Invasive Meningococcal Disease

CDNA National Guidelines for Public Health Units

1. Summary

Public health priority

Urgent

Case management
Isolate case with standard and droplet precautions for 24 hours after initiation of antibiotic treatment. Exclude from child-care, school, other educational institution or work until 24 hours of clearance antibiotics completed.

Contact management
Provide information to identified contacts and urgently arrange for clearance antibiotics to be given to eligible higher-risk contacts. Vaccination may be advised for eligible higher-risk contacts if case confirmed to be caused by some vaccine preventable serogroups (A, C, W135 or Y meningococcus).

2. The disease

Infectious agents
*Neisseria meningitidis*, the meningococcus, is a Gram-negative diplococcus. There are 13 serogroups of *N. meningitidis*, with six serogroups (A, B, C, W-135, X and Y) accounting for the majority of cases of invasive meningococcal disease (IMD) worldwide (1). Serogroup B is currently responsible for most IMD cases in Australia, with small numbers of cases due to serogroups C, Y and W135 (2).

Reservoir
*N. meningitidis* is an obligate commensal of humans, the only natural host. The bacteria normally colonise the mucosa of the upper respiratory tract without causing disease. The mean duration of carriage, in settings where prevalence is stable, has been estimated as about 21 months (3). Carriage rate varies from around 3%–25% of the population, depending primarily on age (4). In European and North American studies carriage rates have been shown to be very low in the first years of life and then to sharply increase in teenagers, reaching a maximum in those aged between 20 and 24 years (5). Meningococcal carriage is also associated with male gender, coincident viral or bacterial respiratory tract infections, low socio-economic status, smoking, frequency of intimate kissing and the number and closeness of social contacts (5, 6).

Mode of transmission
Transmission is primarily by respiratory droplets from the upper respiratory tract. Saliva has been shown to inhibit the growth of meningococci and salivary contact (e.g. by sharing drink bottles) is not considered to be a significant means of transmission (7).

Incubation period
Usually from 1 to 7 days (rarely up to 10 days). Individuals who become asymptomatic carriers of meningococci are very unlikely to develop IMD (1).

Infectious period
Until the organisms are no longer present in discharges from the nose and throat. With effective antibiotic therapy meningococci usually disappear from the nasopharynx within 24 hours (8).
Clinical presentation and outcome

Invasive infections due to *N. meningitidis* can present as a spectrum of clinical illness, with meningitis and septicaemia, or a combination of the two, being the most common. Disease expression can also include pneumonia, septic arthritis, pericarditis, conjunctivitis and urethritis (9).

Meningococcal meningitis typically presents with fever, meningeal signs (e.g. headache, neck stiffness, photophobia) and altered mental status (9).

Septicaemia, with or without meningitis, can have a fulminant and rapidly fatal course (sometimes less than 24 hours) with initial symptoms that are nonspecific (e.g. fever, muscle aches, vomiting), especially in children (10). The septicaemic form can be difficult to diagnose before the onset of the characteristic haemorrhagic (i.e. petechial or purpuric) rash that does not blanch under pressure. Appearance of a rash can be relatively late (median onset 13-22 hours) (11) or there may be no rash at all. Additionally, in the early stages of illness there is sometimes a maculopapular rash that blanches under pressure. This rash may progress to become haemorrhagic and non-blanching or may fade away (12).

Leg pain, cold extremities, and abnormal skin colour – described as pallor or mottling – are frequently reported in the first 12 hours of meningococcal disease (median onset 7-12 hours), particularly in children and adolescents (11).

Infrequently, chronic meningococcal septicaemia can also occur.

Overall mortality for IMD is approximately 5-10% of infected individuals (13). An increase in case fatality rate (CFR) has been associated with a range of factors, including age (14, 15), the *N. meningitidis* serogroup (16, 17), concurrent HIV infection (18) and whether cases are associated with an outbreak (19). Most deaths occur in the first 24 hours (20) and early diagnosis and treatment is associated with reduced CFR (21, 22).

