

Protecting and improving the nation's health

Guidance for public health management of meningococcal disease in the UK Updated August 2019

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Public Health England, Wellington House, 133-155 Waterloo Road, London SE1 8UG Tel: 020 7654 8000 www.gov.uk/phe Twitter: @PHE_uk Facebook: www.facebook.com/PublicHealthEngland

Prepared by: Helen Campbell, Sydel Parikh, Mary Ramsay and Shamez Ladhani of the PHE Immunisation Team together with Steve Grey, Ray Borrow of the PHE Meningococcal Reference Unit, NHS National Services Scotland, Public Health Wales and Public Health Agency in Northern Ireland. We are grateful for the additional contributions made by the PHE Vaccine Preventable Invasive Bacterial Infections Forum and PHE Health Protection Teams in particular Surrey and Sussex Health Protection Unit and North East Health Protection Team.

Amendments in August 2019 are highlighted in pink.

For queries relating to this document, please contact: Shamez Ladhani, Immunisation Hepatitis and Blood Safety Department, Public Health England Colindale, 61 Colindale Avenue, Colindale, London NW9 5EQ. Email: shamez.ladhani@phe.gov.uk

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Executive summary

This guidance on the public health management of individual cases and clusters of invasive meningococcal disease was updated in February 2018 as an amalgamation of the 2014 guidance on preventing secondary cases of MenB disease and the 2012 version of the guidance for public health management of meningococcal disease in the UK. Major changes to earlier guidance are highlighted below.

- ciprofloxacin is the first line chemoprophylaxis; rifampicin is a suitable alternative
- chemoprophylaxis is no longer recommended to eradicate carriage for any case treated with a cephalosporin
- a single dose of ciprofloxacin can be used for the prevention of a secondary case in pregnancy, because short duration treatment for other indications appears to be safe
- cases do not need additional vaccination unless they are unimmunised or partially immunised for their age according to the national immunisation schedule, are in a risk group for meningococcal disease or are part of a defined cluster where vaccination is recommended
- following a single case of confirmed or probable MenB disease, vaccination against MenB is not recommended for close contacts
- for a cluster involving confirmed serogroup A, C, W or Y cases: the quadrivalent conjugate vaccine should usually be offered to all individuals of any age who were offered antibiotics and who have not received the vaccine in the previous 12 months
- following the introduction of the infant MenB immunisation programme the recommendations for MenB vaccination in a cluster setting were revised to offer MenB vaccination to household contacts if two or more MenB cases occur within 28 days; MenB vaccination for clusters arising in a pre-school setting will require careful assessment of the vaccination status of the risk group
- for a cluster involving confirmed serogroup B cases: MenB vaccine should usually be offered to all individuals of any age who were offered antibiotics and who have not received the vaccine in the previous 12 months

Amendments in August 2019 are:

- the definition of a 'probable' IMD case has been clarified
- confirmation that the recent EU review of fluoroquinolones does not affect ciprofloxacin chemoprophylaxis for meningococcal disease
- definition of a cluster has been clarified
- the importance of investigating for underlying risk factors in IMD patients due to unusual meningococcal serogroups, non-groupable strains or recurrent meningococcal disease has been highlighted and appendix 5 added for communication with GPs concerning this.

1. Background

Neisseria meningitidis is a major cause of septicaemia and meningitis worldwide and is associated with significant mortality as well as serious long-term sequelae among survivors ⁽¹⁾. Six meningococcal capsular groups (A, B, C, W, X and Y) distinguished by their polysaccharide capsule cause almost all invasive infections in humans. The meningococcus commonly colonises the nasopharynx and carriage prevalence increases through childhood from around 5% in infants to a peak of 24% in 19-year olds and subsequently decreases in adulthood to around 8% ⁽²⁾. The mean duration of carriage in settings where prevalence is stable has been estimated at about 21 months⁽³⁾. Invasive disease is a rare outcome of acquisition but onward transmission from cases to close contacts can rarely result in secondary cases, as well as clusters of infection ⁽⁴⁻⁶⁾. Fewer than 2% of invasive meningococcal disease (IMD) cases, however, are considered to result from close contact with a primary IMD case ⁽⁷⁾. In 2014 annual IMD incidence across all age groups was approximately 1.2/100,000 in the UK ⁽⁸⁾.

Systemic immunity, as measured by serum bactericidal antibodies, usually develops within 14 days of acquisition of meningococci ⁽⁹⁾. Rarely, acquisition may progress to invasive disease before immunity develops. This incubation period is usually three to five days, based on data from studies of laboratory-acquired infection ⁽¹⁰⁾, from occasional clusters where the date of exposure is known ⁽¹¹⁾ and from carriage studies among military recruits ⁽¹²⁾. Established meningococcal carriers do not usually develop invasive disease ⁽¹²⁾. The risk of invasive disease following acquisition is likely to vary with environmental and host factors, but will also depend critically on the characteristics of the strain acquired. Only a very small proportion of carried strains are responsible for invasive disease ⁽¹³⁾.

Conjugate vaccines against group C meningococci (MenC) have been available since the late 1990s and quadrivalent conjugate vaccines against groups A, C, W and Y (MenACWY) have been licensed in Europe for more than a decade. In early 2013, a new vaccine was developed specifically to prevent disease caused by group B meningococci (MenB) and was licensed in Europe (4CMenB, Bexsero®, GSK Biologicals, Belgium). This vaccine is unlike the existing MenC and MenACWY conjugate vaccines in that it is protein-based and, therefore, has a different mechanism of action compared with conjugate vaccines along with different safety, reactogenicity and immunogenicity profiles in different age groups ⁽¹⁴⁾. In 2017, another MenB vaccine, using bi-valent lipidated fHbp (rLP2086, Trumenba®; Pfizer), was licensed in Europe. Trumenba® is currently licensed for individuals aged 10 years and older. This updated guidance includes the potential use of MenB vaccine in the public health management of cases and contacts of IMD.

1.1 Objectives of guidelines

This updated guidance is an amalgamation of the guidance on preventing secondary cases of MenB disease and the earlier version of the guidance for public health management of meningococcal disease in the UK. The guidance covers pre-admission management, investigation of suspected cases, case definitions, chemoprophylaxis and vaccination of cases and close contacts of sporadic cases, as well as management of IMD clusters and outbreaks.

2. Epidemiology of IMD in the UK

2.1 Meningococcal group C

MenC disease increased from the mid-1990s due to the rapid expansion of a hypervirulent strain belonging to the ST-11 clonal complex that was associated with severe disease, high case fatality and a number of outbreaks in educational and other settings. This situation led to an accelerated programme for the development and licensure of a MenC conjugate vaccine in the UK.

Immunisation against group C disease was introduced into the UK routine infant schedule in November 1999 using newly licensed MenC conjugate vaccines. At the same time, there was a large phased catch-up campaign scheduled for completion by October 2000. The campaign targeted all children up to 18 years of age with the scheduling prioritised according to disease risk by age. Eligibility was later extended up to 24 years of age. The MenC immunisation programme resulted in a rapid decrease in cases under 18 years of age ⁽¹⁵⁾. Cases in older age groups also declined because of vaccine impact on reduced carriage in immunised adolescents, thus providing indirect (herd) protection across the population. MenC disease has remained well controlled, with only around 30-40 cases annually over the last decade. Many current cases are diagnosed in adults who were born outside the UK and may, therefore, not have had the same opportunities to be vaccinated as their UK peers with small numbers arising in children despite MenC immunisation.

2.2 Meningococcal group W

In the UK, a small increase in MenW during the early 2000s was associated with the Hajj pilgrimage, but this was rapidly controlled following mandatory MenACWY vaccination for all pilgrims entering Saudi Arabia. Since then, MenW cases have occurred sporadically, accounting for less than 5% of all IMD cases. From 2010/2011, however, MenW cases began to increase and exceeded 200 cases in 2015/16 ⁽¹⁶⁾. This increase was due to the emergence and rapid expansion of a hypervirulent strain belonging to the ST-11 clonal complex, which was responsible for severe disease and high case fatality rates in South America ⁽¹⁷⁾. In response to this national outbreak, the UK introduced an emergency MenACWY immunisation programme for adolescents from August 2015. This programme included replacement of the routine MenC vaccine at 13-14 years with the MenACWY conjugate vaccine, alongside a catch-up for 14-18 year-olds and new university entrants, up to their 25th birthday. The increase in MenW disease has since slowed and, by August 2016, a 69% decrease was observed among English school leavers in 2015 (the first cohort to be immunised) compared to expected cases from pre-vaccination trends ⁽¹⁸⁾.

2.3 Meningococcal group Y

MenY disease is uncommon in the UK and predominantly affects older adults with underlying health conditions. A small increase in MenY disease was observed in 2008/09 but cases have been relatively stable since 2010/11, with around 100 cases confirmed each year. Teenagers are offered protection against MenY disease through the MenACWY vaccination programme.

2.4 Meningococcal group B

MenB disease has declined over the past decade, most likely because of secular trends ^[9]. MenB accounted for nearly 90% of cases between 2006 and 2011, with an overall incidence of nearly 2/100,000. The highest MenB incidence was observed among infants (~40/100,000), followed by toddlers (13/100,000) and then 15-19 year-old adolescents (3/100,000) ⁽¹⁹⁾. Cases in infants increased from birth and peaked at 5 months then declined gradually until the age of 12 years, before rising to a second smaller peak at 18 years. Around 26% of MenB cases occur in the first year of life and ~60% in children aged <5 years. An early impact on MenB disease in eligible cohorts following the introduction of MenB vaccine (Bexsero[®]) in the infant schedule from September 2015 has been observed ⁽²⁰⁾.

2.5 Other meningococcal groups

Other meningococcal groups rarely cause invasive disease in the UK, with most cases occurring in those with underlying health conditions.

3. Vaccination programmes

3.1 MenC vaccines

MenC vaccine (Meningitec[®], Menjugate[®] or NeisVac[®]) was included in the routine infant programme from November 1999. These conjugate vaccines confer high levels of serum bactericidal antibody and induce immunological memory in individuals from the age of two months ⁽²¹⁾. The vaccine is 88–96% effective against invasive meningococcal disease due to serogroup C infection for all ages within the first year following a primary course. However, protection against MenC disease declines over time, especially in children who were immunised as infants or toddlers ⁽²²⁾. MenC conjugate vaccine confers no protection against other serogroups (eg A, B, W, or Y).

Currently (August 2019), all individuals born since 01 September 1981 should have been offered at least one dose of MenC vaccine.¹ The national MenC vaccine schedule has been revised several times over the past decade. In teenagers, MenC vaccine offered to 13-14 year olds and new university entrants from autumn 2013 was replaced with MenACWY vaccination from August 2015. The remaining infant MenC dose, at 3 months, was removed from the national immunisation schedule in July 2016. A single dose of Menitorix® vaccine (combined MenC-Haemophilus influenzae type B [Hib]) is offered at 12 months of age. NeisVac[®] is the only MenC vaccine now marketed in the UK.

3.2 Quadrivalent MenACWY vaccines

The MenACWY conjugate vaccine (Menveo[®], Nimenrix[®]) replaced the MenC vaccine for 13-14 year-olds and new university entrants up to 25 years of age from August 2015; catch-up vaccination has also been offered during 2015-17 to those who were aged 14-18 years in 2015.

MenACWY conjugate vaccines induce higher antibody responses to all four serogroups after two doses compared with the plain polysaccharide vaccine $^{(23, 24)}$. The response to serogroup C is comparable with that seen with the monovalent MenC conjugate vaccine⁽²⁵⁾.

¹ See MENSV01 for details of expected MenC vaccination history according to date of birth

3.3 MenB vaccine

4CMenB (Bexsero^{®;} GSK) was licensed in Europe in early 2013 and is a protein based vaccine containing 4 main components: factor H binding protein (fHbp) variant 1.1, Neisserial Adhesin A (NadA), Neisseria Heparin Binding Antigen (NHBA) and the New Zealand OMV incorporating Porin A (PorA) P1.4 ⁽¹⁴⁾.

The MenB vaccine (Bexsero[®]) has been included in the routine infant programme since 01 September 2015. Infants born in May 2015 were eligible for the vaccine at 4 and 12 months, those born in June were eligible for the vaccine at 3, 4 and 12 months and those born since 01 July 2015 are offered the vaccine at 2, 4 and 12 months alongside their other routine immunisations. In 2017, another MenB vaccine, using bi-valent lipidated fHbp (Trumenba[®]; Pfizer), was licensed in Europe. Trumenba[®] is licensed for individuals aged 10 years and older; this age restriction is likely to be lowered following favorable data in younger children. The vaccine is licensed to be given as two doses (0.5 ml each) administered at a 6-month interval or as 3 doses (2 doses at least 1 month apart, third dose at least 4 months later).

