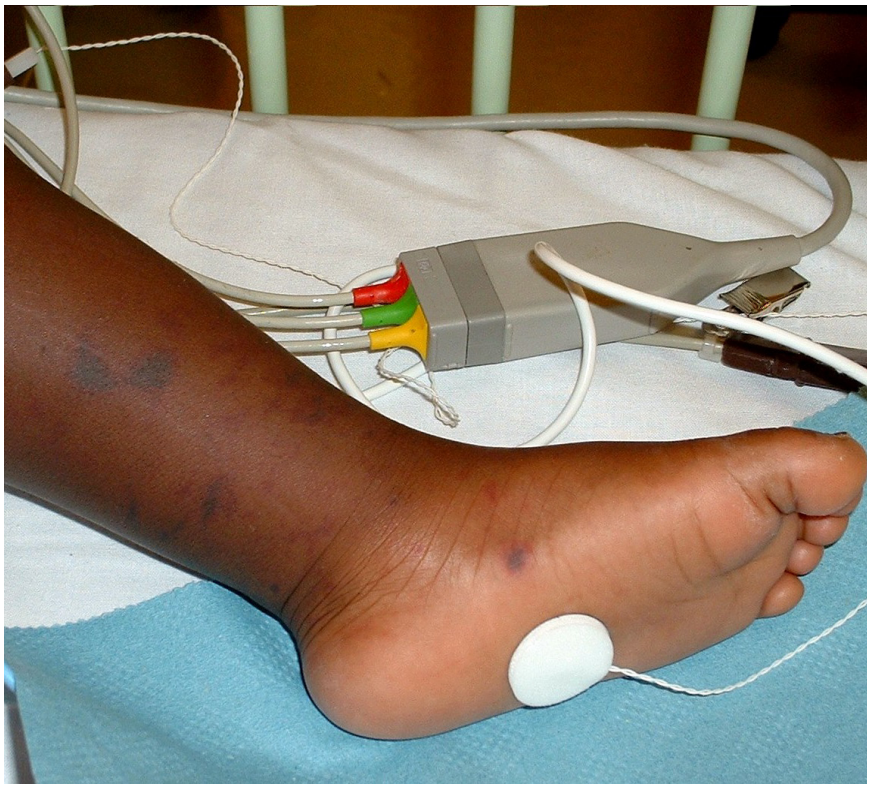
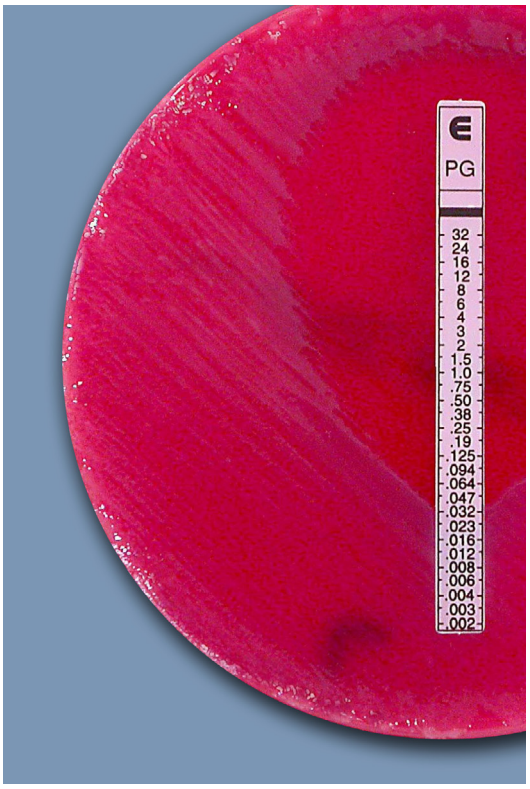
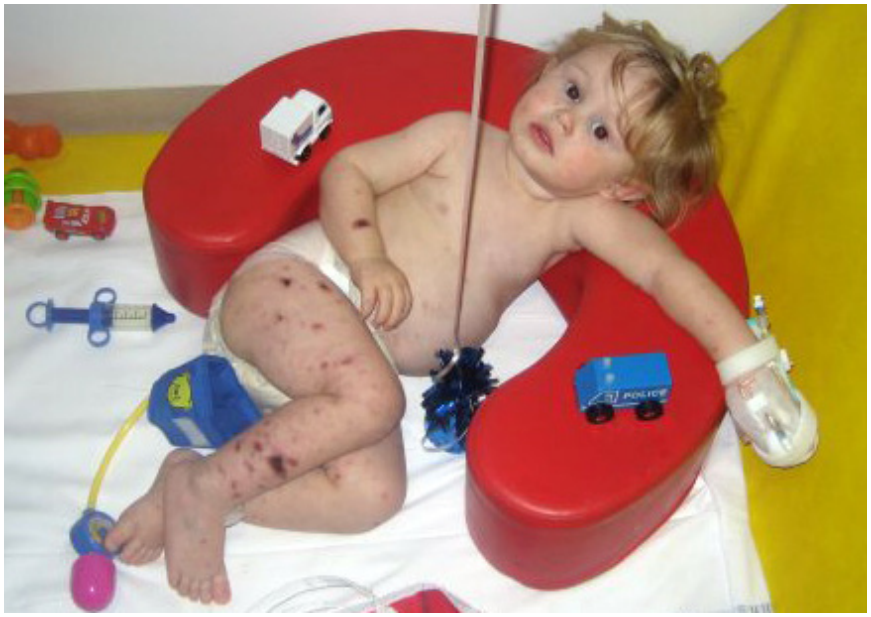
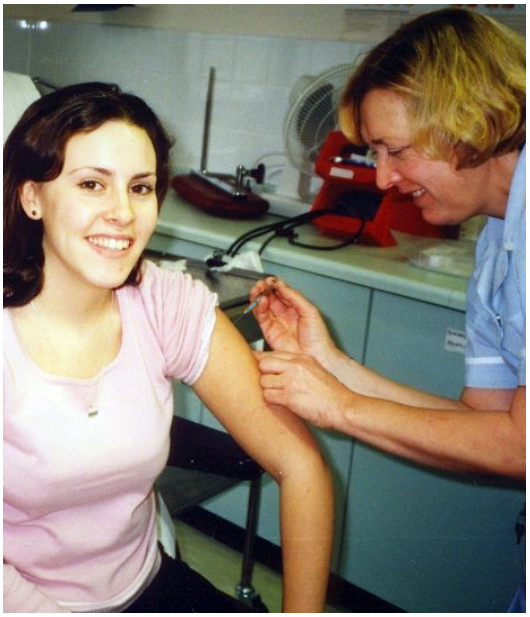
Health Protection Agency

Guidance for public health management of meningococcal disease in the UK









Guidance for public health management of meningococcal disease in the UK

Health Protection Agency Meningococcus and Haemophilus Forum. Updated March 2012

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Contents

1 Introduction

The Health Protection Agency Meningococcus Forum's last major review of the guidance for control measures for meningococcal disease took place in 2006. This review followed changes in the epidemiology of meningococcal disease, the advent of new vaccines, and new evidence on risk and control measures.The 2006 guidelines covered pre-admission management, investigation of suspected cases, the role of public health, public health action after a single case, prophylaxis in healthcare settings, and management of clusters. Links to relevant websites were included. Recommendations were graded according to the level of evidence on which they are based.

In 2011, the HPA Meningococcus and Haemophilus Forum updated several sections of the guidance, on behalf of the Vaccine Programme Board. These latest updates reflect more recent data on the incidence of infection (section 3) and refer to NICE guidance on pre-admission management (section 4, the introduction of new health protection legislation (section 6). The choice of antibiotics for chemoprophylaxis has been modified and information on the effectiveness of antibiotics for chemoprophylaxis and their use during pregnancy and breast-feeding added (section 7.1). The role of conjugate vaccines has been reviewed (section 7.2). The significant changes to the recommendations are summarised overleaf.

2 Specific changes to recommendations

2.1 Recommendation 1: Pre-admission management (section 4)

- 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. 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.

2.2 Recommendation 4: Chemoprophylaxis and choice of antibiotic (section 7.1)

Choice of agent for chemoprophylaxis

Ciprofloxacin

- Ciprofloxacin is recommended for use in all age groups and in pregnancy. Rifampicin has been the drug of choice for meningococcal chemoprophylaxis because it is licensed for chemoprophylaxis. However, rifampicin has several disadvantages. The advantages of ciprofloxacin over rifampicin are that it is given as a single dose, does not interact with oral contraceptives, and is more readily available in community pharmacies. It is contraindicated in cases of known ciprofloxacin hypersensitivity. Ciprofloxacin is usually not recommended in children due to induced arthropathy in juvenile animals. However in studies, the risk of arthropathy due to ciprofloxacin was very low, arthralgia was transient and most were coincidental.

2.3 Recommendation 5: Vaccines (section 7.2)

Close contacts

- Close contacts of any age of a case of meningococcal disease caused by confirmed serogroup C who were only immunised in infancy and those who completed the recommended immunisation course (including the 12-month booster) more than one year before, should be offered an extra dose of MenC conjugate vaccine.
- For contacts of a case of confirmed serogroup A, W135 or Y infection, vaccination with quadrivalent conjugate vaccine should be offered to all close contacts of any age (two doses one month apart if aged less than one year).
- For probable cases with serogroup A, W135 or Y from a nasopharyngeal swab, the quadrivalent conjugate vaccine should be offered to close contacts of any age (two doses one month apart if aged less than one year).