Long term sequelae affect 10-20% of recovered IMD cases, including deafness, other neurological deficits, skin loss requiring grafts and partial or full amputation of limbs (1).

People at increased risk of disease

Transmission from a symptomatic case is uncommon – the vast majority of cases are sporadic with transmission assumed to have occurred from prolonged close contact with an asymptomatic carrier in the network of close contacts.

Household contacts

The contacts most at risk of meningococcal disease are other members of the household of a case of IMD, during the first week after the case is detected (23). Studies carried out in Europe and America before the routine use of clearance antibiotics showed that household contacts of a case of IMD had a 500 to 800-fold greater risk of meningococcal disease than the general population (23, 24). The risk was highest in the first week after onset of illness in the case and fell rapidly thereafter (23).

Intimate contacts

The frequency of intimate kissing, involving close contact with respiratory droplets from the nasopharynx, increases the risk of both carriage (6, 25) and disease (26, 27). However, contact with saliva *per se*, such as through sharing drinks or superficial mouth kissing, is not thought to significantly increase risk of carriage or disease (7).
**Child-care contacts**

There is limited evidence in favour of providing clearance antibiotics to child-care contacts of sporadic cases of IMD. A Belgian study found that the relative risk of secondary IMD among day-care (aged under three years) and pre-school contacts (aged two to five years) was much less than that for similarly aged household contacts of an index case (23). A British study of pre-school settings (including day care, play-groups and other pre-school groups) (most were aged less than four years) found that the relative risk of a cluster of cases in pre-school in the four weeks after an index case was 27.6 and the absolute risk was 49/100,000 contact children (28).

**School and university contacts**

United States (US) and United Kingdom (UK) studies have demonstrated a modestly increased risk of further cases in schools attended by index cases (29, 30). However, subsequent cases do not necessarily occur in the same classroom as the index case, with others occurring, for example, in contacts who share extracurricular activities with index cases (29). In the US the relative risk of further cases among school students (5-18 years of age) was 2.3 (29).

**Healthcare workers and others with close contact with a case after onset of symptoms**

Even though transmission from a symptomatic case is uncommon there is, however, a small increased risk of disease in people who have very close contact with a symptomatic case prior to completion of 24 hours of antibiotic therapy. Those healthcare workers who have unprotected close airway exposure to large particle respiratory droplets (e.g. during airway management) from a case of IMD around the time of admission, are at increased risk of disease in the 10–day period after exposure (31). However, the risk is very low; in one study absolute risk was estimated to be 0.8/100,000 (32), far below the risk in household contacts.

**Other groups/individuals at higher risk**

Laboratory personnel who work with N. meningitidis are at increased risk of IMD (33, 34). Other risk factors for IMD include congenital or acquired immunoglobulin deficiencies and complement deficiencies, anatomic or functional asplenia, travel to or residence in countries where meningococcal disease is hyperendemic or epidemic (35), exposure to cigarette smoke (36, 37), concurrent respiratory tract infections (38, 39) and crowded living conditions or recreation spaces (40-42). Indigenous Australians are at significantly increased risk compared to the non-indigenous population (22, 43).

**Disease occurrence and public health significance**

IMD is endemic in Australia but the incidence has varied dramatically over time, with major epidemics following both world wars. More recently, incidence increased through the 1990s, but has declined to historically low levels since a peak around the early 2000s (44, 45). Cases occur throughout the year, but there is a marked seasonality, with the highest number of notifications and hospitalisations occurring between June and September each year (46). All age groups can be affected, but there is a bimodal age distribution, with the highest rates of disease in children aged under 5 years and a second peak in adolescents and young adults aged 15-19 years (2).

While the overall incidence and mortality associated with IMD is low, the clinical and public health management of the disease can be demanding. This is related to the often dramatic course of the disease, the potential for deaths and serious complications, the fact that incidence is highest in young children, teenagers and young adults, and that clusters of cases may occur, albeit infrequently. Hence, it is essential that the public health follow-up of IMD is undertaken as a priority,
that guidelines are followed closely, and that information provided to families of those affected, contacts and the media is consistent and evidence-based.