Both vaccines were licensed based on immunogenicity data and have been used in university-associated MenB outbreaks, with no additional cases reported after vaccination. The implementation of Bexsero[®] into the UK national immunisation schedule and its recent use in a region of Quebec with high disease incidence ⁽²⁶⁾, has provided more convincing evidence of its effectiveness in the field compared to Trumenba[®], which has yet to be implemented in a national immunisation schedule.

4. Previous guidance

The Public Health Laboratory Service (PHLS) published comprehensive guidance on the control of meningococcal disease in England and Wales in 1995 ^(27, 28). More detailed guidance followed on cluster management ⁽²⁹⁾, prophylaxis in dispersal settings ⁽³⁰⁾, cases and clusters in universities ⁽³¹⁾, use of ciprofloxacin, NICE guidance on preadmission management including antibiotics ⁽³²⁾, prophylaxis for healthcare workers ⁽³³⁾ and new health protection legislation.

This 2019 UK guidance update has been reviewed by the PHE Vaccine Preventable Invasive Bacterial Infections (VaPIBI) Forum. The 2018 updated guidance replaced the 2012 Guidance for public health management of meningococcal disease in the UK and the 2014 guidance on preventing secondary cases of MenB disease. It included more recent data on disease epidemiology, new immunisation programmes and vaccines, together with updated advice on vaccination of cases and close contacts.

Table 1. Levels of evidence

1++ High quality meta analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias.

1+ Well conducted meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.

1- Meta analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.

2++ High quality systematic reviews of case-control or cohort studies. High quality casecontrol or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal.

2+ Well conducted case control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal.

2- Case control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal.

3 Non-analytic studies, e.g. case reports, case series.

4 Expert opinion.

Grades of recommendation

A. At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or a systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results.

B. A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+.

C. A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++.

D. Evidence level 3 or 4; or; extrapolated evidence from studies rated as 2+.

www.sign.ac.uk/guidelines/fulltext/50/section6.html

5. Pre-admission management

5.1 Recommendation

NICE recommends that children and young people with suspected bacterial meningitis without non-blanching rash should be transferred directly to secondary care without giving parenteral antibiotics ⁽³²⁾. If urgent transfer to hospital is not possible, for example, in remote locations or adverse weather conditions, antibiotics should be administered to children and young people with suspected bacterial meningitis.

For suspected meningococcal disease (meningitis with non-blanching rash or meningococcal septicaemia) parenteral antibiotics (intramuscular or intravenous benzylpenicillin) should be given at the earliest opportunity, either in primary or secondary care, but urgent transfer to hospital should not be delayed in order to give the parenteral antibiotics.

The administration of benzylpenicillin in children and young people should only be withheld if they have a clear history of anaphylaxis after a previous dose; a history of a rash following penicillin is not a contraindication.

Recommendation 1: Pre-admission management (British National Formulary)		
Rapid admission to hospital is the highest priority when invasive meningococcal disease is suspected.		
	Evidence grade C	
Immediate single dose of IV/IM benzylpenicillin for suspected meningococcal infections		
Adults and children aged 10 years or over	1.2g	
Children aged 1 to 9 years	600mg	
Children aged under 1 year	300mg	

6. Laboratory investigation of suspected cases

Patients with suspected meningococcal disease should have appropriate samples taken for bacterial culture, ideally prior to antibiotic administration, as well as PCR testing. The source of sampling will depend on clinical presentation and may include blood, cerebrospinal fluid (CSF), joint fluid and/or pleural fluid. A bacterial throat swab should also be taken from all cases with suspected meningococcal disease – a positive meningococcal isolate may provide useful information about the infecting strain in PCR-confirmed cases. If there is a delay in obtaining samples for meningococcal PCR from patients, it may still be possible to retrieve specimens from haematology and chemistry departments. When meningitis is present, CSF is the most appropriate and important sample for confirmatory testing. Whilst it may not be successful, this offers the best chance of yielding an organism for culture and importantly meningococcal DNA can be found in the CSF up to 96 hours after commencing antibiotics ⁽³⁴⁾. When a patient presents with septicaemia with or without meningitis then blood culture and whole blood (EDTA) are extremely useful to support the diagnosis.

Under the Health Protection (Notifications) Regulations (2010), all diagnostic laboratories in England are required to notify PHE when they identify specific infections, including *Neisseria meningitidis*

(http://www.legislation.gov.uk/uksi/2010/659/contents/made). The regulations state that "if the operator of the diagnostic laboratory considers that the case is urgent, the notification must be provided orally as soon as reasonably practicable". Similar legislation applies in Wales and Scotland. Diagnostic laboratories in Northern Ireland voluntarily notify the Public Health Agency (PHA) when they identify specific infections, including *Neisseria meningitidis*. The Public Health (NI) Act 1967 is currently being updated.

The PHE Meningococcal Reference Unit (MRU) offers a national reference service for confirmation and characterisation of invasive meningococcal isolates in England, Wales and Northern Ireland. In Scotland this service is provided by the Scottish Haemophilus, Legionella, Meningococcus and Pneumococcus Reference Laboratory. All invasive meningococcal isolates should be referred to the National Reference Laboratory for confirmation, serogrouping and whole genome sequencing, even if the case has already been confirmed by PCR. The National Reference Laboratories also offer a free service for meningococcal PCR of clinical samples from suspected IMD cases. If IMD is confirmed by a local diagnostic laboratory (including private laboratories), then the original sample, including extracts from PCRs, should be referred to the National Reference Laboratory to allow the capsular group to be confirmed or identified and for

additional characterisation. In addition to the routine testing, further strain characterisation may be undertaken in certain situations, such as outbreaks.

To identify and characterise *N. meningitidis,* a combination of traditional and molecular techniques are used. In general, organisms are cultured from blood, CSF or another sterile site. Strain differentiation is usually performed by PHE MRU and involves characterisation of capsular polysaccharide and some outer membrane proteins using a monoclonal antibody-based internationally-recognised typing scheme. This allows phenotypic classification by capsular group, type and subtype. In Europe, PCR is also widely used and this currently mainly allows capsular group determination. Over 50% of IMD cases in England and Wales are now confirmed by PCR only. PorA and fHbp sequencing is also applied to non-culture samples (if there is sufficient DNA) and has the potential for use in outbreak investigations.

Relatively high resolution genotypic analysis (e.g., Multilocus Sequence Typing (MLST) and whole genome sequencing) can identify genetic relationships between organisms during outbreaks as they evolve over time. Because isolates are batched for genotypic testing, however, their use in outbreak management is limited because decisions regarding immunisation need to be taken rapidly to have an impact on disease transmission. MenB characterisation using Meningococcal Antigen Typing System (MATS) would be ideal for identification of vaccine-preventable strains, but is yet to be implemented on a real-time basis.

In England, the PHE Immunisation Team will request that paediatricians arrange for any child under 5 years of age with confirmed IMD to have an additional blood test at 3-6 weeks after diagnosis for convalescent serology (2 ml serum sample).

There are detailed descriptions of the list of available tests for meningococcal disease including specimen types available here:

https://www.gov.uk/government/publications/meningococcal-reference-unit-mru-usermanual. In Scotland, the user manual is available at http://www.nhsggc.org.uk/aboutus/professional-support-sites/microbiology/scottish-microbiology-referencelaboratories/scottish-haemophilus-legionella-meningococcus-pneumococcus-referencelaboratory/

Recommendation 2: Laboratory investigation

The following specimens should be collected on, or soon after, admission to hospital from all patients (ideally before initiating antibiotics) when meningococcal infection is considered in the differential diagnosis:

- blood for culture
- blood for PCR (ideally EDTA or, alternatively, other unclotted blood specimen)
- If meningitis suspected, CSF for microscopy, culture and PCR lumbar puncture should not be done where contraindicated and should be delayed until the patient's condition becomes stable and raised intracranial pressure is excluded
- for other localised infections, aspirate from sterile site according to clinical indication (e.g. joints) for microscopy, culture, PCR
- nasopharyngeal (throat) swab for meningococcal culture (all suspected cases); a
 positive meningococcal swab should not be used to diagnose meningococcal
 disease (e.g. pneumonia). However, in PCR-confirmed cases, a positive
 nasopharyngeal swab culture provides important information about the infecting
 strain and should, therefore, be submitted to the National Reference Laboratory
 for additional characterisation

All invasive meningococcal isolates should be referred to the National Reference Laboratory for confirmation, serogrouping and whole genome sequencing, even if the case has already been confirmed by PCR.

As part of enhanced national surveillance,

For children aged <5 year-olds:

- acute serum (2ml) and additional EDTA sample (2ml) for non-culture typing of vaccine antigens (ideally within 72 hours of treatment) should be taken & <u>stored</u>
 <u>locally</u> for confirmed cases in England, the PHE Immunisation Team will request both samples to be sent to MRU using the PHE sample submission form (MenSAM01). (https://www.gov.uk/government/publications/meningococcal-disease-enhanced-surveillance-forms)
- in Scotland samples (acute serum and EDTA sample) should be sent to the Scottish Meningococcal Reference Laboratory, Glasgow. Sample submission forms can be found on-line at http://www.nhsggc.org.uk/about-us/professionalsupport-sites/microbiology/scottish-microbiology-reference-laboratories/scottishhaemophilus-legionella-meningococcus-pneumococcus-reference-laboratory/

For children aged \geq 5 years and adults:

- in England, additional EDTA sample (2ml) to be sent to MRU for non-culture typing of vaccine antigens using the PHE sample submission form MenSAM01
- in Scotland samples (EDTA sample) should be sent to the Scottish Meningococcal Reference Laboratory, Glasgow. Sample submission forms can be found on-line at http://www.nhsggc.org.uk/about-us/professional-supportsites/microbiology/scottish-microbiology-reference-laboratories/scottishhaemophilus-legionella-meningococcus-pneumococcus-reference-laboratory/

NB: Other investigations should be performed according to clinical indication

Cases due to rare serogroups, recurrent meningococcal disease or that arise after conjugate vaccination (see section 8.5.1)

In cases with meningococcal disease caused by rare serogroups (especially MenY cases in those aged 5 to <25 years of age), non-encapsulated meningococci (non-serogroupable) or recurrent infection due to any serogroup, additional immunological investigations should be strongly considered (e.g. presence of spleen, splenic function, complement deficiency, HIV testing). IMD after teenage meningococcal conjugate vaccination (e.g. Men A, C, W, or Y disease after MenACWY conjugate vaccine) is uncommon and such cases should therefore also be similarly assessed for possible underlying risk factors. This should be discussed with relevant immunisation and reference laboratory teams. A template letter for the GP is available to use in such circumstances (Appendix documents).

7. Role of public health

Public health departments have a major role in the management of meningococcal disease by ensuring that there are adequate disease prevention and surveillance programmes in place, preventing secondary cases through contact tracing, and rapidly investigating and managing clusters and outbreaks.

Meningococcal meningitis and septicaemia are statutorily notifiable by registered medical practitioners under the health protection legislation (2010) (www.legislation.gov.uk/uksi/2010/659/contents/made), under Health Protection (Wales) Regulations (2010) upon suspicion of meningitis (all forms) and meningococcal disease, under Scottish legislation as meningococcal infection and under Northern Ireland as meningococcal septicaemia or acute meningitis (bacterial). Clinicians should inform the proper officer, usually an experienced member of the local Health Protection Team, as soon as a case of meningococcal disease is suspected in a patient so that appropriate public health assessment and actions can be undertaken.

In England, Scotland and Northern Ireland, Health Protection Teams should enter all the details of the reported cases on HPZone, a web-based software for public health management of infectious diseases, including any public health actions taken. In Wales, the All Wales Acute Response (AWARe) Team (Health Protection) will enter information onto the equivalent case and incident management system (Tarian). To notify a possible/probable/confirmed case in Wales: during office hours (Mon-Fri 9am-5pm) please contact the All Wales Acute Response (AWARe) Team on 0300 00 300 32; outside of office hours (5pm-9am; weekends and bank holidays), contact Public Health Wales' out-of-hours health protection service via local Ambulance Control.