Vaccination of the index case

- Index cases who are in the known risk-groups for meningococcal disease (asplenia and complement deficiency – see Immunisation against infectious disease - 'The Green Book' http://www.dh.gov.uk/en/Publichealth/Immunisation/Greenbook/index.htm) and have not been immunised with the quadrivalent MenACWY conjugate vaccine should complete the recommended immunisation course, whilst those who received the quadrivalent MenACWY conjugate vaccine more than 12 months previously should receive an extra dose of the quadrivalent MenACWY conjugate vaccine.

2.4 Recommendation 7: Prophylaxis in healthcare settings (section 8)

- Routine vaccination of healthcare workers with meningococcal conjugate vaccines is not recommended.

2.5 Recommendation 8: Managing clusters in educational institutions (section 9.1)

- For a cluster involving confirmed serogroup A, W135 or Y cases: the quadrivalent conjugate vaccine should be offered to all individuals of any age who were offered antibiotics.

3 Epidemiology of meningococcal carriage and disease

Neisseria meningitidis is a normal inhabitant of the human nasopharynx and is transmitted from person to person by droplets or secretions from the upper respiratory tract.[1] Saliva is inhibitory to meningococcal growth, and transmission by fomites is considered insignificant.[2,3]

Meningococci are classified according to characteristics of the polysaccharide capsule into serogroup, of outer membrane proteins into serotype and serosubtype, and of chromosomal DNA into genotype. Carriage of meningococci (all strains included) is relatively common. A large community survey in England in 1987 found carriage rates varying from 2% in children under five years to a peak of 25% in 15 to 19 year olds.[4] Conversely, carriage of *Neisseria lactamica,* a non-pathogenic organism believed to confer protection against meningococcal disease, is highest in young children.[5] Increased rates of meningococcal carriage have been observed in smokers, overcrowded households, and military recruits.[6,7,8] The mean duration of carriage in settings where prevalence is stable has been recently estimated as about 21 months.[9]

Systemic immunity, as measured by serum bactericidal antibodies, usually develops within 14 days of acquisition of meningococci.[10] 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,[11] from occasional clusters where the date of exposure is known[12] and from carriage studies among military recruits.[13] Not surprisingly, established meningococcal carriers do not usually develop invasive disease.[13] 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 small proportion of carried strains are responsible for most cases of invasive disease.[14]

In the UK, annual rates of invasive disease usually vary between two and six per 100,000, with case-fatality rates of about 10%.[15] Prior to the use of mass vaccination, most cases were caused by serogroup B or C strains. Disease usually presents as septicaemia, meningitis or both. Age-specific attack rates are highest in infancy and decline during childhood with a secondary rise in teenagers and young adults. The highest incidence is seen in the winter months. Apart from age, risk factors include passive smoking,[16] preceding influenza A infection[17] and overcrowding.[7]

3.1 Changing disease incidence

The reported incidence of meningococcal disease rose to historically high levels during 1998/99, particularly associated with serogroup C strains of the sequence type 11 clonal complex.[18,19] Following the introduction of the UK meningococcal C conjugate vaccination programme in November 1999, there was a marked fall in disease caused by serogroup C strains.[18,20] Two national outbreaks of disease due to W135 strains, previously rare in the UK, followed the Hajj pilgrimages in 2000 and 2001.[21] Incidence of meningococcal disease has declined slightly in recent years, with an average annual incidence of 2.05/100,000 population between 2006/7-2009/10; 88% of these cases were due to serogroup B infections. Cases of serogroup C disease are currently very rare with only 13 cases confirmed in 2008/09 and 17 cases in 2009/10.

3.2 Previous guidance

The Public Health Laboratory Service (PHLS) published comprehensive guidance on the control of meningococcal disease in England and Wales in 1995.[22,23] More detailed guidance followed on cluster management,[24] prophylaxis in dispersal settings,[25] cases and clusters in universities,[26] use of ciprofloxacin[27] pre-admission antibiotics[28] and prophylaxis for healthcare workers.[29] This series of guidance documents was adopted in Northern Ireland and modified slightly for use in Scotland.[30]

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 case-control 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

3.3 Review of guidance

The 1995 guidance was updated in August 2006 to take account of changes in epidemiology, and to incorporate new evidence on risk and control measures. The 2006 review was undertaken by a working group set up by the Health Protection Agency (HPA) Meningococcus Forum. The revisions were based on available evidence, and the levels of evidence were graded according to published guidelines (Table 1). Where the working group considered that insufficient evidence was available on which to base guidance, agreement on recommendations was reached through consensus (expert opinion).

The 2011 revisions have been agreed by the HPA Meningococcal and Haemophilus Forum, which comprises representatives from all HPA divisions, Health Protection Scotland and the Public Health Wales plus experts from academia.

3.4 Objective of guidelines

The objective of these guidelines is to present the rationale and recommendations for the control of meningococcal disease in the UK in one comprehensive document. Guidance is offered on pre-admission management to reduce mortality rate, investigation of suspected cases, case definitions, public health action after a single case and management of clusters. These recommendations now form the definitive UK guidance on public health management of meningococcal disease.

4 Pre-admission management

Recommendation 1

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.* 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.

*http://guidance.nice.org.uk/CG102/NICEGuidance/pdf/English

Recommendation 1: Pre-admission management

Rapid admission to hospital is highest priority when meningococcal disease is suspected.

Evidence grade C

Immediate dose of iv/im benzylpenicillin for suspected meningococcal infections

Adults and children aged 10 years or over	1.2 g
Children aged 1 to 9 years	600 mg
Children aged under 1 year	300 mg

5 Laboratory investigation of suspected cases

Identification and characterisation of meningococci causing infection provides important information to assist the public health response. Whilst traditional microbiological techniques remain an important part of investigating suspected cases, molecular methods have been developed that assist diagnosis and further characterisation of strains from cases where isolates have not been obtained.[31,32,33] Considerable advantages remain in having a cultured isolate available for testing, the most significant of which is a potentially infinite supply of the organism for further study.

Blood samples for culture and polymerase chain reaction (PCR) testing are essential. The chance of obtaining laboratory confirmation is increased by taking samples at the earliest available opportunity. If the possibility of meningococcal disease is not considered until some time after admission, it may still be possible to retrieve earlier specimens from haematology and chemistry departments.

When meningitis is present, cerebrospinal fluid (CSF) offers the best chance of yielding an organism for culture; meningococcal DNA can be found in the CSF up to 96 hours after commencing antibiotics.[34] Lumbar puncture may be contra-indicated for a range of reasons and should not be performed until the patient's condition has been stabilised and appropriate assessment has been made to rule out raised intracranial pressure. Material (preferably fluids) from any other normally sterile site, e.g. pericardial or synovial fluid, can also be tested by culture and PCR.

Immunological abnormalities such as complement deficiency can predispose to meningococcal disease. This may present as recurrent meningococcal infection but should be suspected in teenagers or young children with infection due to rare serogroups.[35]

5.1 Microscopy

Visualising Gram-negative intracellular diplococci in the CSF provides a highly specific confirmatory test. In other sites, e.g. synovial fluid, there is a greater possibility of encountering gonococci and the clinical presentation of the illness should provide important clues to correctly identify the aetiological agent. Specimen collection, prior use of antibiotics and experience of the person performing microscopy are other factors that can affect the sensitivity and specificity.

Cerebrospinal fluid (CSF)

Classically the CSF from a case of meningococcal meningitis reveals a raised neutrophil count and high protein content along with lowered glucose concentration. Gram-negative diplococci (which are usually but not invariably intracellular) confirm meningococcal meningitis.

The typical picture will not always be present. Very occasionally, numerous organisms will be present in the absence of a raised neutrophil count, and in about 8% of culture positive cases, meningococci may be cultured from CSF that is normal on initial analysis.[36] Conversely, high white cell counts may be present in the CSF, but the number of organisms may be too low to be detectable by microscopy. Prior administration of antibiotics will decrease numbers and may alter the Gram staining characteristics of the organisms. CSF collected some time after presentation may contain a higher proportion of lymphocytes than typically is seen in more acute specimens.

The sensitivity of the Gram stain in CSF to detecting meningococcal meningitis is estimated as 65%.[32] This is affected by the stage of disease, number of organisms present and timing of the procedure in relation to antibiotic administration.

Aspirates and biopsies from normally sterile sites

In patients with a clinically compatible illness, Gram stains of aspirates and biopsy material from sterile sites have high specificity and serve to confirm invasive meningococcal disease. However, as for CSF, they are insufficiently sensitive to exclude invasive meningococcal disease on the basis of negative microscopy.

Examination of material from skin lesions

There has been no systematic study of the optimal way to sample from skin. Techniques employed have ranged from simply disrupting and swabbing a rash-affected area to performing punch biopsies. The reported sensitivity of Gram stains of skin lesion aspirates or biopsies ranges from 30% to 70%. It is highest in haemorrhagic lesions of patients with meningococcal septicaemia in whom Gram stains of skin biopsies may remain positive for up to 48 hours after antibiotic administration. False positive Gram stain results may occur.

