1):51-7. http://dx.doi.org/10.1017/S0950268898001769 PMID:10098785
34. MacLennan J, Kafatos G, Neal K, Andrews N, Cameron JC, Roberts R, et al.; United Kingdom Meningococcal Carriage Group. Social behavior and meningococcal carriage in British teenagers. Emerg Infect Dis. 2006;12(6):950-7. http://dx.doi.org/10.3201/eid1206.051297 PMID:16707051
35. Morgan K, McGee H, Watson D, Perry I, Barry M, Shelley E, et al. SLAN 2007: Survey of Lifestyle, Attitudes & Nutrition in Ireland: Main Report. Dublin: Department of Health and Children; 2008.
36. First vaccine approved by FDA to prevent serogroup B Meningococcal disease. United States Food and Drug Administration (FDA); 2014. Available from http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm420998.htm
37. European Medicines Agency. Bexero. Meningococcal group-B vaccine (rDNA, component, adsorbed). Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002333/human_med_001614.jsp&mid=WC0b01ac058001d124
38. Dull PM, McIntosh ED. Meningococcal vaccine development--from glycoconjugates against MenACWY to proteins against MenB--potential for broad protection against meningococcal disease. Vaccine. 2012;30(Suppl 2):B18-25. http://dx.doi.org/10.1016/j.vaccine.2012.01.062 PMID:22607895
39. Donnelly J, Medini D, Boccadifuoco G, Biolchi A, Ward J, Frasch C, et al. Qualitative and quantitative assessment of meningococcal antigens to evaluate the potential strain coverage of protein-based vaccines. Proc Natl Acad Sci USA. 2010;107(45):19490-5. http://dx.doi.org/10.1073/pnas.1013758107 PMID:20962280
40. Zalmanovici Trestioreanu A, Fraser A, Gafter-Gvili A, Paul M, Leibovici L. Antibiotics for preventing meningococcal infections. Cochrane Database Syst Rev. 2011; (8):CD004785. PMID:21833949
41. Centers for Disease Control and Prevention (CDC). Serogroup B Meningococcal Vaccine and Outbreaks; 2014. Atlanta: CDC. Available from: http://www.cdc.gov/meningococcal/outbreaks/vaccine-serogroupB.html