Recommendation 3: Role of public health

The PHE Health Protection Team should ensure that policies are in place, ideally through a mechanism such as a service level agreement, which recognises the corporate responsibility of the NHS. Policies should ensure that:

- cases are referred early to hospital
- cases are reported promptly to the Health Protection Team
- cases in hospital are investigated appropriately
- contacts are traced and given appropriate information
- appropriate chemoprophylaxis and vaccination is accessible

- information can be cascaded to others, as appropriate, including primary care, schools/universities, education authorities, National Health Service helplines, meningitis charities, employers
- communication with the media is appropriate and efficient giving due consideration to case (and family) confidentiality

All cases where a diagnosis of meningococcal disease is suspected should be promptly notified by clinicians to the Health Protection Team, without waiting for microbiological confirmation. N.B. Notification is a legal requirement.

Evidence grade D

An experienced member of the Health Protection Team should ensure that comprehensive information on cases is gathered to contribute to local public health management and surveillance in I with detail set out in the national enhanced surveillance of vaccination programmes targeting invasive meningococcal disease in England www.gov.uk/government/publications/meningococcal-disease-enhanced-surveillance-plan.The data set should include epidemiological, laboratory and clinical information. This should be recorded on HPZone (England, Scotland and Northern Ireland) or Tarian (Wales).

For cases that require public health action, it is important to request appropriate additional enhanced surveillance samples as soon as possible after hospital admission as detailed in the national enhanced surveillance for meningococcal disease in England document www.gov.uk/government/publications/meningococcal-disease-enhanced-surveillance-plan

For confirmed cases, the PHE national surveillance form (MENSV01) detailed in the national enhanced surveillance for meningococcal disease in England document (www.gov.uk/government/publications/meningococcal-disease-enhanced-surveillance-plan) or local equivalent covering the same detail should be completed and uploaded to HPZone. Surveillance forms for Scotland are available at

www.hps.scot.nhs.uk/immvax/meningococcaldisease.aspx. In Wales the national enhanced surveillance form should be completed for all confirmed cases. No additional surveillance forms require completion in Northern Ireland.

Data for local management and audit programmes should include:

Case – name and address including post code, telephone number, details of general practitioner, dates and times of disease onset/hospital admission/reporting, ethnic group, occupation/workplace, school/college/nursery attended, meningococcal vaccination history, antibiotics given prior to admission, name of hospital/ward, name of consultant, specimens and dates and types of specimens, recent travel history and underlying risk factors (asplenia/splenic dysfunction/complement deficiency/HIV status)

Contacts – addresses and telephone numbers, details of antibiotics/vaccine/information given and by whom; details of general practitioner

Notifier - name, address and occupation

8. Public health action after a case

8.1 Risk to close contacts

Around 97% of cases are sporadic ⁽³⁵⁾. Although the risk to contacts is low, the highest absolute and relative risk is to people who live in the same household as a case of meningococcal disease ^(35, 36). This risk is highest in the first seven days after a case and falls rapidly after this period ⁽³⁵⁾. The absolute risk (AR) of developing a second case of IMD within 30 days of an index case is 1 in 300 if chemoprophylaxis is <u>not</u> administered ⁽⁷⁾. Beyond this period, the risk of meningococcal disease among household contacts is near background levels ⁽³⁵⁾, although later secondary cases have been observed. The increased risk to household members is thought to be due to shared exposure to meningococci in the contact group, although environmental factors and genetic susceptibility in the family may contribute.

The rationale for giving antibiotic chemoprophylaxis to close contacts of IMD cases is to eliminate established carriage from the close contact group and, thereby, to reduce onward transmission. This strategy reduces the risk of secondary cases in household contacts by up to 89% (95%, 42-98%) ⁽³⁷⁾. In such circumstances, the number needed to treat (NNT) – ie the number of close contacts receiving chemoprophylaxis to prevent one IMD case – is estimated to be 218 (95% CI, 121 to 1135) ^[4].

The case is likely to have acquired the invasive strain from a close contact, typically in the same household, who is an asymptomatic carrier ^(38, 39). The incubation period is usually three to five days ⁽¹⁰⁾ and cases do not usually have detectable carriage until admission to hospital or shortly beforehand ⁽¹²⁾. As the highest risk of illness in close contacts is in the first 48 hours after onset of disease in the index case ⁽³⁶⁾ the source of infection in these secondary cases is most likely to be from the same (or another) carrier and not from the index case.

Antibiotic chemoprophylaxis also eradicates carriage in those who have newly acquired the invasive strain and who may themselves be at risk of IMD. In this instance, individuals who have prolonged close contact with the case after the onset of illness but before the case is treated with antibiotics would also benefit from antibiotic chemoprophylaxis.

It follows that transient contact with the index case before acute illness is unlikely to be a significant risk factor for disease; therefore, mere proximity to the case (e.g. during travel in a plane, bus or car) does not justify prophylaxis. Although ECDC guidance indicates flight contact tracing only where there has been intense exposure to nasopharyngeal secretions, the value of this may be limited once the individuals have dispersed ⁽⁴⁰⁾.

Whilst the United States guidance recommends that passengers seated next to the index case on a plane for more than eight hours should be offered prophylaxis, only one such possible on-board transmission was detected in a review by ECDC with onset of symptoms two and five days after landing in two passengers who had sat 12 rows apart. A further possible on-board transmission was identified during an international Scouts outbreak where a Japanese couple developed symptoms 3-4 days after the flight. In both these scenarios, it is unlikely that the ECDC-recommended post-exposure prophylaxis (contact tracing for those sitting next to and/or directly exposed to oral secretions of the index case) would have prevented these cases⁽⁴⁰⁾.

Box One: Case definitions Cases requiring public health action Confirmed case

Clinical diagnosis of meningitis, septicaemia or other invasive disease (e.g. orbital cellulitis, septic arthritis) AND at least one of:

- Neisseria meningitidis isolated from a normally sterile site
- gram negative diplococci identified in a normally sterile site
- meningococcal DNA in a normally sterile site
- meningococcal antigen in blood, CSF or urine

Although not meeting the definition of a confirmed case, *meningococcal infection of the conjunctiva* is considered an indication for public health action (i.e. treatment for the case and antibiotic prophylaxis for close contacts, but not vaccination) because of the high immediate risk of invasive disease.

Probable case

- clinical diagnosis of meningitis or septicaemia or other invasive disease where an experienced member of the Health Protection Team, in consultation with the physician and/or microbiologist, considers that meningococcal infection is the most likely diagnosis (see: Box Three for sources of materials on characteristic symptoms and signs of meningococcal disease in different age groups). Some microbiological tests (e.g. rising antibody levels) that are not considered sufficient to confirm the diagnosis may change the case category from 'possible' to 'probable'
- in cases of meningitis or septicaemia with clinical and laboratory evidence of bacterial infection but where the causative pathogen is not known, meningococcal disease should be considered in the differential diagnosis, especially in previously healthy children and young adults; where *Neisseria*

meningitidis could be responsible and there is no alternative diagnosis at that time, the case should be considered as "probable" IMD

Cases not requiring public health action

Possible case

Clinical diagnosis of meningitis or septicaemia or other invasive disease where an experienced member of the Health Protection Team, in consultation with the clinician and microbiologist, considers that another diagnosis, such as a viral illness, is a more likely diagnosis than meningococcal disease. Information dissemination after a possible case may still be considered (see Recommendation 8).

Isolation of meningococci from non-sterile sites

- isolation of meningococci from sputum, nasopharynx, bronchoalveolar lavage or genital tract is not by itself an indication for public health action because asymptomatic carriage is common
- non-bacteraemic meningococcal pneumonia is not an indication for public health action but may carry a small risk of transmission in healthcare settings, especially to the immunocompromised ^(41, 42)

As the source of the meningococcal strain may sometimes be outside of the defined population – be it a household or a school – it may not be possible to prevent strains from re-entering the group and, consequently, leading to additional cases in the group. Vaccination of close contacts of an index case can help prevent secondary IMD cases occurring more than 14 days after disease onset in the index case (see section 8.5 Aim of vaccination) ⁽⁴³⁾.

Other contacts (that do not meet the close contact definition)

After a single case of meningococcal disease, the risk of additional linked cases outside of the close contact group is low; this is presumably related to lower likelihood of exposure to the responsible strain ⁽³⁹⁾. In England and Wales from 1995 to 2001, after one case in a pre-school group, a primary school or a secondary school, the absolute risks to each child/pupil in the same institution of becoming a case within the next 28 days were approximately one in 1,500, one in 18,000 and one in 33,000, respectively ⁽⁶⁾.

Antibiotics are not recommended in educational settings after a single case because the benefits in this setting are largely unknown. The potential for risk reduction is limited by the interval between disease confirmation in the case and time to antibiotic administration within the institution; moreover, harm may arise from drug side-effects, development of antibiotic resistance, and eradication of naturally immunising strains from the nasopharynx. This particularly applies in young children who are more likely to be carrying the commensal, *Neisseria lactamica*, than *Neisseria meningitidis* ⁽⁴⁴⁾. Reports of clusters in other settings (e.g. the workplace) are rare and the level of risk is considered to be much lower than in educational settings. As explained previously, transient contact with the index case before acute illness is unlikely to be a significant risk factor for disease, so that mere proximity to the case may not justify prophylaxis. Low-level salivary contact is also not considered to be a risk factor ⁽⁴⁵⁾. No cases have been reported following post-mortem contact with a case of meningococcal disease. Embalming is not considered a hazard for transmission.

For recommendations following a case in a healthcare worker see Section 9 (Recommendation 9).

Box Two: Definition of close contacts Close contact

Close contact is defined as *prolonged close contact* with the case in *a household type setting* during the seven days before onset of illness. Examples of such contacts would be those living and/or sleeping in the same household, pupils in the same dormitory, boy/girlfriends, or university students sharing a kitchen in a hall of residence (Evidence Grade B)

The definition of close contact does not include (Evidence Grade C):

- staff and children attending same nursery or crèche
- students/pupils in same school/class/tutor group
- work or school colleagues
- friends
- residents of nursing/residential homes
- kissing on cheek or mouth (intimate kissing would normally bring the contact into the close, prolonged contact category)
- food or drink sharing or similar low level of salivary contact
- attending the same social function
- travelling in next seat on same plane, train, bus, or car (in the absence of intense exposure to nasopharyngeal secretions – see text)

Contact in an educational setting

educational settings include pre-schools, primary schools, secondary schools, colleges and universities. The term "pre-school" is used synonymously with child-minders, playgroup, nursery, day care or crèche. Within an educational setting, however, it may be possible to define a group that fulfils the definition of a close contact (e.g. in a child-minder setting) and, therefore, have a higher risk of developing secondary IMD. Such groups might benefit from public health action (Evidence Grade D)

8.2 Risk reduction through chemoprophylaxis

A recent systematic review suggested an 84% reduction in the risk of subsequent cases of IMD among household contacts given chemoprophylaxis within 30 days with 200 household contacts needing to be treated to prevent one subsequent case of IMD within 30 days ⁽⁴⁶⁾. A review of retrospective observational studies found a significantly reduced risk of additional cases in the household during the month after a case among household members given rifampicin prophylaxis ⁽³⁷⁾. Two randomised controlled trials found no difference in the protection afforded by ciprofloxacin compared to rifampicin ⁽⁴⁷⁾. In relatively small studies, a single dose of intramuscular ceftriaxone was more effective in eradicating pharyngeal carriage than four doses of rifampicin over two days, while other studies found oral cefixime and azithromycin to be as effective as rifampicin ⁽⁴⁸⁻⁵⁰⁾.

In an ECDC review ⁽⁵¹⁾, rifampicin, ciprofloxacin, ceftriaxone, cefixime and azithromycin were all recommended for preventing secondary cases of meningococcal disease. In the UK, ciprofloxacin is the recommended chemoprophylaxis of choice and rifampicin is a suitable alternative ⁽⁵²⁾. Ceftriaxone must be given by injection.

In the past, ciprofloxacin was not recommended in children due to induced arthropathy in juvenile animals, but abundant evidence of lack of joint damage has been found in young children given ciprofloxacin. In one RCT on carriage eradication, ciprofloxacin when compared to rifampicin did not lead to a higher rate of side effects ⁽⁵³⁾. Multiple controlled prospective and retrospective studies, using higher doses of ciprofloxacin, showed that the rate of adverse events of ciprofloxacin in children was similar to that seen using other antibiotics, and that long-term cartilage damage was not seen in humans ^(54, 55). In all studies, the risk of arthropathy due to ciprofloxacin was very low; arthralgia was transient and most cases were coincidental. A controlled study of 116 neonates receiving ciprofloxacin also showed similar clinical growth compared to 100 controls, even at one year of follow-up (⁵⁶). The risk of tendon disorders in a large retrospective study involving 4,531 children given ciprofloxacin was similarly low compared to children given azithromycin (0.8%) ⁽⁵⁷⁾. In all studies, side effects resolved after cessation of therapy.