While these investigations have been employed successfully in a few centres abroad,[37,38,39] they have not found popularity in the UK. Several units that have undertaken assessments report no improved ascertainment over that provided by culture and PCR of blood and CSF (personal communications – R Read, Sheffield; G Jones, Southampton; R Heyderman, Bristol and M Cafferkey, Dublin).

5.2 Culture

Culture of *N. meningitidis* from blood, CSF or another normally sterile site represents the optimal confirmation of invasive meningococcal disease. Isolates are amenable to relatively straightforward strain characterisation and additional investigations such as antibiotic susceptibility testing. Isolates submitted to UK reference units are characterised phenotypically by serogroup, serotype and serosubtype. Genotypic characterisation of some determinants can also be performed.

Blood culture

Blood for culture should be obtained from all suspected cases. However, the sensitivity falls to 5% or less if antibiotics have been given more than one to two hours before collection.[40] Other factors that affect the sensitivity of blood cultures include the number of blood cultures collected, the volume of the samples and their timing, but perhaps most critically, the bacterial load, which can vary enormously.[41]

CSF culture

The sensitivity of CSF culture is about 70% in cases of untreated meningococcal disease.[40] Nevertheless, while antibiotics take somewhat longer to act in CSF than in blood, successful culture is unlikely unless specimens are collected within two to three hours of treatment commencing.

Aspirate from a normally sterile site, skin rash aspirate or biopsy culture

Culture of meningococci from these sites confirms invasive infection.

Nasopharyngeal (throat) swabs

Nasopharyngeal swabs are less affected by prior antibiotic therapy and have been found to yield meningococci in 40–50% of cases of invasive meningococcal disease.[40] They should be collected from all suspected cases and the request form should specify that meningococci are being sought. Nasopharyngeal swabs to detect meningococci are usually taken through the mouth (sweeping posterior pharynx behind uvula). A review of patients on the PHLS Meningococcus Reference Unit (MRU) database between 1994 and 1997, where both nasopharyngeal and systemic isolates were submitted, showed the organisms from both sites were identical in 97% (134/138) of cases. However, in 3% of cases they were different, and a nasopharyngeal isolate in the absence of a systemic isolate does not confirm invasive disease but may help support the clinical diagnosis alongside other signs and symptoms. Crucially, results of nasopharyngeal swabs afford the possibility of identifying a strain in the event of a cluster that requires identification.

5.3 Non-culture diagnostic tests

Polysaccharide antigen testing

Demonstrating meningococcal polysaccharide antigen in CSF, blood or other normally sterile fluid using latex agglutination provides confirmatory evidence of invasive infection in patients with a clinically compatible presentation.

PCR

PCR-based assays for detecting specific DNA sequences of *N. meningitidis* have been developed and made widely available through reference laboratories in the UK. Experience has been based largely on experience with CSF and blood specimens. Other material from sterile sites, however, and indeed throat swabs and material from rashes can also be tested. The sensitivity of the ctrA (screening) assay currently used at the MRU has been estimated to be 89% for whole blood samples and 96% for CSF. Samples positive by this assay are submitted for further testing for serogroup determination, initially for serogroups B and C and, if negative for these, then for serogroups W135, Y and A.[32,33,42]

For blood specimens, whole blood (unclotted) specimens are preferred and current DNA extraction methods mean that heparinised specimens can now be handled along with EDTA and citrated samples.

5.4 Strain differentiation of N. meningitidis

Strain characterisation is generally performed at national reference laboratories. Laboratories who culture the organism should refer all strains to the reference laboratory for urgent serogrouping to inform the management of the contacts. Attempts to more finely differentiate meningococcal strains from cases of invasive disease can be undertaken for public health reasons, e.g. to confirm or to exclude a suspected outbreak of cases. A true epidemiological link between cases can only be established by public health investigations. Laboratory typing results can categorically rule out true relatedness of apparently linked cases if they emerge as being distinct, but provide no more than supporting evidence when case isolates are indistinguishable.

The most widely applied differentiation techniques involve characterisation of surface structures in the capsule and outer cell membrane. Capsular polysaccharide antigens separate meningococci into serogroups among which A, B, C, W135, X and Y account for the overwhelming majority of invasive infections worldwide.

Further differentiation can be made by identification of outer membrane proteins (OMPs). Of the five OMP classes present, three porin proteins have been used to produce reagents for an internationally recognised typing scheme. All meningococci have class 1 (PorA) and also either class 2 or 3 OMPs (PorB) – these last are mutually exclusive. Using monoclonal antibodies which detect the different antigens, the class 2/3 OMPs designate the serotype, while the class 1 porin OMPs define the serosubtype. The serogroup, serotype, and serosubtype together make up the most commonly used phenotypic designation of meningococci. Panels of monoclonal antibodies used in the UK, most European countries and Australasia have been lodged with the National Institute for Biological Standards and Controls, which prepares and distributes the reagents to national reference centres.[43,44]

5.5 Genotypic characterisation of strains (including non-culture-based applications)

Genotypic (molecular) procedures are now supplanting phenotypic (serology-based) typing methods. The best described and most widely available include pulsed field gel electrophoresis (PFGE), *porA, feta or fHBP (factor H binding protein)* sequencing and multi-locus sequence typing (MLST).

Recommendation 2 : Laboratory investigation

The following specimens should be collected on, or soon after, admission to hospital from all patients when meningococcal infection is included in the differential diagnosis.

- Blood for culture
- Blood for PCR (EDTA or other unclotted blood specimen)
- Serum (on admission and 2-6 weeks later)
- CSF for microscopy, culture, PCR
- Aspirate from other sterile sites suspected of being infected (e.g. joints) for microscopy, culture, PCR
- Nasopharyngeal (throat) swab normally taken through the mouth

Evidence grade D

- Lumbar puncture should not be done where contraindicated and should be delay until the patient's condition has been stabilised and assessment made to rule out raised intracranial pressure.

NB: Where appropriate, specimens should be taken to check for alternative diagnoses, e.g. nasopharyngeal swabs and stool for viral culture.

Cases due to rare serogroups or recurrent infection

In children and young adults with meningococcal disease caused by rare serogroups or recurrent infection due to any serogroup, the CCDC/CPHM should discuss immunological investigation with the physician.

PorA sequence typing is becoming increasingly available and can also be applied for outbreak investigation. The antigens defined by *porA* stimulate production of bactericidal antibody and so represent potential vaccine candidates.[45] The MRU and the Scottish Meningococcus and Pneumococcus Reference Laboratory have now developed *porA* sequencing as a non-culture-based method, which can be applied to the majority of 'non-viable' samples for which serogroup can be determined by PCR. Laboratories who conduct diagnostic PCR for *N. meningitidis* should refer clinical samples to the national reference laboratories for further typing.

MLST can occasionally provide information useful for identifying outbreaks but is usually more appropriately applied to study long-term clonal relationships of meningococcal populations since it examines parts of the genome defining cell components which are not surface expressed and hence not under selection pressure. MLST is now also available as a non-culture-based method for cluster investigation. [46,47,48,49] Two other antigen genes, feta and fHBP, are now becoming more widely used for strain typing and outbreak investigation.

6 Role of public health

Recommendation 3

Public health departments have a major role in the management of meningococcal disease, ensuring that there are adequate disease prevention and surveillance programmes, and in the prevention of secondary spread through contact tracing. Usually the lead is through the consultant in communicable disease control (CCDC)/consultant in public health medicine (CPHM). Based on revised health protection legislation (2010), it is a legal requirement in England for all diagnostic laboratories to notify the HPA when they identify evidence of infection caused by specified causative agents, including *Neisseria meningitidis,* (http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_114510). The legislation describes how such notifications should be made as well as the relevant timescales for making them, including provision for urgent oral reporting. In general, the notification requirements on laboratories in England can be met by continuing to use CoSurv.

Recommendation 3: Role of public health

The CCDC/CPHM should ensure that policies are in place and implemented through a mechanism such as a service level agreement that recognises the corporate responsibility of the NHS. Policies should ensure that:

- Cases are referred early to hospital.
- Cases are reported promptly to CCDC/CPHM.
- Cases in hospital are investigated appropriately.
- Contacts are traced and given appropriate chemoprophylaxis.
- Information is given to others including primary care, schools/universities, education authorities, National Health Service helplines, meningitis charities, employers.
- Communication with the media is appropriate and efficient.

Evidence grade D

All cases where a diagnosis of meningococcal disease is suspected should be promptly notified to the communicable disease control team without waiting for microbiological confirmation.
N.B. Notification is a legal requirement.
Evidence grade D

The CCDC/CPHM should ensure that comprehensive information on cases is gathered to contribute to local public health management and surveillance. The data set should include epidemiological, laboratory and clinical information This information should be recorded.
Evidence grade D
Data for local management and audit programmes may 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, antibiotics given prior to admission, name of hospital/ward, name of consultant, specimens and dates and types of specimens.
- *Contacts* – addresses and telephone numbers, details of antibiotics/vaccine/information given and by whom; details of general practitioner.
- *Notifier* – name, address and occupation.

CCDCs/CPHMs receive reports of cases from local clinicians in the course of managing the public health aspects of cases. In addition, meningitis and meningococcal septicaemia are statutorily notifiable by registered medical practitioners under the new health protection legislation (2010) ((http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_114510), and under Scottish legislation as meningococcal infection. Therefore clinicians are required to notify suspected cases to the proper officer, usually the CCDC/CPHM.