Universal childhood vaccination using the conjugate serogroup C vaccine, introduced in 2003, along with catch-up vaccination of children and adolescents through school based programs, has been associated with a marked reduction in serogroup C IMD cases in Australia. In 2011, 84% of cases in Australia were caused by serogroup B organisms, with much smaller proportions caused by serogroups C (4.2%), W135 (5.2%) and Y (7%) (2). Serogroup Y in Australia is a more common cause of IMD in those over 65 years of age compared to those under 65 years (15).

3. Routine prevention activities

Vaccination
A single dose of a meningococcal C conjugate-containing vaccine (MenCCV) is recommended as part of the National Immunisation Program (NIP) for all children at 12 months of age. MenCCV\(^1\) is also recommended for people at high risk of meningococcal disease (refer to the current edition of the Australian Immunisation Handbook). Quadrivalent meningococcal conjugate (4vMenCV) and polysaccharide vaccines cover several serogroups not often seen in Australia and 4vMenCV is recommended and may be required for travellers to places such as Africa and Asia and pilgrims to the Haj.\(^2\)

Quadrivalent conjugate vaccines can be used in infants and children, with the minimum recommended age varying between brands (see Australian Immunisation Handbook for current recommendations). Polysaccharide vaccines are not recommended for children under the age of two, and they only provide protection for about three years.

In Australia the Therapeutic Goods Administration (TGA) included a 4CMenB vaccine on the Australian Register of Therapeutic Goods on 14 August 2013. The vaccine is registered for use in persons ≥2 months of age for the prevention of invasive disease caused by serogroup B meningococci. It is available through purchase on the private market. This vaccine is not funded under the NIP. 4CMenB is a recombinant multicomponent meningococcal B (MenB) vaccine that induces specific bactericidal antibodies against a range of MenB strains. In Australia, based on laboratory tests, about 76% of MenB strains are predicted to be covered by this vaccine, but clinical effectiveness has not yet been shown.

For further information on meningococcal disease vaccination refer to the Australian Immunisation Handbook at:

For further details specifically on 4CMenB vaccination see:

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\(^1\) This refers to any vaccine containing MenCCV; at the time of writing NIP funds a MenCCV and Hib vaccine combination

\(^2\) Currently these vaccines are not funded under the NIP

Risk mitigation
The main aims of public health measures for meningococcal disease are:

- to provide information to contacts to allay anxiety and provide advice on the action to take should they develop symptoms consistent with IMD; and
• to identify and provide clearance antibiotics to household-like close contacts of cases in order to reduce the risk of further cases resulting from transmission of a virulent strain of the organism.

4. Surveillance objectives

• To promptly identify cases and their close contacts in order that appropriate public health action can be taken
• To identify clusters of cases and outbreaks in order that appropriate public health action can be taken
• To monitor the epidemiology of the disease, including the impact of immunisation, to inform prevention strategies
• To monitor the effectiveness of current control measures and to provide an evidence base for further review of national guidelines.

5. Data management

Probable and confirmed cases of meningococcal disease should be entered into NCIMS within one working day of notification. Ensure that data on Aboriginality and vaccination history are collected and entered into the jurisdictional database. Serogroup, subserogroup and case outcome should be added to the database when available.

6. Communications

Where applicable in a jurisdiction the laboratory or clinician advises the state/territory communicable diseases branch or public health unit (PHU) of the case’s age, sex, date of onset, clinical status, laboratory findings and vaccination history (if relevant).

7. Case definition

Probable and confirmed cases of meningococcal disease are notifiable.