Recommendation 4: Indications for antibiotic prophylaxis

Prophylaxis indicated

Chemoprophylaxis should be offered to *close contacts*, irrespective of vaccination status, of cases that require public health action (see case definitions Box One) in the following categories:

- those who have had prolonged close contact with the case (including conjunctivitis) during the seven days before onset of illness (See Box Two for definitions)
- those who have had *transient close contact* with a case *only* if they have been directly exposed to large particle droplets/secretions from the respiratory tract of a case around the time of admission to hospital

Evidence grade B

Evidence grade C

Prophylaxis for the case

Cases treated with intravenous or intramuscular cephalosporins (e.g. ceftriaxone, cefotaxime) do not require antibiotic chemoprophylaxis^(58, 59). If the case (including conjunctivitis cases) is treated with any other antibiotic, chemoprophylaxis should be offered when the case is able to take oral medication and, ideally, before discharge from hospital.

Prophylaxis uncertain

The division between those who do and do not receive prophylaxis can be arbitrary as evidence on risk and benefit is limited outside of the household setting. The Health Protection Team will need to use their judgement to decide whether or not to advise prophylaxis for those who do not clearly fall into the close contact or excluded categories in Box Two. For example, when a case occurs in a group of children looked after by the same child minder or among a circle of close friends, an assessment should be made as to whether these exposures meet the definitions of a close contact.

Timing

Antibiotic prophylaxis should be given as soon as possible (ideally within 24 hours) after the diagnosis of the index case.

Recording of antibiotic administration

When antibiotics are prescribed outside general practice for contacts, the GP practice of each recipient of antibiotic prophylaxis should be informed so that an up-to-date medical record can be retained for their registered patient.

Other situations:

Dispersal settings

In settings where close contacts have been identified and *where contact has now finished*, e.g. those sleeping in the same room on holiday or at university, attempts should be made to arrange chemoprophylaxis within one week of dispersal *if practicable*.

Evidence grade D

Post-mortem contact with a case

Prophylaxis is not indicated. Kissing the body is not considered to be a risk. Body bags are not necessary, and transport to other countries for burial or cremation does not pose a risk. There is no restriction on embalming.

Guidance for public health management of meningococcal disease in the UK: updated August 2019

Evidence grade D

Contacts of possible cases Contacts of possible cases do not need prophylaxis unless or until further evidence emerges that changes the diagnostic category to confirmed or probable.

Evidence grade D

Delayed diagnosis

If the Health Protection Team receives a delayed report of the case, close contacts (as defined above) should be offered chemoprophylaxis, and vaccine if appropriate, up to 28 days after onset of illness (*low risk of further cases after this period*).

Evidence grade D

Cases in contacts who have received prophylaxis If further cases occur within a group of close contacts in the 28 days after receiving prophylaxis, an alternative agent should be used for repeat prophylaxis.

8.3 Choice of agent for chemoprophylaxis

The recent EU-wide restrictions and precautions on the use of systemic fluoroquinolone antibiotics (including ciprofloxacin), due to very rare reports of serious side-effects, do not apply to the single dose of ciprofloxacin recommended for chemoprophylaxis of meningococcal disease.²

Ciprofloxacin, therefore, remains the recommended choice for meningococcal chemoprophylaxis because it has a number of advantages over rifampicin ⁽⁴⁷⁾. It is given as a single dose, does not interact with oral contraceptives, and is more readily available in community pharmacies; it is now licensed for this indication in adults. It is contraindicated in cases of known ciprofloxacin hypersensitivity.

Rifampicin is a suitable alternative although disadvantages include; rapid induction of resistance, inhibition of contraceptives, requirement for multiple doses over two days and availability usually only from hospital pharmacies. Both products are available in preparations suitable for children.

Although benzylpenicillin suppresses meningococcal growth in the throat, it does not reliably eradicate carriage. Around 5% of cases treated with benzylpenicillin still carry the invasive strain after completing treatment and before discharge from hospital ^{(60-62).}

² See EC final decision Quinolone and fluoroquinolone Article 31 referral – PRAC recommends restrictions on use (updated 19/03/2019) page 24, table 11.

https://www.ema.europa.eu/en/medicines/human/referrals/quinolone-fluoroquinolone-containing-medicinal-products#all-documents-section

Convalescent cases may then pose a risk to household contacts unless given a course of antibiotic treatment to eradicate carriage.

Recommendation 5: Choice of agent for antibiotic prophylaxis

Ciprofloxacin

Recommended for use in all age groups and in pregnancy.

The administration of ciprofloxacin may rarely be followed by anaphylactic reactions (^{63, 64}). Healthcare staff should give out information sheets that include the risk of side effects iii and be prepared to deal with allergic reactions. Ciprofloxacin can also interact with other drugs but a single dose is unlikely to have a significant effect. It has an unpredictable effect on epilepsy but may be preferable to rifampicin if the patient is on treatment with phenytoin (see notes below). Dosage (for one dose):

All to be given as a single dose

- adults and children aged 12 years and over: 500 mg stat
- children aged 5–11 years:
- children aged 1-4 years:
- infants <1 year~:

*Ciprofloxacin suspension contains 250mg/5ml

~prescribed off-label

Rifampicin

Recommended for use in all age groups.

Evidence grade B Rifampicin is contraindicated in the presence of jaundice or known hypersensitivity to rifampicin. Interactions with other drugs, such as anticoagulants, phenytoin, and hormonal contraceptives should be considered. Side effects should be explained including staining of urine and contact lenses. Written information for patients should be supplied with the prescription. This is the responsibility of the prescriber.

Dosage

All doses below to be given twice daily for 2 days: Adults and children aged 12 years and over 600 mg

ⁱⁱⁱ See Meningococcal public health communication templates

250 mg stat

- 125 mg stat
 - 30mg/kg to a maximum 125mg stat

Evidence grade B

https://www.gov.uk/government/publications/meningococcal-disease-guidance-on-public-health-management

Children aged 1–11 years Infants (under 12 months of age) 10 mg/kg (maximum dose of 600mg) 5 mg/kg

Suitable Rifampicin doses in children based on average weight for age are:

0-2 months 20 mg (1 ml*) 3-11 months 40 mg (2 ml*) 1-2 years 100 mg (5 ml*)

3–4 years 150 mg (7.5 ml*)

5–6 years 200 mg (10 ml*)

7–12 years 300 mg (as capsule/or syrup)

* Rifampicin syrup contains 100 mg/5 ml

8.4 Pregnancy and breastfeeding

The safety of antibiotic regimens for chemoprophylaxis in pregnant and lactating women is poorly described. Animal reproduction studies have failed to demonstrate a risk to the foetus but there are no well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, antibiotic chemoprophylaxis should be used during pregnancy only if clearly needed. A single dose of ciprofloxacin can be used for the prevention of a secondary case in pregnancy [see British National Formulary], because short duration treatment for other indications appears to be safe ⁽⁶⁵⁻⁶⁸⁾. Of the alternative antibiotics, rifampicin teratogenicity has been reported in animals receiving high doses, but epidemiological studies have not revealed any measurable risk in humans when administered for tuberculosis treatment ⁽⁶⁹⁾. Another clinical trial involved 176 pregnant and lactating women, administered ceftriaxone (2 g) via the intra-muscular route, and only five subjects reported mild side effects; there was, however, no control group ⁽⁵³⁾. For breastfeeding infants, a systematic review of antibiotic use in lactation considered ciprofloxacin and rifampicin as compatible with breastfeeding; other antibiotics were not studied ⁽⁷⁰⁾.

Recommendation 6: Antibiotic Chemoprophylaxis for Pregnant Women

Either ciprofloxacin, ceftriaxone or azithromycin can be used as chemoprophylaxis in pregnancy.

Evidence grade C

Ciprofloxacin

Ciprofloxacin has the advantage of being easy to access in the community and in short duration usage appears to be safe in pregnancy.

Ceftriaxone

Ceftriaxone can only be given by injection and can be painful. Potential side effects include diarrhoea, allergies, hepatic and blood disorders.

AzithromycinEvidence grade BA single dose of azithromycin may be offered for chemoprophylaxis for pregnantwomen.Dosage:Azithromycin 500 mg stat

8.5 Aim of vaccination

Meningococcal vaccination is offered to those at close prolonged contact with the index case to reduce the risk of late cases through longer-term direct protection. The risk of late cases may be due to increased exposure to virulent meningococci, to environmental factors or to increased susceptibility in the family. In cases caused by vaccine preventable strains, vaccination would be expected to reduce the long-term risk of disease in close contacts. The estimated number of unimmunised close contacts needed to vaccinate to prevent a case was estimated to be approximately 1,000 cases based on confirmed serogroup C cases ⁽⁴³⁾.

For MenB, the numbers needed to vaccinate to prevent a single case are substantially higher because at least two doses are required for protection ⁽⁷¹⁾. More importantly, the protein-based MenB vaccines are unlikely to afford adequate protection rapidly enough after a single dose (especially for young children who are at highest risk) and most secondary cases occur within a few days of onset in the index case ⁽⁶⁾.

Vaccine is not indicated for those who received chemoprophylaxis for transient contact, in dispersal settings or for close contacts of conjunctivitis cases.

Meningococcal cases provide an opportunity to complete the national vaccination schedule in cases and contacts who are eligible according to current national recommendations for their age

(https://www.gov.uk/government/publications/immunisation-schedule-the-green-bookchapter-11). Health Protection Teams should ensure that all unimmunised and partially immunised cases receive meningococcal vaccination according to national recommendations for their age (Recommendation 7, page 26).

Recommendation 7: Vaccination

Vaccination of the index case

Unimmunised or partially immunised index cases should receive all their vaccinations according to the nationally recommended schedule for their age when they have recovered from their illness. **Fully immunised cases do not require additional vaccination.**

Evidence grade D

At-risk index cases (e.g. asplenia, complement-deficiency) who are unimmunised or partially immunised should be appropriately immunised. Current recommendations include the MenACWY conjugate vaccine (2 doses one month apart if aged <1 year; 1 dose after first birthday) and MenB vaccine (2 doses two months apart with a booster at 12 months for <1 year-olds, 2 doses 2 months apart for 1-10 year-olds and 2 doses 1 month apart for older children and adults)

Evidence Grade C.

The importance of daily penicillin prophylaxis should be emphasised.

Evidence Grade B.

Vaccination of close contacts

MenACWY

For confirmed serogroup A, C, W or Y infections, close contacts of any age should be offered the MenACWY conjugate vaccine, unless they are confirmed to have been immunised against the relevant meningococcal serogroup within the preceding 12 months (2 doses one month apart if aged <1 year; 1 dose after first birthday). For close contacts of MenC cases, another MenC-containing conjugate vaccine (e.g. Menitorix®, NeisVac®) would be a suitable alternative. *Evidence grade D*

MenB

After a single case of confirmed or probable serogroup B infection, vaccination against MenB is not recommended for close contacts, even if the strain is identified as vaccinepreventable.

At-risk close contacts

Eligible at-risk close contacts (eg asplenia, complement-deficiency) who are unimmunised or partially immunised should be appropriately immunised for their age. Current recommendations include the MenACWY conjugate vaccine (2 doses one month apart if aged <1 year; 1 dose after first birthday) and MenB vaccine (2 doses two months apart with a booster at 12 months for <1 year-olds, 2 doses 2 months apart for 1-10 year-olds and 2 doses 1 month apart for older children and adults). For confirmed serogroup A, C, W or Y infections, fully immunised at-risk close contacts should be offered the MenACWY conjugate vaccine, unless they have received a MenACWY vaccine in the previous 12 months (2 doses one month apart if aged <1 year; 1 dose after first birthday).

The importance of daily penicillin prophylaxis for at-risk individuals should be emphasised.

(Evidence Grade B).

National recommendations for vaccination against meningococcal disease are available here:

https://www.gov.uk/government/publications/routine-childhood-immunisation-schedule

https://www.gov.uk/government/publications/vaccination-of-individuals-with-uncertainor-incomplete-immunisation-status

Other Contacts (who do not meet the definition for close contact – see Box Two)

After a single confirmed or probable case of meningococcal disease, vaccination is not recommended for this group, including those who received chemoprophylaxis for transient contact or in a dispersal setting.