7 Public health action after a case

Case definitions (Box 1)

Box 1 defines those cases that require public health action and those that do not.

Box 1: Case definitions

Case 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 normally sterile site
- Gram negative diplococci in normally sterile site
- Meningococcal DNA in 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 because of the high immediate risk of invasive disease. [50]

Probable case
Clinical diagnosis of meningitis or septicaemia or other invasive disease where the CCDC/CPH, in consultation with the physician and microbiologist, considers that meningococcal infection is the most likely diagnosis. Some microbiological tests (e.g. rising antibody levels) that are not considered sufficient to confirm the diagnosis of meningococcal disease may change the case category from 'possible' to 'probable'.

Case not requiring public health action

Possible case
Clinical diagnosis of meningitis or septicaemia or other invasive disease where the CCDC/CPH, in consultation with the clinician and microbiologist, considers that diagnoses other than meningococcal disease are at least as likely. This category includes cases who may have been treated with antibiotics but whose probable diagnosis is viral meningitis.

In such cases, prophylaxis for contacts is not indicated, but giving out information about meningococcal disease may be helpful (see recommendation 7).

Infection in non-sterile sites
Isolation of meningococci from sputum or from swabs taken from nasopharynx or genital tract is not by itself an indication for public health action because asymptomatic carriage in the respiratory and genital tract is common. However, when assessed together with other clinical and microbiological parameters, a positive nasopharyngeal swab may increase the index of suspicion that this is a probable case, especially if the isolate is a virulent strain. Meningococcal pneumonia is not an indication for public health action but may carry a low risk of transmission in healthcare settings especially to the immunocompromised[51,52] (see section 8)

7.1 Chemoprophylaxis

7.1.1 Risk to household contacts

About 97% of cases are sporadic.[53] Although the risk to contacts is low, the highest documented absolute and relative risk is to people who live in the same

household as a case of meningococcal disease.[53,54] The Office for National Statistics defines a household as one person living alone or a group of people who share common housekeeping or a living room. The risk is highest in the first seven days after a case and falls rapidly during the following weeks.[53] If prophylaxis is not given, the absolute risk to an individual in the same household one to 30 days after an index case is about one in 300.[55,56,57] Beyond this four week period the risk is probably close to background levels.[53] The increased risk to household members may be due to a combination of genetic susceptibility in the family, increased exposure to virulent meningococci and environmental factors.

The case is likely to have acquired the invasive strain from a close contact, typically in the same household, who is an asymptomatic carrier.[58,59] The incubation period is usually three to five days[3,11] and cases do not usually have detectable carriage until admission to hospital or shortly beforehand.[13] As the highest risk of illness in untreated households is observed in the first 48 hours after onset of disease in the index case,[54] the source of infection in these further cases is most likely to be from the same (or another) carrier and not from the case.

It follows that transient contact with the index case before acute illness is unlikely to be an important risk factor for disease, so that mere proximity to the case (e.g. during travel in a plane, bus or car) may not justify prophylaxis. Guidance for the USA suggests that passengers seated next to the index case on a plane for more than eight hours should be offered prophylaxis, but only one possible transmission was detected in a recent review by ECDC. (http://ecdc.europa.eu/en/publications/Publications/0906_TER_Risk_Assessment_Guidelines_for_Infectious_Diseases_Transmitted_on_Aircraft.pdf)

Low-level salivary contact should not be considered as a risk factor.[60] No cases have been reported following post-mortem contact with a case of meningococcal disease. Embalming is not considered a hazard for transmission.[61]

7.1.2 Aim of chemoprophylaxis

Chemoprophylaxis aims to reduce the risk of invasive disease by eradicating carriage in the group of close contacts at highest risk. It may act in two ways: (i) by eradicating carriage from established carriers who pose a risk of infection to others and (ii) by eradicating carriage in those who have newly acquired the invasive strain and who may themselves be at risk. The short- and medium-term reduction in risk among household contacts who are given antibiotics suggest that both mechanisms may operate.[55,56,62]

7.1.3 Risk reduction

Rifampicin and ciprofloxacin were shown to be more effective in eliminating carriage than placebo in six and two RCTs respectively.[63] Rifampicin continued to be effective compared to placebo for up to four weeks of follow-up in two studies. Ciprofloxacin and rifampicin showed non-significant differences in effectiveness in two RCTs. In single studies, ceftriaxone was more effective than rifampicin, and cefixime and azithromycin were as effective as rifampicin.[64,65,66] A review of retrospective observational studies found a significantly reduced risk of further cases in the household during the month after a case among household members given rifampicin prophylaxis.[67] The approximate number needed to treat to prevent a case was estimated to be about 200 individuals.

In a recent ECDC review,[68] rifampicin, ciprofloxacin, ceftriaxone, cefixime and azithromycin were all recommended for use in preventing secondary cases of meningococcal disease, but only Ciprofloxacin and Rifampicin are

recommended for this purpose in the BNF.[69] Ceftriaxone must be given by injection.

Ciprofloxacin was not previously 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.[70] 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.,[71,72] In all studies, the risk of arthropathy due to ciprofloxacin was very low; arthralgia were transient and most 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.[73] 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%).[74] In all studies, side effects resolved after cessation of therapy.

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. [75,76,77] Convalescent cases may then pose a risk to household contacts unless given a course of antibiotic treatment to eradicate carriage.

Information given out with antibiotics should include an explanation that such treatment is not fully protective.

7.1.4 Contacts outside the household

After a single case of meningococcal disease, the risk of linked cases outside the household is low; this is presumably related to lower intensity of exposure to virulent strains.[59] In England and Wales from 1995 to 2001, after one case in a pre-school group, a 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 four weeks were approximately one in 1,500, one in 18,000 and one in 33,000, respectively.[78] A retrospective study in European countries suggested that there may be some benefit from a policy of giving chemoprophylaxis to the whole nursery compared to treating only close contacts, but the data were inconsistent between countries and the difference between policies was not statistically significant.[79]

The Meningococcus Forum considered the revised estimates of risk and benefit particularly with reference to the treatment of pre-school groups. The forum recommended that UK policy not to give antibiotics to pre-school groups after a single case should be maintained. The reasons are that: the benefit of giving antibiotics in this setting is not known; clusters in pre-school groups are rare (about three per annum in England and Wales); the potential for risk reduction by intervention is reduced according to the time from identification of a case to administration of prophylaxis within the institution; and harm may arise from drug side effects, development of antibiotic resistance, and eradication of naturally immunising strains from the nasopharynx. The further one goes outside the case household, the lower the chance of finding a carrier of a pathogenic meningococcal strain and the greater the chance of treatment doing harm by eradicating carriage of non-pathogenic organisms that may generate cross-protective immunity.[52,59] This particularly applies in young children who are more likely to be carrying *Neisseria lactamica* than *Neisseria meningitidis.*[5]

Reports of clusters in other settings, e.g. the workplace, are rare and the level of risk is considered to be much lower than educational settings.

Recommendation 4: Chemoprophylaxis and choice of antibiotic

Prophylaxis indicated

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

(a) Those who have had *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 (including extended household), pupils in the same dormitory, boy/girlfriends, or university students sharing a kitchen in a hall of residence.

Evidence grade C

(b) 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 (see section 8).

Evidence grade D

Prophylaxis for the case

The case should receive chemoprophylaxis when able to take oral medication and before discharge from hospital, unless the disease has already been treated with ceftriaxone. Those treated with cefotaxime should still receive prophylaxis because it is not known whether cefotaxime eradicates carriage.

Evidence grade C

Prophylaxis NOT indicated (unless already identified as close contacts) for

- 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.

Evidence grade D

Prophylaxis uncertain

The working group recognised that the division between those who do and do not receive prophylaxis is arbitrary as evidence on risk and benefit is limited. CsCDC/CsPHM* will need to use their judgement in reaching a decision on whether or not to advise prophylaxis for those who do not clearly fall into the above categories. For example, when a case occurs in a group of children looked after by the same childminder or among a circle of close friends, an assessment should be made as to whether these exposures meet the definitions of a close contact.

Evidence grade D

Timing

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

Evidence grade C

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.

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 public health physician receives a delayed report of the case, close contacts (as defined above) should be offered chemoprophylaxis, and vaccine if appropriate, up to four weeks 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 four weeks after receiving prophylaxis, an alternative agent should be used for repeat prophylaxis.

Choice of agent for chemoprophylaxis
Both rifampicin and ciprofloxacin are recommended for chemoprophylaxis, although several factors now favour the use of ciprofloxacin in most individuals. The use of single dose ciprofloxacin is recommended by a Cochrane review. [80] Ciprofloxacin has a number of advantages over rifampicin because 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 was the drug of choice for meningococcal chemoprophylaxis because it has been licensed for chemoprophylaxis for many years. However, the disadvantages of rifampicin are that it is associated with rapid induction of resistance, inhibits contraceptives, has a longer regime duration and is usually only available from hospital pharmacies. Both products are available in preparations suitable for children.