8.5.1 Vaccine failure

The term 'vaccine failure' should be used cautiously in previously immunised IMD cases. No vaccine is 100% effective and vaccine-induced antibodies will wane with time since vaccination. The duration of protection offered by conjugate vaccines, especially in infants and toddlers, is much shorter than originally estimated (¹⁵). The vast majority of children and adults who develop meningococcal disease, including those who are immunised with any of the meningococcal vaccines, are healthy and have no underlying medical problems. However, IMD after teenage meningococcal conjugate vaccination (e.g. Men A, C, W, or Y disease after MenACWY conjugate vaccine) is uncommon and such cases should therefore be assessed for possible underlying risk factors, including asplenia and complement deficiency (72). HIV – undiagnosed or treated - is also a rare but important risk factor for meningococcal disease (73). Those with 2 or more IMD episodes and those with IMD due to unusual capsular groups are also more likely to have underlying risk factors and should be similarly investigated.

Since Bexsero® only aims to protect against 73-88% of group B meningococcal strains causing invasive disease in the UK, Bexsero® failure can only be confirmed in a fully immunised individual if the responsible isolate is identified to be MATS-positive.

Bexsero® coverage cannot be determined for cases confirmed by PCR only, unless the strain possesses the PorA P1.4 antigen or fHbp peptide 1 or 4 or 232.

8.6 Disseminating information

Following a single case of meningococcal disease, it is important to give out information as early diagnosis and treatment should improve outcome. There is a small but real risk of further linked cases (35). Vigilance for signs and symptoms among close contacts is important especially in the immediate high-risk period (one week) after a case. It is important that this information makes it clear that; there is more than one kind of meningococcal disease, vaccines do not protect against all kinds of meningococcal disease and awareness of symptoms and signs can be critical. Accurate and timely information should help to limit the spread of false rumours and anxiety and may help early identification should a further case arise.

Recommendation 8: Disseminating information

Leaflets or other information about meningococcal disease should be widely available and quickly distributed after reporting of a confirmed or probable case. This may also be helpful after a possible case depending on levels of concern, and is a matter for local judgment. See Box Three for useful sources for free leaflets etc and appendix documents can be found on this page .(Appendix document).

Evidence grade D

An experienced member of the Health Protection Team should ensure that information about a case of meningococcal disease is shared with other NHS colleagues and external agencies as necessary. It is important to inform any appropriate general practitioner(s) and out-of-hours services, so that they know what public health action has been taken and to promote early recognition of any further cases. An experienced member of the Health Protection Team may also wish to inform NHS helplines and the meningitis charities.

Evidence grade D

Cases in educational institutions

Heads of pre-school groups, schools, colleges and universities should be informed when there is a confirmed or probable case of meningococcal disease in someone attending their institution. With the advice of an experienced member of the Health Protection Team, letters are usually sent to other parents/students to inform them of the situation (Appendix document). It is recommended to inform and seek support for this action from the case or their relatives, as the letters may result in identification of the case. The purpose of the letter is to give information about meningococcal disease, assist parents and others in the early detection of the disease, allay anxiety and prevent uninformed rumours. The information given should be sufficient to ensure that parents are aware of the situation whilst preserving the confidentiality of the patient. It is usually helpful to explain what public health action has been taken.

If a *possible* case attends an educational institution, consider informing the head of the institution at an early stage. The head will then be in a good position to respond immediately to local concerns and will be able to access advice from the HPTs. Letters to other parents / students may be considered.

Please also see Meningitis and septicaemia prevention and management in higher education institutions $^{\mbox{\scriptsize iv}}$

In Wales there are contingency plans for communicable disease cases/clusters in educational establishments available to the AWARe Team (Health Protection).

Dispersal

If a case is reported within one week of date of last attendance at the institution, distributing information should be considered where practical. This is consistent with chemoprophylaxis in dispersal settings.

Evidence grade D

^{iv} www.gov.uk/government/publications/meningitis-and-septicaemia-prevention-and-management-in-higher-educationinstitutions

9. Chemoprophylaxis in healthcare settings

The risk of meningococcal disease in healthcare workers is very low ⁽⁷⁴⁾. Healthcare workers who were more heavily exposed to nasopharyngeal secretions of cases around the time of admission to hospital were considered to be at higher risk ⁽⁷⁵⁻⁷⁸⁾. UK guidelines for preventing hospital-acquired infections recommend wearing face masks and eye protection when there is a risk of secretions splashing into face and eyes ^(76, 78). Laboratory studies suggest that surgical masks can protect the wearer against droplet transmission ^(79, 80).

Meningococcal pneumonia may carry a low risk of transmission in healthcare settings especially to the immunocompromised ^(35, 41). Meningococcal pneumonia cannot be diagnosed from a sputum sample or from a nasopharyngeal (throat) swab culture because carriage is relatively common in the community. Diagnosis is usually made after the meningococcus is identified in a normally sterile site (typically, blood) – such cases of bacteraemic pneumonia should be managed as invasive disease.

Recommendation 9: Prophylaxis in healthcare settings

In Scotland please refer to National Infection Prevention Control Manual for Scotland http://www.nipcm.scot.nhs.uk

Healthcare workers should reduce the possibility of exposure to large particle droplets (eg by wearing surgical masks, using closed suction) especially when carrying out airway management procedures, so that chemoprophylaxis is not needed.

Evidence grade D

Chemoprophylaxis is recommended only for those healthcare workers whose mouth or nose is directly exposed to large particle droplets/secretions from the respiratory tract of a probable or confirmed case of meningococcal disease during acute illness until completed 24 hours of systemic antibiotics. This type of exposure will only occur among healthcare staff who are working close to the face of the case without wearing a mask or other mechanical protection. In practice this implies a clear perception of facial contact with droplets/secretions and is unlikely to occur unless using suction during airway management, inserting an airway, intubating, or if the patient coughs in your face. General medical or nursing care of cases is not an indication for prophylaxis. Ciprofloxacin 500 mg as a single dose (or, alternatively, rifampicin 600 mg orally twice daily for 2 days) is recommended for prophylaxis.

Evidence grade D

Exposure of the eyes to respiratory droplets is not considered an indication for prophylaxis. Such exposure may, however, carry a low risk of meningococcal conjunctivitis and subsequent invasive disease. Staff should be counselled about this risk and advised to seek early treatment if conjunctivitis should develop within 10 days of exposure.

Evidence grade D

Routine vaccination of healthcare workers with meningococcal vaccines is not recommended because the exposure is invariably transient and those at increased risk will be offered chemoprophylaxis.

Evidence grade D

Vaccination after contact with a confirmed or probable case of meningococcal disease is also not recommended because the exposure is invariably transient and those at increased risk will be offered chemoprophylaxis.

Evidence grade D

The above recommendations also apply to contacts of cases in healthcare workers (including dentists), and to contacts of cases on a hospital ward where the diagnosis is initially unsuspected and not treated with systemic antibiotics. Chemoprophylaxis is not usually indicated for patient or staff contacts of such cases. A hospital ward is not equivalent to a household setting. However, the threshold for giving prophylaxis should be lower for immunocompromised contacts who may be at increased risk of invasive disease. Risk assessment is advised.

10. Clusters and Management

Clusters of IMD occur most commonly within households. In a systematic review assessing the effectiveness of vaccinating household contacts in addition to chemoprophylaxis in outbreaks caused by Men A, C, W or Y, six eligible studies reporting a total of 4,730 primary cases and 30 household clusters with 40 secondary cases were identified ⁽⁴³⁾. The attack rate using a fixed effects Poisson model for meta-analysis was 1.08/1000 contacts (95% CI, 0.7-1.7) in the 14-365 days after disease onset in the index case. Using data from the four studies with a follow-up period of >31 days, the secondary attack rate after chemoprophylaxis was 20-90 per 100,000 household contacts ⁽⁴³⁾. The authors estimated that between 640 and 1,680 household contacts would need vaccinating to prevent a secondary case ^(6, 43).

IMD clusters can also occur in a variety of community settings, particularly in institutions such as pre-schools, schools and colleges/universities. Enhanced national surveillance indicated that there were approximately 16 IMD clusters annually in school settings and a further 3 in pre-school settings in England and Wales during 1995-2001 ⁽⁶⁾. Over the same period (prior to and during the introduction of universal MenC conjugate vaccination), the overall risk of a cluster was similar for MenB and MenC disease. Most MenC cases occurred in secondary schools, while MenB clusters were more common in primary schools ⁽⁶⁾.

An increase in the relative risk (RR) and absolute risk (AR) of a cluster due to any capsular group following an initial case in these educational settings has been reported, with the risk being highest in pre-school (RR, 27.6; AR, 70/100,000) and lowest in secondary school (RR 3.6; AR, 3/100,000) settings ⁽⁶⁾. In most clusters, secondary cases occurred within one week of the index case (29% within 2 days, 68% within 7 days) and, by the end of the third week, the RR of a secondary case was similar to baseline. The majority of clusters (89%) had only 2 cases and, where third cases did occur, 93% were diagnosed within 6 days of a secondary case (although, in one cluster, a third case occurred 21 days after the second case).

A case-control analysis of school children in the USA (1989-1994) estimated the secondary incidence of IMD as 2.5/100,000 in school children aged 5-18 years, with relative risk of 2.3 ⁽⁷⁾. One third of cases occurred within 48 hours of the index case and 75% within 2 weeks. In secondary schools, where 75% of clusters occurred, 73% of secondary cases occurred within 2 weeks of the index case. When more than two cases were identified, in school-based clusters, the mean time between second and third cases was 1.6 days (range 0-5 days). No attempt was made in these studies to estimate any additional benefit of vaccination over chemoprophylaxis in preventing further cases.

In educational settings, once a second case has occurred, the risk of a third case may be as high as 30-50% (6, 81). The risks are highest in the week after the second case. The risk to staff in such clusters is not known. However, of six clusters that contained confirmed cases among both staff and children in educational settings in England and Wales from 1995–2001, five involved pre-school groups or primary schools ⁽⁸²⁾, suggesting a greater risk to teachers of young children.

Relative risk of further cases in other settings has not been formally assessed, but outbreaks in definable social groups, civilian communities and military recruits are well described ⁽⁸³⁾. Although one trial of mass chemoprophylaxis in a closed community (military barracks) showed a significant effect on disease reduction (84), whether such interventions work in schools or civilian communities is not known (85, 86). The aim of such interventions is to eradicate carriage of the outbreak strain from a population at high risk of invasive disease ⁽⁸⁷⁾.

If an outbreak is caused by strains of a serogroup for which an effective vaccine exists, vaccination should be considered. Data from England and Wales showed that if the serogroup of one case had been identified and another case was diagnosed within four weeks in the same school, the second case was likely to be of the same strain as the first case ⁽⁶⁾. In the USA, vaccination of whole communities in community serogroup C outbreaks is considered when a defined threshold is reached ⁽⁸¹⁾.

Assessment of the likely benefits and costs of interventions must then lead to a decision on public health action. External factors such as availability of staff, antibiotics, vaccine and feasibility of action (such as holidays just started) may well influence the decisions made ⁽⁸⁸⁾. More evidence is needed on the effectiveness of such interventions.

10.1 Clusters in a household setting

An IMD household cluster is defined as 2 or more cases confirmed within 28 days in the same household. Such clusters are rare and occasionally may occur after longer intervals. They may indicate increased susceptibility of family members to IMD and/or on-going transmission within the household setting. Following the introduction of the infant MenB immunisation programme in September 2015, the recommendations for MenB vaccination in a cluster setting were revised as set out in Recommendation 11.

Recommendation 10: Vaccination following a household cluster

- when two or more cases of IMD occur within 28 days in the same household and fulfil the definition of a cluster, then all close contacts (including the case) are recommended to receive the appropriate vaccine (MenACWY or MenB) in addition to antibiotic prophylaxis unless they are confirmed to have been immunised against the relevant meningococcal serogroup within the preceding 12 months.
- if additional cases occur within 28 days of receiving antibiotic prophylaxis, then an alternative agent should be used for repeat antibiotic prophylaxis (See Recommendation 4: Indications for antibiotic prophylaxis)

(Evidence Grade D).

10.2 Management of clusters in an educational or residential setting

If 2 or more cases of confirmed/probable IMD occur within 28 days in an educational or residential setting, the following should be considered:

- do the cases fulfil the definition of a cluster? Cases are more likely to be linked if a common social network can be identified, if there is a close geographical and temporal relationship and if the infecting strains are indistinguishable
- is there a clearly identifiable group at increased risk of meningococcal disease that may be benefit from public health action such as wider antibiotic prophylaxis and or vaccination?

Evidence suggests that increased risk of a second case arising in an educational setting following the first case persists for up to around 3 weeks ⁽⁶⁾. Cases arising more than 30 days apart in an educational setting are most likely to be due to different capsular groups or strains of the meningococcus and, therefore, unrelated ⁽²⁶⁾. Thus where intervals exceed the 28 day cluster definition, it is more than likely to represent two separate introductions into the population or indicate that circulation of that particular meningococcal strain is occurring more widely in the local community.