Ciprofloxacin
Recommended for use in all age groups and in pregnancy. *Evidence grade B*

The administration of ciprofloxacin may, however, be followed by anaphylactic reactions[,81,82] (P Monk, M Evans, unpublished data). Healthcare staff should give out information sheets that include the risk of side effects (Appendix A), and be prepared to deal with allergic reactions. It 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:
Adults and children over 12 years 500 mg stat
Children aged 5–12 years 250 mg stat
Children under 5yrs 30mg/kg up to maximum of 125 mg stat
*Ciprofloxacin suspension contains 250mg/5ml

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 (Appendix A). This is the responsibility of the prescriber.

Dosage
All to be given twice daily for 2 days:

Adults and children over 12 years of age	600 mg
Children aged 1–12 years	10 mg/kg
Infants (under 12 months of age)	5 mg/kg

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

0–2 months	20 mg (l 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

Pregnancy and breast feeding

Either Ciprofloxacin, Ceftriaxone or Azithromycin can be used as chemoprophylaxis in pregnancy.

Evidence grade C

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

The safety of antibiotic regimens for chemoprophylaxis in pregnant and lactating women is poorly described. Category B: Animal reproduction studies have failed to demonstrate a risk to the foetus and there are no adequate and well controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. The only RCT, involved 176 pregnant and lactating women, administered ceftriaxone (2 g) via the intra-muscular route, and only five subjects reported mild side effects; however, there was no control group.[70] Rifampicin teratogenicity has been demonstrated in high doses in animals, but epidemiological studies did not reveal any notable risk in humans when administered for tuberculosis treatment .[83] Whilst Ciprofloxacin is contra-indicated in its SPC for use in pregnancy, short duration treatment for other indications appears to be safe. [84,85,86]

Safety of antibiotic regimen for the nursing infant is poorly studied, and a drug that is safe for use during pregnancy may not be safe for the infant. A systematic review of antibiotic use in lactation considered ciprofloxacin and rifampicin as compatible with breastfeeding; other antibiotics were not studied.[87]

Ceftriaxone

As ceftriaxone can only be given by injection and is painful, its main indication is when preferred for specific reasons, e.g. in pregnancy. Potential side effects include diarrhoea, allergies, hepatic and blood disorders.

Azithromycin *Evidence grade B*

A single dose Azithromycin can be advised for chemoprophylaxis for pregnant women.

Dosage

Azithromycin 500 mg stat

7.2 Vaccines

7.2.1 Meningococcal serogroup C (MenC) conjugate vaccines

The MenC conjugate vaccine was introduced into the UK childhood vaccination programme in late 1999[18] and scheduled for all under the age of 18 years. In 2002 these vaccines were also made available to those aged 20–24 years. These vaccines confer high levels of serum bactericidal antibody and induce immunological memory in individuals from the age of two months.[18] Preliminary estimates of efficacy suggest that the vaccine is 88–96% effective against invasive meningococcal disease due to serogroup C infection. MenC conjugate vaccine confers no protection against other serogroups of meningococcal disease, such as serogroups A, B, W135, or Y. A 12–month MenC booster in combination with *Haemophilus influenzae* serotype b (Hib/MenC) was introduced into the national childhood immunisation programme in September 2006. Protection against MenC infection declines over time, especially in children who were only immunised prior to September 2006 and who did not receive the 12–month booster.[88] Previous serogroup C disease is not a contra-indication to MenC vaccination. The immune response to natural infection may be inferior to that observed after conjugate vaccines,[89] particularly in young children.

7.2.2 Vaccines against other serogroups

Meningococcal polysaccharide vaccines offer protection against infection with serogroups A, C, W135 and Y but, unlike conjugate vaccines, they do not induce immune memory. In addition, polysaccharide vaccine may induce immune hyporesponsiveness following subsequent doses of the same vaccine.

One quadrivalent MenACWY conjugate vaccine (Menveo®) has recently been licensed for use in adults and children aged over 11. Although the conjugate vaccine is not yet licensed for infants and young children, it induces a higher antibody response to all four serogroups after two doses compared with the plain polysaccharide vaccine.[90,91] The response to serogroup C is comparable with that seen with the monovalent MenC conjugate vaccine.[92] Based on this and the experience with other conjugate vaccines, immunity is expected to be higher, longer-lasting and confer less risk of immunological tolerance than the plain polysaccharide vaccine. For this reason, the conjugate vaccine is recommended in preference to the plain polysaccharide vaccine across all age groups.

The meningococcal polysaccharide vaccines do not offer ANY protection against serogroup B organisms.

7.2.3 Aim of prophylactic vaccination

Meningococcal vaccination is offered to those at close prolonged contact to reduce the risk of late cases. The latter risk may be due to a combination of genetic susceptibility in the family, increased exposure to virulent meningococci and environmental factors. 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 is approximately 1,000 in cases due to confirmed serogroup C infection.[93] Vaccine is not indicated for those who received chemoprophylaxis for transient contact and in dispersal settings.

A case of meningococcal disease provides an opportunity to complete the national vaccination schedule in cases and contacts who are eligible according to current Department of Health recommendations (http://www.dh.gov.uk/en/Publichealth/Immunisation/Greenbook/index.htm).

Vaccination is recommended for cases of serogroup C disease who are eligible for routine vaccination. Vaccine failure implies an inadequate response to the vaccine and may reflect host factors or suboptimal storage or administration of the vaccine. Immunological investigation of the case and testing convalescent serum prior to re-immunisation (available at HPA Meningococcal Reference Unit) should be considered. Although recurrent serogroup C disease is rare, this policy ensures that persons in this age group are given equivalent protection to their age-matched immunised peers.

Recommendation 5: Vaccines

Close contacts
Individuals who were identified as close prolonged contacts of cases due to vaccine preventable strains of *N. meningitidis* who received chemoprophylaxis should be offered an appropriate vaccine once diagnosis has been confirmed and up to four weeks after illness onset.

For confirmed serogroup C infection, MenC conjugate vaccination should be offered to all close contacts who are previously unimmunised with MenC conjugate vaccine. Close contacts who are partially immunised should complete a course of MenC conjugate vaccination. Close contacts of any age who were only immunised in infancy and those who completed the recommended immunisation course (including the 12–month booster) more than one year before should be offered an extra dose of MenC conjugate vaccine.

Evidence grade B

For confirmed serogroup A, W135 or Y infection, vaccination with quadrivalent conjugate vaccine [i] should be offered to all close contacts of any age (2 doses one month apart if aged <1 year).

Evidence grade B

For probable cases with serogroup A, W135 or Y from a nasopharyngeal swab, the quadrivalent conjugate vaccine[i] should be offered to close contacts of any age (2 doses one month apart if aged <1 year).

Evidence grade D

Vaccination of the index case
MenC conjugate vaccine should also be offered according to the recommended national schedule to any unimmunised index cases under the age of 25 years (whatever the serogroup).

Evidence grade D

Cases of confirmed serogroup C disease who have previously been immunised with MenC conjugate (or polysaccharide) vaccines should be offered a booster dose of MenC conjugate vaccine around the time of discharge from hospital.

Evidence grade D

Index cases who are in the risk-group for meningococcal disease (e.g. asplenia, complement-deficiency) and have not been immunised (or are incompletely immunised for age) with the quadrivalent MenACWY conjugate vaccine should complete the recommended immunisation course (2 doses one month apart if aged <1 year; 1 dose after first birthday), while those who received the quadrivalent MenACWY conjugate vaccine more than 12 months previously should receive an extra dose of the quadrivalent MenACWY conjugate vaccine.[i]

Evidence grade D

i Currently (Menveo®) is available from Novartis® (Tel: 08457 451500).

7.3 Disseminating information

Following a case of meningococcal disease, it is important to give out information because early diagnosis and treatment should improve outcome. There is a small but real risk of further linked cases.[53] Vigilance for signs and symptoms among contacts and their cases is important especially in the immediate high risk period (one week) after a case. Accurate and timely information should help to limit the spread of false rumours and anxiety.

Recommendation 6: Disseminating information

Leaflets or other printed 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 judgement.

Evidence grade D

The CCDC/CPHM 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 the 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. The CCDC/CPHM 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 case of meningococcal disease in someone attending their institution. With the advice of the CCDC/CPHM, letters are usually sent to other parents/students to inform them of the situation (Appendix B). It is recommended to inform and seek support for this action from relatives of the case, 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, it is still advisable to discuss the situation with the head of the institution at an early stage. The head will then be in a good position to respond immediately to parental concerns.

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

8 Prophylaxis in healthcare settings

Healthcare workers in contact with cases of meningococcal disease are at increased relative risk of disease in the 10–day period after exposure, although absolute risks are very low; in one study absolute risk was estimated as $0.8/10^5$ and relative risk as 25.[94] The data were consistent with a higher (but unquantifiable) risk in those more heavily exposed to nasopharyngeal secretions of cases around the time of admission to hospital.

After starting treatment of the case with intravenous benzylpenicillin, carriage rates decrease rapidly so that meningococci are undetectable by nasopharyngeal swabbing after 24 hours on treatment.[77] Third generation cephalosporin antibiotics would be expected to have a similar or more rapid effect on suppression of carriage. Both ceftriaxone and rifampicin are known to be effective in eradicating carriage,[95,64] whereas penicillin is thought to suppress but not eradicate carriage.[77]

Recently published 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.[96] In the USA, masks are recommended when working within one metre of patients known or suspected to be infected with micro-organisms transmitted by large-particle droplets (> 5 micrometres diameter) that can be generated during coughing, sneezing, talking or the performance of clinical procedures.[97] Laboratory studies suggest that surgical masks can protect the wearer against droplet transmission. [98,99]

Meningococcal pneumonia may carry a low risk of transmission in healthcare settings especially to the immunocompromised.[51,52]

Recommendation 7: Prophylaxis in healthcare settings

Healthcare workers should reduce the possibility of exposure to large particle droplets (e.g. 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 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 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 rifampicin 600 mg orally twice daily for 2 days are 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 conjugate vaccines is not recommended for two reasons. First, at the time of exposure, the serogroup of the infecting strain is not usually known, so previous vaccination would not obviate the need for chemoprophylaxis. Second, most cases are caused by serogroups other than A, C, Y and W135 and would, therefore, not be prevented by the quadrivalent conjugate vaccine.

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.

Evidence grade D

9 Management of clusters

Outbreaks of meningococcal disease often generate high levels of public alarm.[100,101] Contributing to this alarm are the lack of predictability and speed of development of outbreaks that can frustrate the efforts of public health authorities. The speed of public health response is thus important both to implement preventive measures and reduce public anxiety.

In educational settings, once a second case has occurred, the risk of a third case may be as high as 30-50%.[78,102] 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 (N Syed, unpublished data), 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.[101]

Although one trial of mass chemoprophylaxis in a closed community (military barracks) showed a significant effect on disease reduction,[103] whether such interventions work in schools or civilian communities is not known.[104,105] The aim of such interventions is to eradicate carriage of the outbreak strain from a population at high risk of invasive disease.[106]

If an outbreak is caused by strains of a serogroup for which an effective vaccine exists, vaccination should be considered. Recent 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.[78] In the USA, vaccination of whole communities in community serogroup C outbreaks is considered when a defined threshold is reached.[107]

Assessment of 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.[108] More evidence is needed on the effectiveness of such interventions.

9.1 Management of clusters in a single educational institution

In this context, a cluster is defined as two or more cases of meningococcal disease occurring in the same pre-school group, school, or college/university within a four-week period.

Recommendation 8: Managing clusters in educational institutions

Assess the information
When two or more cases are reported from an educational institution, 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.
- Numbers of students in the school and in each school year.

Consider the options
The public health management options include:

- No further action (e.g. if two possible cases).
- Giving out information only.
- Giving out information and offering wider prophylaxis in the institution.

The main decision to be taken by the CCDC/CPHM* is whether to offer wider prophylaxis, and, if so, when and to whom. The principle is to try to define a group at high risk of acquiring meningococcal infection and disease, and to target that group for prophylaxis in order to reduce 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 suggests a need to act promptly.

Evidence grade D

Make a decision
If two *possible* cases attend the same institution, whatever the interval between cases, prophylaxis to any contacts is not indicated.

Evidence grade D

If two *confirmed* cases caused by different strains attend the same institution, they should be regarded as two sporadic cases, whatever the interval between them. Only close contacts of each case should be offered prophylaxis.

Evidence grade D

If two *confirmed/probable* cases who attend the same preschool group, school, college or university arise within a four-week period and are, or could be, caused by the same serogroup, public health action is indicated. It is not necessary to wait for microbiological results on probable cases (*high immediate risk of further cases).*

Evidence grade D

Information should be given out widely within the institution to parents and students as appropriate (see Appendix B).

Evidence grade D

For clusters in pre-school groups, both staff and children would normally be offered prophylaxis.

For clusters in schools/colleges/universities, if a clear subgroup can be defined that contains the cases, 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 they are confirmed or not.

If uncertain, seek expert advice from Health Protection Services (HPS) Colindale (Tel: 020 8200 4400) or Health Protection Scotland (Tel: 0141 300 1100).

For clusters among children at preschool groups and primary schools, staff should normally be included in the target group (*some evidence of increased risk*) but not in clusters among students at secondary schools, colleges, universities (*no evidence of increased risk*).

Evidence grade D

For a cluster involving confirmed serogroup A, W135 or Y cases: the quadrivalent conjugate vaccine should be offered to all individuals of any age who were offered antibiotics.[ii]

Evidence grade D

For a cluster involving one or more cases of confirmed serogroup C infection: MenC conjugate vaccine should also be offered to all previously unimmunised individuals who were offered antibiotics. If the cluster involves MenC conjugate vaccine failures, further investigation may be required and discussion with HPS Colindale or Health Protection Scotland is recommended (see section 7.2, vaccines).

Implement the decision
If antibiotics +/– vaccine are to be offered, make urgent arrangements with:

• Community medical/nursing staff to deliver medicines/vaccine/information.
• Head of the institution to inform parents/students and seek consent (Appendix B).
• Pharmacists to supply antibiotics (in correct formulation, dosage and information sheets) and vaccines.[109]

Ciprofloxacin or rifampicin are the recommended antibiotics (see section 7.1, chemoprophylaxis). Patient group directions may be helpful (Appendix C).

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; application and success of intervention 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.

*****CCDC **–** Consultant in communicable disease control, CPHM – Consultant in public health medicine

ii Emergency vaccine supply for use in clusters of serogroup A, W135 or Y infections should be discussed with HPS Colindale

9.2 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.

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 above).

Recommendation 9: Managing clusters in wider community
Assess carefully all the epidemiological information at your disposal: confirmed and probable cases, serotyping and/or molecular typing data, dates of onset, links between cases, size of population containing the cases, and MenC vaccination uptake rates (where relevant).

Calculate age specific attack rates.
The numerator is the number of confirmed cases in the population at risk caused by strains of the same serogroup and that are not distinguishable. Count multiple cases in the same household or in the same institutional setting (if this setting is considered to be the focus of a separate outbreak) as a single case.
The denominator is the population at risk. This population should be clearly defined and make sense to the people who live within and without the selected boundaries. It may not be easy to define such a population. Examples are a rural town/village or a secondary school with its feeder schools. The target age group within this population should contain all or most of the outbreak cases. If the outbreak is mainly in children, the denominator should be based on the age range of children at school or preschool and, where relevant, ages in whom vaccine should be effective
Only consider intervention 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 2–16 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 - about 20 times the annual incidence of disease in 1–19 year olds in England and Wales during 1995/96.

Evidence grade D

Seek advice from national experts through Health Protection Services Colindale (Tel: 020 8200 4400) or Health Protection Scotland** (Tel: 0141 300 1100) if attack rates approach this level.

Decide whether or not to embark on a community immunisation and/or chemoprophylaxis programme at a full meeting of the outbreak control team.

Disseminating information
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.
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 the CCDC/CPHM should liaise closely with the manager or head teacher. In college/university settings liaison will be with a member of the senior management team. 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.

A public relations strategy will be required. If high levels of interest are anticipated or already evident, prepare to set up telephone helplines (section 6, box 2, for helpline contact details), to allow controlled media access to vaccination sites, to release regular coordinated press briefings and to hold press conferences.[101]

Evidence grade D

10 Authorship

10.1 Membership of HPA Meningococcus and Haemophilus Forum

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10.2 Review of guidelines

The guidelines will be reviewed by the HPA Meningococcus and Haemophilus Forum every three years. Any modifications will be updated on the HPA website, www.hpa.org.uk.

10.3 Acknowledgements

The 2006 guidelines received comments from the Royal College of Physicians, the Royal College of General Practitioners, the Royal College of Pathologists, the Royal College of Paediatrics and Child Health, the British National Formulary, the Meningitis Research Foundation and many individual members of the PHMEG. We also thanked Dr Erika Duffell, Kelly Alexander and Janet McCulloch for their assistance in revising information on drug interactions and developing patient group directions.

Appendix A: Examples of drug information leaflets

Rifampicin

The antibiotic you will be given is called Rifampicin. It comes as either tablets or syrup and is suitable for people of all ages. The meningococcal germs that cause meningitis and septicaemia can be carried in the nose and throat, this antibiotic will kill them.

Rifampicin must be taken twice a day for two days (morning & evening), the instructions will be clearly written on the box or bottle. ***It is important that you take a two-day course. It is taken by mouth and should be taken one hour before a meal to obtain the best effect.*** You may have extra medicine left, which should be disposed of safely.

Rifampicin is an antibiotic that is frequently used to treat lots of different conditions. It is recommended in national guidelines for close contacts of someone with meningococcal disease.

The **side effects** of Rifampicin may include:

- Orange/reddish staining of urine, saliva and tears. ***This is normal – so do not be alarmed. Rifampicin may permanently stain some contact lenses so you should not wear contact lenses whilst on treatment or for the following week.***

- Tummy upset, diarrhoea and nausea.

- Skin flushing and itching, with or without a rash.

- Very rarely, jaundice (yellowing of the skin or whites of the eyes).

Rifampicin may reduce the effect of several medicines including

- blood thinning medication (anticoagulants)

- diabetic medication

- some types of epilepsy medication (anticonvulsants).

Rifampicin can interact with oral contraceptives. If you are taking an oral contraceptive pill, you should use an additional method of birth control (such as condoms) as well as your oral contraceptive pill during treatment with rifampicin and for at least 4 weeks after finishing the treatment

Please tell the public health doctor or nurse if you:

- ***take any medication***

- ***are allergic to rifampicin***

as you may need an alternative medicine.