These considerations should be discussed by an Incident Management Team (IMT) and will inform the choice of public health interventions that should be undertaken:

- antibiotic prophylaxis leads to short-term meningococcal clearance and, therefore, offers the greatest benefit if given as soon as possible after a cluster is defined and the risk group is identified
- vaccination provides longer-term direct protection to individuals in clusters. Conjugate vaccines such as the MenC and MenACWY vaccines can also interrupt transmission of the respective serogroups within a network; it is not known whether the current MenB vaccines, which are protein-based, have any impact on carriage

Irrespective of whether the cases in a cluster are linked or not, early dissemination of information should be undertaken to raise awareness of signs and symptoms of IMD because of the importance of being informed and seeking early medical advice if symptoms arise. Please see Appendix documents (Appendix 6, 7 and 8).

Different educational settings are considered; pre-schools, primary schools, secondary schools and universities. Residential setting includes, for example military barracks, asylum centres, nursing/residential homes etc. If indicated, vaccination of contacts in the educational/residential setting should be offered as early as possible because the attack rates are much higher within the first week after the index case is diagnosed.

Where cases do not fulfil the cluster definition (see *Section 10.2*), dissemination of information should still be considered. It may also be possible to identify a clearly defined social network where further intervention could be beneficial. If there is no clear group at increased risk of disease, identifying a potential group to be vaccinated becomes difficult. In the absence of a closed or semi-closed network, wider chemoprophylaxis is also unlikely to be beneficial because chemoprophylaxis provides short-term clearance of the nasopharynx but the bacteria can be reintroduced into the network from those outside the network as soon as protection from chemoprophylaxis declines. Decisions related to public health action in such circumstances should generally be made by experienced members of the Health Protection Team or by the Incident Control Team.

Protective immune response after conjugate vaccines (MenC or MenACWY) is rapid, typically within a week after a single dose of vaccine. Conjugate vaccines also prevent acquisition of carriage, which may help control the spread of infection within the local setting. On the other hand, only 73-88% of MenB strains in the UK are predicted to be preventable by vaccination and at least two doses of MenB vaccine are required to afford adequate protection ⁽⁴⁾. Where Bexsero® is the vaccine of choice in an outbreak situation; the two doses can be offered with a four-week interval for those aged 1 year and older because of the need for early protection. Whilst there are currently no data comparing four week versus eight week intervals in terms of immunogenicity or long-term persistence in those aged 1-10 years, the need for rapid protection would, in these circumstances, outweigh the need for longer-term protection. The effect of MenB vaccination on carriage is not known. This needs to be taken into consideration when assessing the potential benefit of vaccination to control clusters and outbreaks.

Recommendation 11: Managing clusters in educational and residential institutions

Expert advice is available for managing clusters from: Public Health England, Colindale (Tel: 020 8200 4400) AWARe (all Wales Acute Response team) (Tel: 0300 00 300 32) Health Protection Scotland (Tel: 0141 300 1100) or Northern Ireland Public Health Agency Health Protection Duty Room (Tel: 0300 555 0119) Please alert the appropriate organisation to any cluster situation.

Assess the information

When two or more cases are reported in an educational or residential setting, careful and rapid assessment should be made. This should include a review of:

- clinical features of the cases
- microbiological data (serogroup and sequence-based typing)
- dates of onset of illness and of last attendance
- links between cases by age, school year, home address, social activities, and friends
- the type of setting (pre-school, primary school, secondary school or university)
- numbers of students in the school and in each school year

Consider the public health management options

The usual course of action should include dissemination of information to raise awareness of symptoms and signs of IMD because of the need for early medical intervention. Information should be distributed widely using all available platforms to parents and students, as appropriate (see Appendix document).

Evidence grade D

The main decision to be taken by an IMT is whether a high-risk group can be identified that might benefit from public health action, including antibiotic prophylaxis and vaccination to reduce that risk.

The target group should be a discrete group that contains the cases and makes sense to staff/parents/students; for example, children and staff of the same preschool group, children of the same school year, children or students who share a common social activity, or a group of friends. The evidence on risk indicates a need to act promptly with the agreed public health action to prevent additional cases.

Evidence grade D

Make a decision on antibiotic prophylaxis

For clusters in an educational or residential setting, if a clear high-risk group can be defined that contains the cases, antibiotic prophylaxis should be offered to that group. If a subgroup cannot be defined, then a decision may be needed on offering prophylaxis to the whole institution. This will depend on factors such as the size of the population, the time interval and age difference between cases, whether the cases are confirmed or not, etc.

For clusters among children at pre-school groups and primary schools, both children and staff should normally be included in the group offered chemoprophylaxis and vaccination (some evidence of increased risk) but not in clusters among students at secondary schools, colleges, or universities (no evidence of increased risk).

Where ciprofloxacin is recommended, Patient Group Directions may be helpful: https://www.gov.uk/government/publications/meningococcal-disease-pgd-template-forsupply-of-ciprofloxacin.

Evidence grade D

Make a decision on vaccination

Template patient group directives are available for meningococcal vaccines at https://www.gov.uk/government/collections/immunisation-patient-group-direction-pgd

For a cluster involving confirmed serogroup A, C, W or Y cases: the quadrivalent conjugate vaccine should be offered to all individuals of any age who were offered antibiotics unless they are confirmed to have been immunised against the relevant meningococcal serogroup within the preceding 12 months. In the case of a MenC outbreak, another MenC-containing conjugate vaccine (e.g. Menitorix®, NeisVac®) would be a suitable alternative.

Evidence grade D

For a cluster involving confirmed serogroup B cases: vaccination against MenB should be considered and would usually be offered to the same group that would receive antibiotic chemoprophylaxis as soon as practically possible based on the schedule table below. However, vaccination should target those in the group identified as potentially being at ongoing increased risk of disease; for example, if there are 2 MenB cases in a nursery, then nursery contacts may be offered MenB vaccination, but the household contacts of each case would not be considered as have ongoing increased risk.

Evidence grade D

Choice of MenB vaccine

Two vaccines are licensed against MenB; 4CMenB (Bexsero®; GSK) and Trumenba® (Pfizer Ltd). The vaccination dosing and schedule for Bexsero®, as well as the licensed age indication, is more suitable for outbreak control than Trumenba®. Bexsero® also has proven efficacy in the field. Therefore, until more data become available, Bexsero® is the vaccine of choice unless the outbreak strain is predicted not to be prevented by this vaccine (using Meningococcal Antigen Typing System [MATS], for example, if isolates are available). MATS results, however, are not timely and should not delay public health decisions.

Evidence grade D

In a cluster or outbreak situation, MenA,B,C,W and Y cases should also be vaccinated as part of the social network when the cluster/outbreak is declared, unless they have received the vaccine in the previous 12 months.

Evidence grade D

In line with Recommendation 7, in a cluster situation, vaccine is not indicated for those who received chemoprophylaxis for transient contact **in dispersal settings** as they would not usually be considered to have ongoing increased risk.

Evidence grade D

Age	4CMenB Vaccination Status	Schedule for secondary prevention of MenB disease
<8 weeks	Unvaccinated	Vaccinate in accordance with routine vaccination schedule at the appropriate ages
≥8 weeks and < 1 year old	Unvaccinated	Give 2 doses eight weeks apart with a booster at 1 year of age
1-10 year- olds	Unvaccinated	Give 2 doses four weeks apart*
>10 year old and adults	Unvaccinated	Give 2 doses four weeks apart
< 1 year old	Vaccinated	Continue and complete routine vaccination schedule
≥1 year old	Received only a single dose of 4CMenB in infancy	Give a second dose of MenB providing at least four weeks* have elapsed since the last dose. A further dose should be given four weeks* later.
≥1 year old	Completed only primary vaccination with two doses in infancy	Give a single booster dose providing at least four weeks* have elapsed since the last dose.
≥1 year old	Completed only a single dose in infancy and a booster after first birthday	Give a single dose of MenB providing at least four weeks* have elapsed since the last dose.
≥1 year old	Fully vaccinated, have received two or more doses in infancy plus a booster after 1 st birthday	If the final dose was given more than 12 months previously give a single booster dose of MenB vaccine. If the final dose was given within the past 12 months no further vaccination is needed.
≥1 year old	Partially vaccinated (outside the national programme), one dose only received after 1 st birthday	Give a single dose of MenB providing at least four weeks* have elapsed since the last dose.

Table of vaccination schedule for MenB cases and contacts

	≥1 year old	Fully vaccinated (outside the national programme), two doses received after 1 st birthday	If the final dose was given more than 12 months previously give a single booster dose of MenB vaccine. If the final dose was given within the past 12 months no further vaccination is needed.
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*There is no accelerated immunisation schedule for 4CMenB but the interval between doses for 1-10 year olds should be reduced to four weeks for secondary prevention of MenB disease because of the need for rapid protection.

Evidence grade D

For a cluster involving two or more "*probable*" cases: every attempt should be made to determine the meningococcal capsular group for at least one case before any decision to offer vaccination is made. If this is not possible, then a vaccine with broad coverage such as 4CMenB (Bexsero®) or Trumenba® (both vaccines may also help protect against other capsular groups) may be considered.

If antibiotics and/or vaccine are to be offered, make urgent arrangements in line with local procedures with:

- community medical/nursing staff to deliver medicines/vaccine/information
- head of the institution to inform parents/students and seek consent
- pharmacists to supply antibiotics (in correct formulation, dosage and information sheets) and vaccines ⁽⁸⁹⁾

NB: Closing the school is not advised as no reduction in risk would be expected (levels of contact among social networks are unlikely to be reduced and may be increased; also, application and success of public health actions will be assisted if school attendance is high).

Swabbing to measure carriage of outbreak strains is not usually recommended in acute outbreaks because decisions have to be taken before results are available and because carriage rates often bear no relationship to risk of further cases.

NB: If two or more cases occur within a clearly defined social group outside an educational setting, the same principles as for a school cluster apply.

Recording of antibiotic and vaccine administration

When antibiotics are prescribed or vaccinations given outside general practice in an outbreak setting, the GP practice of each recipient of antibiotic prophylaxis and vaccination (with batch and product information) should be informed so that an up-to-date medical record can be retained for their registered patient.

Emergency vaccine supply for use in an outbreak situation

In England and Wales, if there is no vaccine stock available from the manufacturers or if there is any delay, then discuss with colleagues in the Immunisation Department at PHE Colindale and/or email Vaccinesupply@phe.gov.uk for advice. In Scotland, vaccine supply should be obtained from local hospital pharmacy departments. Details of these are available from Procurement, Commissioning & Facilities of NHS National Services Scotland 0131 275

6725. Vaccine supply for use in clusters in Northern Ireland should be discussed with the Public Health Agency Health Protection Duty Room 0300 555 0119.

Linked cases that do not meet the cluster definition (See Section 10.2) In such circumstances, a broad 'warn and inform' approach would be indicated. Public health action following linked cases that do not meet the cluster definition will need to be decided based on the specific circumstances.

10.3 Management of clusters in the wider community

One of the major difficulties in targeting a wider community for intervention is deciding on the population boundaries, often defined by age group and geography. Such boundaries will of necessity be arbitrary. As far as possible, use existing administrative boundaries that make sense to the people who live within and without them. In any case, there are likely to be people living on the other side of the boundary who may feel unjustifiably excluded. The extent of public concern and press interest can be extensive. There have been examples of extended clusters of disease within sociallyrelated groups over a poorly defined geographical area. Such clusters may be difficult to define as there may be more than one link by recreational activity (e.g. sports club) or through regular social groups.

Although school outbreaks must be handled quickly in order to control alarm and reduce immediate risk of further cases, wider community outbreaks usually build up more slowly and by their nature are more diffuse. The same principles and management steps apply (see recommendations 11, 12 and 13).

In such situations, age-specific attack rates should be calculated.

10.3.1 Calculating age-specific attack rates

The numerator would be the number of confirmed cases in the population at risk caused by strains of the same capsular group and that are not distinguishable by standard molecular typing. Multiple cases in the same household or in the same institutional setting would be considered (if this setting is considered to be the focus of a separate outbreak) as a single case.

The denominator would be the population at risk, which must be clearly defined if meningococcal vaccination is to be offered, and make sense to the people who live within and outside the selected boundaries (eg a rural town/village, a secondary school with its feeder schools, etc.). It may not be easy to define such a population. If the outbreak is mainly in children, the denominator should be based on the age range of children at risk (e.g. 2-4 year olds, 2-16 year olds, etc.) in whom the vaccine should be effective.

Vaccine should only be considered if the age-specific attack rate (number of confirmed outbreak strain cases [suggested minimum of four] divided by the number in target age group) in a three-month period is "high". Although a precise threshold for intervention has not been set, age-specific attack rates among 2 to 16 year olds targeted for intervention in two community outbreaks during the winter of 1995/6 caused by serogroup C strains were over 40/100,000.

The vaccination dosing and schedule for Bexsero®, as well as the current licensed age indication, is more suitable for outbreak control than Trumenba®. Bexsero® also has proven efficacy in the field ⁽²⁰⁾. Therefore, until more data become available, Bexsero® is the vaccine of choice unless the outbreak strain is predicted not to be prevented by this vaccine (using Meningococcal Antigen Typing System [MATS], for example).

Recommendation 12: Managing clusters in the wider community

Any decision to offer meningococcal vaccines to wider communities will require careful assessment of all the available epidemiological information, such as the number of confirmed and probable cases, molecular information on infecting meningococcal strains, dates of onset, links between cases, size of the community, and routine vaccination uptake rates.

Evidence grade D

Vaccination against clusters of the same serogroup of IMD may be considered in the community if the age-specific attack-rate (for a vaccine preventable strain in the case of MenB) within a defined geographical boundary over a three-month period exceeds 40/100,000.

10.4 Disseminating information in cluster management

It is essential that clear, consistent and accurate information is provided to parents, students and staff, and the wider community. The target group should be clearly identified and information to this group should emphasise the importance of early recognition of symptoms and prompt access to medical services. (see appendix 5-7 for templates).

Local general practitioners and out-of-hours services should be advised to be on the alert for any new cases associated with the cluster. It may also be helpful to alert receiving Accident and Emergency Departments and admitting clinicians.

As far as possible, information that may need to be disseminated should be prepared in advance. In pre-school and school settings an experienced member of the Health Protection Team should liaise closely with the manager or head teacher. In college/university settings liaison will usually be with a member of the senior

management team (See Higher Education Institution Guidance available from: https://www.gov.uk/government/publications/meningitis-and-septicaemia-preventionand-management-in-higher-education-institutions). It is advisable for one person within the college/university to coordinate operations, and to receive and disseminate all information. Registry departments can aid in tracing students and getting information to them, and personnel or occupational health departments can help disseminate information to staff groups. In Wales there are institution-specific contingency plans for educational settings available to the AWARe team and OOH teams.

A communication strategy will be required. If high levels of interest are anticipated or already evident, consider; telephone helplines (See Box Three for helpline contact details), allowing controlled media access to vaccination sites, and regular coordinated press briefings and to hold press conferences ⁽⁸³⁾.

Box Three: Helplines and leaflets

Meningitis charities and NHS111/NHS 24/NHS Direct

The meningitis charities may be contacted when there is a case of meningococcal disease. They need to have sufficient information so that they can support callers with appropriate advice. The information given to these bodies should include anonymised details of the case and of public health action taken.

Leaflets and posters available from Health and Social Care Publications orderline

Ordering from the Department of Health (DH) Health and social care order line is easy and the service is free of charge. Anyone can register for an account. Once you have registered you will then be allocated an account and can place orders. You will need your full postal address and an email address.

www.orderline.dh.gov.uk/ecom_dh/public/newAccount.jsf

Meningitis Now 01453 768000 Meningitis Research Foundation: 0333 4056262 for England and Wales 0131 5102345 for Scotland 028 90321283 for Northern Ireland

Helplines

Meningitis Now 0808 80 10 388 (Freephone) 9am to 8pm every day. • In addition to obtaining leaflets and posters by calling the Meningitis Now office, they can also be viewed and downloaded from the website: https://www.meningitisnow.org/how-wehelp/resources/view-download-order/

Meningitis Research Foundation 0808 800 3344 (Freefone). Information and support is also offer by email and on social media: helpline@meningitis.org; www.facebook.com/meningitisresearch; @M_R_F

NHS 111 (England) NHS 24 (Scotland) Dial 111 NHS Direct Wales 0845 46 47

Websites

Meningitis Research Foundation www.meningitis.org Meningitis Now www.meningitisnow.org NHS Choices http://www.nhs.uk/conditions/Meningitis/Pages/Introduction.aspx Public Health England https://www.gov.uk/government/collections/meningococcal-diseaseguidance-data-and-analysis Public Health Agency, Northern Ireland- http://www.publichealth.hscni.net/ Health Protection Scotland http://www.hps.scot.nhs.uk/immvax/meningococcaldisease.aspx?subjectid=103,104 Scotland NHS Inform https://www.nhsinform.scot/ Immunisation Scotland http://www.immunisationscotland.org.uk/ Public Health Wales http://www.publichealthwales.wales.nhs.uk/ The Green Book https://www.gov.uk/government/publications/meningococcal-the-green-bookchapter-22.

References

1. Halperin SA, Bettinger JA, Greenwood B, Harrison LH, Jelfs J, Ladhani SN, et al. The changing and dynamic epidemiology of meningococcal disease. Vaccine. 2011;30 Suppl 2(1873-2518 (Electronic)):B26-B36.

2. Christensen H, May M, Bowen L, Hickman M, Trotter CL. Meningococcal carriage by age: a systematic review and meta-analysis. Lancet Infect Dis. 2010;10(12):853-61.

3. Trotter CL, Gay NJ, Edmunds WJ. The natural history of meningococcal carriage and disease. EpidemiolInfect. 2006;134(0950-2688 (Print) LA - eng PT - Journal Article SB - IM):556-66.

4. Ladhani SN, Cordery R, Mandal S, Christensen H, Campbell H, Borrow R, et al. Preventing secondary cases of invasive meningococcal capsular group B (MenB) disease using a recently-licensed, multi-component, protein-based vaccine (Bexsero(®)). The Journal of infection. 2014(July).

5. Granerød J, Davison K, Stuart J, Crowcroft N. Clusters of meningococcal disease in educational establishments in the United Kingdom: April 2001 to March 2002. Communicable disease and public health / PHLS. 2004;7(1):51-5.

6. Davison KL, Andrews N, White JM, Ramsay ME, Crowcroft NS, Rushdy AA, et al. Clusters of meningococcal disease in school and preschool settings in England and Wales: what is the risk? Archives of Disease in Childhood. 2004;89(3):256-60.

7. Zangwill KM, Schuchat A, Riedo FX, Pinner RW, Koo DT, Reeves MW, et al. School-based clusters of meningococcal disease in the United States. Descriptive epidemiology and a case-control analysis. Jama. 1997;277(5):389-95.

8. Whittaker R, Dias JG, Ramliden M, Kodmon C, Economopoulou A, Beer N, et al. The epidemiology of invasive meningococcal disease in EU/EEA countries, 2004-2014. Vaccine. 2017;35(16):2034-41.

9. Goldschneider I, Gotschlich EC, Artenstein MS. Human immunity to the meningococcus. II. Development of natural immunity. The Journal of experimental medicine. 1969;129(6):1327-48.

10. Boutet R, Stuart JM, Kaczmarski EB, Gray SJ, Jones DM, Andrews N. Risk of laboratoryacquired meningococcal disease. J Hosp Infect. 2001;49(4):282-4.

11. Orr H, Kaczmarski E, Sarangi J, Pankhania B, Stuart J. Cluster of meningococcal disease in rugby match spectators. Commun Dis Public Health. 2001;4(4):316-8.

12. Edwards EA, Devine LF, Sengbusch GH, Ward HW. Immunological investigations of meningococcal disease. III. Brevity of group C acquisition prior to disease occurrence. Scandinavian journal of infectious diseases. 1977;9(2):105-10.

13. Bygraves JA, Urwin R, Fox AJ, Gray SJ, Russell JE, Feavers IM, et al. Population Genetic and Evolutionary Approaches to Analysis of Neisseria meningitidis Isolates Belonging to the ET-5 Complex. Journal of Bacteriology. 1999;181(18):5551-6.

14. Bai X, Findlow J, Borrow R. Recombinant protein meningococcal serogroup B vaccine combined with outer membrane vesicles. Expert Opin Biol Ther. 2011;11(7):969-85.

15. Campbell H, Borrow R, Salisbury D, Miller E. Meningococcal C conjugate vaccine: the experience in England and Wales. Vaccine. 2009;27 Suppl 2:B20-9.

16. Ladhani SN, Beebeejaun K, Lucidarme J, Campbell H, Gray S, Kaczmarski E, et al. Increase in endemic Neisseria meningitidis capsular group W sequence type 11 complex associated with severe invasive disease in England and Wales. Clin Infect Dis. 2015;60(4):578-85.

17. Lucidarme J, Hill DM, Bratcher HB, Gray SJ, du Plessis M, Tsang RS, et al. Genomic resolution of an aggressive, widespread, diverse and expanding meningococcal serogroup B, C and W lineage. J Infect. 2015;71(5):544-52.

18. Campbell H, Edelstein M, Andrews N, Borrow R, Ramsay M, Ladhani S. Emergency Meningococcal ACWY Vaccination Program for Teenagers to Control Group W Meningococcal Disease, England, 2015-2016. Emerg Infect Dis. 2017;23(7).

19. Ladhani SN, Flood JS, Ramsay ME, Campbell H, Gray SJ, Kaczmarski EB, et al. Invasive meningococcal disease in England and Wales: implications for the introduction of new vaccines. Vaccine. 2012;30(24):3710-6.

20. Parikh SR, Andrews NJ, Beebeejaun K, Campbell H, Ribeiro S, Ward C, et al. Effectiveness and impact of a reduced infant schedule of 4CMenB vaccine against group B meningococcal disease in England: a national observational cohort study. Lancet. 2016;388(10061):2775-82.

21. Miller E, Salisbury D, Ramsay M. Planning, registration, and implementation of an immunisation campaign against meningococcal serogroup C disease in the UK: a success story. Vaccine. 2001;20 Suppl 1:S58-67.

22. Trotter CL, Andrews NJ, Kaczmarski EB, Miller E, Ramsay ME. Effectiveness of meningococcal serogroup C conjugate vaccine 4 years after introduction. Lancet. 2004;364(9431):365-7.

23. Snape MD, Kelly DF, Lewis S, Banner C, Kibwana L, Moore CE, et al. Seroprotection against serogroup C meningococcal disease in adolescents in the United Kingdom: observational study. Bmj. 2008;336(7659):1487-91.

24. Perrett KP, Snape MD, Ford KJ, John TM, Yu L-MM, Langley JM, et al. Immunogenicity and Immune Memory of a Nonadjuvanted Quadrivalent Meningococcal Glycoconjugate Vaccine in Infants. The Pediatric Infectious Disease Journal. 2009;28(3):186-93.

25. Southern J, Borrow R, Andrews N, Morris R, Waight P, Hudson M, et al. Immunogenicity of a reduced schedule of meningococcal group C conjugate vaccine given concomitantly with the Prevenar and Pediacel vaccines in healthy infants in the United Kingdom. Clinical and Vaccine Immunology: {CVI}. 2009;16(2):194-9.

26. De Wals P, Deceuninck G, Lefebvre B, Tsang R, Law D, De Serres G, et al. Impact of an Immunization Campaign to Control an Increased Incidence of Serogroup B Meningococcal Disease in One Region of Quebec, Canada. Clin Infect Dis. 2017;64(9):1263-7.

27. Control of meningococcal disease: guidance for consultants in communicable disease control. PHLS Meningococcal Infections Working Group and Public Health Medicine Environmental Group. Commun Dis Rep CDR Rev. 1995;5(13):R189-95.

28. Kaczmarski EB, Cartwright KA. Control of meningococcal disease: guidance for microbiologists: CCDC. Consultant in Communicable Disease Control, England. Commun Dis Rep CDR Rev. 1995;5(13):R196-8.

29. Stuart JM, Monk PN, Lewis DA, Constantine C, Kaczmarski EB, Cartwright KA. Management of clusters of meningococcal disease. PHIS Meningococcus Working Group and Public Health Medicine Environmental Group. Commun Dis Rep CDR Rev. 1997;7(1):R3-5.

30. Prophylaxis for holiday contacts of single cases of meningococcal disease. Communicable disease report CDR weekly. 1998;8(35):307.

31. England PH. Guidance on the prevention and management of meningococcal meningitis and septicaemia in higher education institutions: Raising awareness, promoting immunisation and planning ahead. London: Public Health England; 2016.

32. NICE. Bacterial Meningitis and Meningococcal Septicaemia: Management of Bacterial Meningitis and Meningococcal Septicaemia in Children and Young People Younger than 16 years in Primary and Secondary Care: RCOG Press; 2010.