Ciprofloxacin

The antibiotic you will be given is called Ciprofloxacin. The meningococcal germs that cause meningitis and septicaemia can be carried in the nose and throat. This antibiotic will kill them.

It comes in tablet or liquid form. You will receive either one or two tablets of Ciprofloxacin or one dose of a liquid. Tablets are taken by mouth as a one-off dose with a glass of water. It is important to drink plenty of fluids for the rest of the day after taking this antibiotic.

Do not take the tablet or medicine if you have taken antacid/indigestion medicines or preparations containing iron or mineral supplements within the last four hours. Please see the doctor or nurse if this is the case.

You should also avoid drinking alcohol with this medication as it may make you drowsy, affecting your ability to drive or operate machinery.

Ciprofloxacin is an antibiotic that is frequently used to treat lots of different conditions. It is recommended in national guidelines for close contacts of someone with meningococcal disease.

The **side effects** of Ciprofloxacin may include:

- Tummy ache, diarrhoea and nausea.
- Tiredness and headaches.
- Rash and itching.
- **Facial swelling** - very rarely breathing difficulties may occur with the facial swelling. **You should seek medical attention urgently if this occurs.**
- Pain and inflammation around the joints.

Please tell the public health doctor or nurse if you are:

- ***allergic to ciprofloxacin***
- ***have a history of epilepsy or G6PD deficiency***

so that they can arrange an alternative medicine.

Ciprofloxacin does **not** interfere with the contraceptive pill.

If you are unclear or would like further information, please contact: -

Appendix B: Example of information letter to parents after a case

** Delete/modify as appropriate*

Dear Parent or Guardian,
I am writing to inform you that one **pupil/child* from the **school/nursery* has been admitted to hospital with **meningitis/septicaemia*, *probably/possibly* caused by the meningococcal bacteria. The child is *(*status – responding well to treatment etc.).* No further action is necessary at the present time. There is no reason to make any change in the **school/nursery* routine and no reason for children to be kept at home.

Meningococcal bacteria are carried in the back of the throat of about one in ten people at any one time but only very rarely cause illness. Most people who carry the bacteria become immune to them. The bacteria do not spread easily and those who have had prolonged, close contact with the person are at a slightly greater risk of getting ill. These people have been identified and given antibiotics to stop the bacteria spreading.

Although the risk of another case in the **school/nursery* is very small, it is sensible to be aware of the signs and symptoms **which are detailed in the attached leaflet / outlined below.*

Meningitis	***Septicaemia***
Fever	Fever
Vomiting	Vomiting
Severe Headache	Bruising / Rash
Stiff Neck	Rapid Breathing
Dislike of bright light	Joint/Muscle Pain
Seizures	Cold Hands and Feet
Confusion/delirium	Confusion/delirium
Extreme sleepiness / difficulty waking	Extreme sleepiness / difficulty waking

NOT ALL OF THESE SIGNS AND SYMPTOMS MAY SHOW AT ONCE, but someone with this illness will become very ill. The illness may progress over one or two days. **BUT IT CAN DEVELOP VERY RAPIDLY**, sometimes in a matter of hours.

Diagnosis in the early stages can be difficult. The early signs can be like bad 'flu' symptoms but be **WATCHFUL** and use your instincts. **IF SOMEONE BECOMES ILL WITH SOME OF THESE SIGNS OR SYMPTOMS**, **CONTACT THE DOCTOR URGENTLY** and ask for advice.

If you have individual worries about this case, you can speak to a member of the public health team on …….. during normal working hours.

Further information is available from:
The Meningitis Research Foundation, www.meningitis.org, 0808 800 3344 (24hr Helpline)
The National Meningitis Trust, www.meningitis-trust.org, 0800 028 1828 (24hr Support Line)
NHS Direct, www.nhsdirect.nhs.uk, 0845 46 47

Yours sincerely
**Head Teacher/Manager/ Public Health Physician*

Example of parent letter if antibiotics and/or vaccine programme

Dear Parent or Guardian,

I am writing to inform you that **two/three pupils/children* from the **school/nursery* have been admitted to hospital with **meningitis/ septicaemia*, *probably/definitely* caused by the meningococcal bacteria. The children are **(status – responding well to treatment etc.).*

In accordance with national expert guidance, we will be offering preventive antibiotics **and vaccination* to all pupils in the **school/ school year*. A special session for this will be held on ……. from ….. to …. in ……..

Your child should attend this session and bring with them the enclosed consent form, signed by you. I also enclose an information sheet on **meningitis/ ciprofloxacin/ rifampicin/ vaccine* for your information.

For further information, a telephone helpline is available on …….

Yours sincerely

Public health physician

Example of consent form

……*School/Nursery*

Name of pupil /student …… Date of birth……/……/……

Address ……

School year ……

**I consent to *my child/ receiving meningococcal vaccine*

**I consent to *my child/ receiving preventive antibiotic tablets*

I have read the information leaflet attached

**Relationship to child: (Mother, Father, Legal Guardian) ……..*

NAME (Capitals, please) ……..

Date:	Signed:

Appendix C: Examples of Patient Group Directions

Administration of Rifampicin by Registered Nurses employed by …….Trust/Agency for the prevention of secondary cases of meningococcal disease

1. This Patient Group Direction relates to the following drug:

Name of medicine	Rifampicin
Legal Status	POM (Prescription only medicine)
Storage	Rifampicin capsules 300mg: store below 25^0 C Rifampicin syrup 100mg in 5ml: store below 30^0 C Protect from light and moisture Shake syrup before use and do not dilute
Dose	Adults and children over 12 years: 600mgs twice daily for 2 days Children aged 1 to 12 years: 10mg per kg twice daily for 2 days Infants under 12 months: 5mg per kg twice daily for 2 days **Children's doses based on average weight for age:** 0-2 months 20mg (1ml syrup*) twice daily for 2 days 3-11 months 40mg (2ml syrup*) twice daily for 2 days 1-2 years 100mg (5ml syrup*) twice daily for 2 days 3-4 years 150mg (7.5ml syrup*) twice daily for 2 days 5-6 years 200mg (10ml syrup*) twice daily for 2 days 7-12 years 300mg (1 capsule) twice daily for 2 days * Rifampicin syrup contains 100mg in 5ml
Route/method	Oral The doses should be taken at least 30 minutes before a meal or 2 hours after a meal to ensure rapid and complete absorption
Frequency	Twice daily
Duration	Two days
Total dose number	Four doses
Advice to the patient or carer	• Patients on oral contraceptives should be advised to use alternative, non-hormonal methods of birth control during the therapy and continued for at least 4 weeks after stopping the rifampicin. • Pregnancy – use only if potential benefit outweighs the potential risk (see below for further detail) • Stress the importance of completing the 2 day course • Soft contact lenses should not be worn for 1 week following completion of the course or they may be permanently stained. • Treatment is not fully protective and close contacts must be alert to symptoms and signs of meningococcal disease. • **Provide written patient information sheet on rifampicin and meningococcal disease**

Side effects **See BNF for full details**	Nausea, diarrhoea, urticaria and rash, fatigue, headache or drowsiness • Orange/reddish staining of urine, sputum and tears, may stain contact lenses and nappies • Respiratory symptoms, including shortness of breath • Collapse and shock • Haemolytic anaemia • Acute renal failure • Thrombocytopenic purpura • Alterations to liver function, jaundice • Also, oedema, muscular weakness and myopathy, exfoliative dermatitis, toxic epidermal necrolysis, pemphigoid reactions, leucopenia, oesinophilia
Overdose	Gastric lavage should be performed as soon as possible. Intensive support measures should be instituted and individual symptoms treated as they arise.

2. Clinical condition

Clinical condition to be treated	Prophylaxis following close contact with a case of meningococcal disease to eliminate meningococci in the nasopharynx of asymptomatic carriers
Criteria for inclusion	All children and adults at risk of meningococcal disease, including: • People who have had close, prolonged contact with the confirmed or probable case during the 7 days before the case became ill • During local outbreaks of the disease Ideally, prophylaxis should be given within 24 hours of the index case being diagnosed
Criteria for exclusion	• Refusal of treatment or parental decline to give consent • Jaundice • Hypersensitivity to rifampicin or any of the ingredients • Hepatic impairment (may require reduced dose) • Anticoagulants or phenytoin • Transplant patients receiving ciclosporin, tacrolimus or sirolimus • HIV positive patients receiving antiretroviral therapy
Action if excluded	• Explain clinical reasons for exclusion • Consider alternative prophylaxis and if necessary refer to relevant GP or Consultant in Communicable Disease Control • Advise on risks of infection, the need for vigilance for symptoms of meningococcal disease and the need to seek urgent medical

	attention should symptoms occur • Document all actions
Action if refused	• Advise on risks of infection, the need for vigilance for symptoms of meningococcal disease and the need to seek urgent medical attention should symptoms occur • Inform GP • Respect wishes • Document actions in patient's records
Drug interactions (Further interactions are outlined in the BNF)	Rifampicin has been shown to have liver enzyme inducing properties and may reduce the effectiveness of: • Anticoagulants • Corticosteroids • Ciclosporin • Digitalis preparations • Oral contraceptives • Oral hypoglycaemics • Dapsone • Phenytoin • Quinidine • Narcotics • Analgesics It may be necessary to adjust the dosage of these drugs if they are given concurrently with rifampicin, especially when it is initiated or withdrawn. Patients may need advice or referral to a doctor.
Cautions	Hepatic impairment – consider risks and benefits
Pregnancy and lactation	Pregnancy – use only if the potential benefit outweighs the potential risks. If used within the last few weeks of pregnancy it may cause post-natal haemorrhages in the mother and infant, for which treatment with vitamin K1 may be indicated. Ciprofloxacin or ceftriaxone recommended by HPA for prophylaxis in pregnancy or lactation. Rifampicin is excreted in breast milk – only use if the potential benefit outweighs the potential risks

3. Records

3.1 The following paper or computer-based records should be kept:

• Verbal consent agreeing to the administration of the drug is required from an appropriate person

• Patient name and contact details

• Name and brand of the drug

• Batch number and expiratory date (if available)

• Dose given

• Route of administration

• Signature & date

• Adverse effects reported

Note: The nurse administering the drug must ensure that the patient's name and date of administration is written on the box/bottle. The patient must also be provided with written advice on the effects of rifampicin.