33. Stuart JM, Gilmore AB, Ross A, Patterson W, Kroll JS, Kaczmarski EB, et al. Preventing secondary meningococcal disease in health care workers: recommendations of a working group of the PHLS meningococcus forum. Commun Dis Public Health. 2001;4(2):102-5.

34. Ragunathan L, Ramsay M, Borrow R, Guiver M, Gray S, Kaczmarski EB. Clinical features, laboratory findings and management of meningococcal meningitis in England and Wales: report of a 1997 survey. Meningococcal meningitis: 1997 survey report. JInfect. 2000;40(0163-4453 (Print)):74-9.

35. Hastings L, Stuart J, Andrews N, Begg N. A retrospective survey of clusters of meningococcal disease in England and Wales, 1993 to 1995: estimated risks of further cases in household and educational settings. Commun Dis Rep CDR Rev. 1997;7(13):R195-200.

36. De Wals P, Hertoghe L, Borlee-Grimee I, De Maeyer-Cleempoel S, Reginster-Haneuse G, Dachy A, et al. Meningococcal disease in Belgium. Secondary attack rate among household, day-care nursery and pre-elementary school contacts. J Infect. 1981;3(1 Suppl):53-61.

37. Purcell B, Samuelsson S, Hahné SJM, Ehrhard I, Heuberger S, Camaroni I, et al. Effectiveness of antibiotics in preventing meningococcal disease after a case: systematic review. BMJ. 2004;328(7452):1339.

38. Cartwright KA, Stuart JM, Robinson PM. Meningococcal carriage in close contacts of cases. Epidemiol Infect. 1991;106(1):133-41.

39. Kristiansen B, rn E, Tveten Y, Jenkins A. Which contacts of patients with meningococcal disease carry the pathogenic strain of Neisseria meningitidis? A population based study. BMJ. 1998;317(7159):621.

40. Control ECfDPa. Risk assessment guidelines for diseases transmitted on aircraft. Stockholm: ECDC; 2010 January 2011.

41. Cohen MS, Steere AC, Baltimore R, von Graevenitz A, Pantelick E, Camp B, et al. Possible nosocomial transmission of group Y Neisseria meningitidis among oncology patients. Annals of internal medicine. 1979;91(1):7-12.

42. Riewerts Eriksen NH, Espersen F, Laursen L, Skinhøj P, Høiby N, Lind I. Nosocomial outbreak of group C meningococcal disease. BMJ : British Medical Journal. 1989;298(6673):568-9.

43. Hoek MR, Christensen H, Hellenbrand W, Stefanoff P, Howitz M, Stuart JM. Effectiveness of vaccinating household contacts in addition to chemoprophylaxis after a case of meningococcal disease: a systematic review. Epidemiol Infect. 2008;136(11):1441-7.

44. Gold R, Goldschneider I, Lepow ML, Draper TF, Randolph M. Carriage of Neisseria meningitidis and Neisseria lactamica in infants and children. J Infect Dis. 1978;137(2):112-21.

45. Orr HJ, Gray SJ, Macdonald M, Stuart JM. Saliva and Meningococcal Transmission. Emerging Infectious Diseases. 2003;9(10):1314-5.

46. Telisinghe L. Systematic review of the effect of antibiotics and/or vaccination in preventing subsequent disease among household contacts of cases of meningococcal disease WHO; 2014 May 2014. Report No.: 1.7.

47. Fraser A, Gafter-Gvili A, Paul M, Leibovici L. Antibiotics for preventing meningococcal infections. The Cochrane database of systematic reviews. 2006(4):Cd004785.

48. Schwartz B, Al-Tobaiqi A, Al-Ruwais A, Fontaine RE, A'Ashi J, Hightower AW, et al. Comparative efficacy of ceftriaxone and rifampicin in eradicating pharyngeal carriage of group A Neisseria meningitidis. Lancet. 1988;1(8597):1239-42.

49. Podgore JK, Girgis N, L-Refai E, Abdel-Moneim A. A double-blind randomized trial of cefixime compared to rifampin in the eradication of meningococcal pharyngeal carriage in a closed population. Journal of Tropical Medicine. 1993;2(5):41-5.

50. Girgis N, Sultan Y, Frenck RW, Jr., El-Gendy A, Farid Z, Mateczun A. Azithromycin compared with rifampin for eradication of nasopharyngeal colonization by Neisseria meningitidis. Pediatr Infect Dis J. 1998;17(9):816-9.

51. Control ECfDPa. Public health management of sporadic cases of invasive meningococcal disease and their contacts. Stockholm: ECDC; 2010.

52. Committee JF. British National Formulary 73. London: BMJ Publishing Group; 2017.

53. Cuevas LE, Kazembe P, Mughogho GK, Tillotson GS, Hart CA. Eradication of nasopharyngeal carriage of Neisseria meningitidis in children and adults in rural Africa: a comparison of ciprofloxacin and rifampicin. J Infect Dis. 1995;171(3):728-31.

54. Drew TM, Altman R, Black K, Goldfield M. Minocycline for prophylaxis of infection with Neisseria meningitidis: high rate of side effects in recipients. J Infect Dis. 1976;133(2):194-8.

55. Burkhardt JE, Walterspiel JN, Schaad UB. Quinolone arthropathy in animals versus children. Clin Infect Dis. 1997;25(5):1196-204.

56. Drossou-Agakidou V, Roilides E, Papakyriakidou-Koliouska P, Agakidis C, Nikolaides N, Sarafidis K, et al. Use of ciprofloxacin in neonatal sepsis: lack of adverse effects up to one year. Pediatr Infect Dis J. 2004;23(4):346-9.

57. Yee CL, Duffy C, Gerbino PG, Stryker S, Noel GJ. Tendon or joint disorders in children after treatment with fluoroquinolones or azithromycin. Pediatr Infect Dis J. 2002;21(6):525-9.

58. Clark J, Lakshman R, Galloway A, Cant A. Does cefotaxime eradicate nasopharyngeal carriage ofN meningiditis. Archives of Disease in Childhood. 2002;87(5):449.

59. Simmons G, Jones N, Calder L. Equivalence of ceftriaxone and rifampicin in eliminating nasopharyngeal carriage of serogroup B Neisseria meningitidis. J Antimicrob Chemother. 2000;45(6):909-11.

60. Barroso D. Neisseria meningitidis nasopharynx colonization of diseased patients on presentation and on discharge. Tropical doctor. 1999;29(2):108-9.

61. Alvez F, Aguilera A, Garcia-Zabarte A, Castro-Gago M. Effect of chemoprophylaxis on the meningococcal carrier state after systemic infection. Pediatr Infect Dis J. 1991;10(9):700.

62. Abramson JS, Spika JS. Persistence of Neisseria meningitidis in the upper respiratory tract after intravenous antibiotic therapy for systemic meningococcal disease. J Infect Dis. 1985;151(2):370-1.

63. Davis H, McGoodwin E, Reed TG. Anaphylactoid reactions reported after treatment with ciprofloxacin. Annals of internal medicine. 1989;111(12):1041-3.

64. Burke P, Burne SR. Allergy associated with ciprofloxacin. BMJ. 2000;320(7236):679.

65. Connell WR. Safety of drug therapy for inflammatory bowel disease in pregnant and nursing women. Inflammatory Bowel Diseases. 1996;2(1):33-47.

66. Ferrero S, Ragni N. Inflammatory bowel disease: management issues during pregnancy. Archives of gynecology and obstetrics. 2004;270(2):79-85.

67. Cassina M, Fabris L, Okolicsanyi L, Gervasi MT, Memmo A, Tiboni GM, et al. Therapy of inflammatory bowel diseases in pregnancy and lactation. Expert opinion on drug safety. 2009;8(6):695-707.

68. Lin KJ, Mitchell AA, Yau WP, Louik C, Hernandez-Diaz S. Safety of macrolides during pregnancy. American journal of obstetrics and gynecology. 2013;208(3):221.e1-8.

69. Dautzenberg B, Grosset J. [Tuberculosis and pregnancy]. Revue des maladies respiratoires. 1988;5(3):279-83.

70. Nahum GG, Uhl K, Kennedy DL. Antibiotic use in pregnancy and lactation: what is and is not known about teratogenic and toxic risks. Obstetrics and gynecology. 2006;107(5):1120-38.

71. Ladhani SN, Cordery R, Mandal S, Christensen H, Campbell H, Borrow R, et al. Preventing secondary cases of invasive meningococcal capsular group B (MenB) disease using a recently-licensed, multi-component, protein-based vaccine (Bexsero((R))). J Infect. 2014;69(5):470-80.

72. Ladhani SN, Campbell H, Lucidarme J, Gray S, Parikh S, Willerton L, et al. Invasive meningococcal disease in patients with complement deficiencies: a case series (2008-2017). BMC Infect Dis. 2019;19(1):522.

73. Simmons RD, Kirwan P, Beebeejaun K, Riordan A, Borrow R, Ramsay ME, et al. Risk of invasive meningococcal disease in children and adults with HIV in England: a population-based cohort study. BMC Med. 2015;13(1):297.

74. Ricco M, Vezzosi L, Odone A, Signorelli C. Invasive Meningococcal Disease on the Workplaces: a systematic review. Acta bio-medica : Atenei Parmensis. 2017;88(3):337-51.

75. Gilmore A, Stuart J, Andrews N. Risk of secondary meningococcal disease in health-care workers. Lancet. 2000;356(9242):1654-5.

76. Coia JE, Ritchie L, Adisesh A, Makison Booth C, Bradley C, Bunyan D, et al. Guidance on the use of respiratory and facial protection equipment. Journal of Hospital Infection. 2013;85(3):170-82.

77. Bunyan D, Ritchie L, Jenkins D, Coia JE. Respiratory and facial protection: a critical review of recent literature. Journal of Hospital Infection. 2013;85(3):165-9.

78. Loveday HP, Wilson JA, Pratt RJ, Golsorkhi M, Tingle A, Bak A, et al. epic3: national evidencebased guidelines for preventing healthcare-associated infections in NHS hospitals in England. J Hosp Infect. 2014;86 Suppl 1:S1-70.

79. Weber A, Willeke K, Marchioni R, Myojo T, McKay R, Donnelly J, et al. Aerosol penetration and leakage characteristics of masks used in the health care industry. American journal of infection control. 1993;21(4):167-73.

80. Chen CC, Willeke K. Aerosol penetration through surgical masks. American journal of infection control. 1992;20(4):177-84.

81. CDC. Control and prevention of meningococcal disease and control and prevention of serogroup C meningococcal disease: evaluation and management of suspected outbreaks. MMWR Morb Mortal Wkly Rep. 1997;46(RR-5):1-21.

82. Davison KL, Andrews N, White JM, Ramsay ME, Crowcroft NS, Rushdy AA, et al. Clusters of meningococcal disease in school and preschool settings in England and Wales: what is the risk? Arch Dis Child. 2004;89(3):256-60.

83. Stuart JM. Managing outbreaks the public health response. In: Pollard AJ, Maiden MCJ, editors. Meningococcal disease: methods and protocols. Totowa, NJ: Humana Press Inc; 2001. p. 257-72.

84. Kuhns DM, Nelson CT, Feldman HA, Kuhn LR. The prophylactic value of sulfadiazine in the control on meningococcic meningitis. JAMA. 1943;123(6):335-9.

85. Jackson LA, Alexander ER, DeBolt CA, Swenson PD, Boase J, McDowell MG, et al. Evaluation of the use of mass chemoprophylaxis during a school outbreak of enzyme type 5 serogroup B meningococcal disease. Pediatr Infect Dis J. 1996;15(11):992-8.

86. Shehab S, Keller N, Barkay A, Leitner L, Leventhal A, Block C. Failure of mass antibiotic prophylaxis to control a prolonged outbreak of meningococcal disease in an Israeli village. European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology. 1998;17(11):749-53.

87. Irwin DJ, Miller JM, Milner PC, Patterson P, Richards RG, Williams DA, et al. Community immunization programme in response to an outbreak of invasive *Neisseria meningitidis* serogroup C infection in the Trent region of England 1995-1996. Journal of Public Health Medicine. 1997;19(2): 162-70.

88. Ardern K, Bowler S, Hussey RM, Regan CM. Managing meningococcal disease case clusters: art or science? J Epidemiol Community Health. 1999;53(9):565-71.

89. Barker RM, Shakespeare RM, Mortimore AJ, Allen NA, Solomon CL, Stuart JM. Practical guidelines for responding to an outbreak of meningococcal disease among university students based on experience in Southampton. Commun Dis Public Health. 1999;2(3):168-73.