3.2 Drug audit trail data collection:

Reconciliation: Stock balances should be reconciled with receipts, administration and records on a patient-by-patient basis.

Storage: Standards must be consistent with the Summary of Product Characteristics.

4. Professional responsibility of nurses

4.1 The nurse will ensure that she/he has the relevant training and is competent in administering POM, including contra-indications and anaphylaxis. She/he will attend training updates as appropriate.

4.2 The nurse will have due regard to the Nursing and Midwifery Council Code of Professional Conduct, the Scope of Professional Practice and Guidelines for the Administering of Medicines.

5. Administration of rifampicin:

All nurses involved in the administration of rifampicin must read and sign the appropriate Patient Group Direction.

6. This Patient Group Direction has been peer reviewed by:

Name	Position	Date

Sources:

- British National Formulary (2010) British Medical Association and Royal Pharmaceutical Society of Great Britain: London.
- Department of Health (2007) Immunisation Against Infections Diseases: Meningococcal Chapter. Accessed on 17 January 2011: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_079917 Electronic Medicines Compendium. Accessed 17 January 2011, at: http://www.emc.medicines.org.uk
- NHS Executive (2000) Health Service Circular HSC2000/026: Patient Group Directions (England only)
- Health Protection Agency Meningococcus and Haemophilus Forum (2011) Guidance for public health management of meningococcal disease in the UK http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/MeningococcalDisease/Guidelines/
- Resuscitation Council UK (2008) Emergency treatment of anaphylactic reactions. Guidelines for healthcare providers. www.resus.org.uk/pages/reaction.pdf

Patient Group Direction
Supply and administration of RIFAMPICIN by nurses employed by ….Trust/Agency in the ….Unit

This Patient Group Direction for use in ….Trust/….Agency is authorised by:

Job Title	Name	Signed	Date
Senior PCT Doctor			
Senior PCT Pharmacist			
Senior PCT Nurse			

The nurses named below, being employees of ….Trust/….Agency, are authorised to supply and administer RIFAMPICIN as specified in this Patient Group Direction

We agree to supply and administer the above drug in accordance with this Patient Group Direction

Name	Job Title	Signed	Date

This Patient Group Direction comes into effect: Date
Review date (every two years): Date

Administration of Ciprofloxacin by Registered Nurses employed by ……..Trust/Agency

1. This Patient Group Direction relates to the following drug:

Name of medicine	Ciprofloxacin
Legal Status	POM (Prescription only medicine) **NB The use of Ciprofloxacin for prophylaxis of meningococcal disease is an unlicensed indication.** The Health Service Circular HSC2000/026 states that medicines used outside the terms of the Summary of Product Characteristics may be included in PGDs provided such use is exceptional, justified by current best clinical practices and that a direction clearly describes the status of the product. The use of ciprofloxacin for prophylaxis of meningococcal meningitis is described in the British National Formulary and XXXX local policy. Please refer to these documents.
Storage	No special storage precautions are necessary. Protect from contamination, sunlight, atmospheric moisture and adverse temperatures.
Dose	Adults and children over 12 years: 500mg Children 5-12 years: 250mg* Children 1 months - 4 years 125mg * Following a risk assessment only
Route/method	Oral
Frequency	Single dose
Total dose number	1 dose
Advice to the patient or carer	• Swallow tablets whole with an adequate amount of liquid. Do not take with dairy products or with mineral fortified drinks alone, (e.g. milk, yoghurt, calcium fortified orange juice). • Drink plenty of fluids for rest of the day to avoid excessive alkalinity of urine. • Treatment is not fully protective and close contacts must be alert to symptoms and signs of meningococcal disease. • May impair driving and skilled tasks, effects are enhanced by alcohol • Provide patient information leaflet on ciprofloxacin.
Cautions and Side effects See BNF for full details	• History of epilepsy or conditions predisposing to seizures • History of glucose-6-phosphate dehydrogenase (G6PD)deficiency • Renal impairment: avoid excessive alkalinity of urine and ensure adequate fluid intake (risk of crystalluria). • Myasthenia gravis • Children and young adolescents (Ciprofloxacin has been shown to cause arthropathy in weight-bearing joints of immature *animals*). The benefit of its use in children for the prophylaxis of meningococcal disease must be considered against the risks. Recommend for prophylaxis. • Side effects may include nausea, diarrhoea, rash, fatigue or facial swelling, and tendon damage. Rarely, breathing difficulties – urgently refer to doctor.

2. Clinical condition

Clinical condition to be treated	Ciprofloxacin may be used as an alternative agent to rifampicin for chemoprophylaxis of meningococcal meningitis in adults and children aged 1 month and above.
Criteria for inclusion	All children and adults at risk of meningococcal disease, including: • People who have had close, prolonged contact with the confirmed or probable case during the 7 days before the case became ill • During local outbreaks of the disease Ideally, prophylaxis should be given within 24 hours of the index case being diagnosed
Criteria for exclusion	• Hypersensitivity to any of the ingredients. • History of epilepsy or conditions that predispose to seizures, unless on treatment with phenytoin (benefit outweighs risk) • Patients with myasthenia gravis
Action if excluded	• Advise of reasons for exclusion • Consider alternative prophylaxis and if necessary refer to relevant GP or Consultant in Communicable Disease Control • Advise of risks of infection and recognising symptoms • Document all actions
Action if refused	• Advise on risks of infection, the need for vigilance for symptoms of meningococcal disease and the need to seek urgent medical attention should symptoms occur • Inform GP • Respect wishes • Document actions in patient's records
Drug interactions (Refer to latest edition of BNF for full list of drug interactions)	Significant drug interactions that may require advice or referral to a doctor. These include: • Anticoagulants • Ciclosporin • Theophylline • interacts with phenytoin but considered preferable to rifampicin Others include: antacids, iron, zinc, , calcium salts, coumarins, methotrexate, didanosine, duloxetine, oral nutritional solutions, dairy products, , NSAIDs, glibenclamide, probenecid, metoclopramide, ropinirole, sucralfate,. Should not be administered within 4 hours of medications that contain magnesium, or iron salts. Avoid if taking Theophylline. Patients should be monitored for 30 minutes after administering the dose in case of anaphylaxis.

3. Records
3.1 The following paper or computer-based records should be kept:

• Verbal consent agreeing to the administration of the drug is required from an appropriate person

• Patient name and contact details

• Name and brand of the drug

• Batch number and expiratory date (if available)

• Dose given

• Route of administration

• Signature & date

• Adverse effects reported

Note: The nurse administering the drug must ensure that the patient's name and date of administration is written on the box/bottle. The patient must also be provided with written advice on the effects of Ciprofloxacin.

3.2 Drug audit trail data collection:
Reconciliation: Stock balances should be reconciled with receipts, administration and records on a patient by patient basis.

Storage: Standards must be consistent with the Summary of Product Characteristics.

4. Professional responsibility (all nurses)
4.1 The nurse will ensure that she/he has the relevant training and is competent in administering POM, including contra-indications and anaphylaxis. She/he will attend training updates as appropriate.

4.2 The nurse will have due regard to the Nursing and Midwifery Council Code of Professional Conduct, the Scope of Professional Practice and Guidelines for the Administering of Medicines.

5. Administration of Ciprofloxacin:
All nurses involved in the administration of Ciprofloxacin must read and sign the appropriate Patient Group Direction.

6. This Patient Group Direction has been peer reviewed by:

Name	Position	Date

Sources:

- British National Formulary (2010) British Medical Association and Royal Pharmaceutical Society of Great Britain: London.
- Department of Health (2007) Immunisation Against Infections Diseases: Meningococcal Chapter. Accessed on 17 January 2011: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_079917
- Electronic Medicines Compendium. Accessed 17 January 2011, at: http://www.emc.medicines.org.uk

- NHS Executive (2000) Health Service Circular HSC2000/026: Patient Group Directions (England only)
- Health Protection Agency Meningococcus and Haemophilus Forum (2011) Guidance for public health management of meningococcal disease in the UK http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/MeningococcalDisease/Guidelines/
- Resuscitation Council UK (2008) Emergency treatment of anaphylactic reactions. Guidelines for healthcare providers. www.resus.org.uk/pages/reaction.pdf

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