<table>
<thead>
<tr>
<th>Confirmed case</th>
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</thead>
<tbody>
<tr>
<td>A confirmed case requires either:</td>
</tr>
<tr>
<td>1. <strong>Laboratory definitive evidence</strong></td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>2. <strong>Laboratory suggestive evidence AND clinical evidence</strong>.</td>
</tr>
<tr>
<td>Laboratory definitive evidence</td>
</tr>
<tr>
<td>1. Isolation of <em>Neisseria meningitidis</em> from a normally sterile site</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>2. Detection of specific meningococcal DNA sequences in a specimen from a normally sterile site by nucleic acid amplification testing.</td>
</tr>
<tr>
<td>Laboratory suggestive evidence</td>
</tr>
<tr>
<td>1. Detection of Gram-negative diplococci in Gram stain of specimen from a normally sterile site or from a suspicious skin lesion</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>2. High titre IgM or significant rise in IgM or IgG titres to outer membrane protein antigens of <em>N. meningitidis</em></td>
</tr>
</tbody>
</table>

Clinical evidence (for a confirmed case)
Disease which in the opinion of the treating clinician is compatible with invasive meningococcal disease.

Probable case
A probable case requires **clinical evidence** only.

Clinical evidence (for a probable case)
A probable case requires:
1. The absence of evidence for other causes of clinical symptoms
   AND EITHER
2. Clinically compatible disease including haemorrhagic rash
   OR
3. Clinically compatible disease AND close contact with a confirmed case within the previous 60 days.


Although meningococcal conjunctivitis is not included in the IMD surveillance case definition, cases should still be notified in order to enable a public health response as, on occasion, it may precede invasive disease (54) or IMD in a contact (55) (refer to Section 12 Special Situations).

8. Laboratory testing

Testing guidelines
All patients with suspected meningococcal infection should have blood collected as soon as possible for culture, polymerase chain reaction (PCR) testing, c-reactive protein and full blood count. Where appropriate, a sample of cerebrospinal fluid (CSF) should be collected for PCR, microscopy and culture. For meningococcal conjunctivitis refer to Section 12. Special situations. For further details of specimen collection, handling requirements and availability of testing, which may vary between locations, contact the relevant laboratory (refer to Appendix 4 National Neisseria Network (NNN) Laboratories).

**Molecular testing by Polymerase Chain Reaction (PCR)**
PCR-based diagnosis provides confirmation of IMD from blood, CSF or other normally sterile sites with validity comparable to that of culture-based diagnosis. Additionally, PCR methods can provide diagnostic information pertinent to patient care and public health management. For these reasons it is recommended that CSF and/or EDTA blood samples from which DNA was extracted for PCR-based diagnosis as well as the remaining DNA extract, both be sent to the appropriate NNN laboratory (refer to Appendix 4).

Early antibiotic therapy has contributed to PCR, particularly in blood specimens, now being the most common means of laboratory diagnosis of IMD. PCR-based assays are generally directed at the *ctrA* gene. Test sensitivity is >95% for CSF using *ctrA* gene PCR (47) and approximately 87% when testing blood samples (48). Data are not available for skin lesions.

PCR tests for serogroup determination should be performed both from a confirmatory and epidemiological point of view. Serogroup identification can guide the public health response, particularly vaccination recommendations. PCR-assays for detecting regions in the *siaD* gene specific for serogroups B, C, W135 and Y are widely performed in Australia.
Although meningococcal DNA can be detected up to 72 hours after initiation of systemic antibiotics, caution should still be taken when interpreting negative PCR results. In probable cases results should be assessed in conjunction with clinical presentation, duration and severity of disease and the timing of the initiation of systemic antibiotics in relation to collection of the specimen (48).

**Microscopy**
Detection of Gram-negative diplococci by Gram stain of CSF or specimens from other normally sterile sites constitutes laboratory suggestive evidence in the CDNA case definition. In conjunction with a clinically compatible illness, this fulfils criteria for a confirmed case of IMD. The reported sensitivity of Gram stain on CSF is about 62% (49, 50) and of skin lesion aspirates or biopsies about 50% (50, 51). Prior use of antibiotics reduces the likelihood of a positive Gram stain and culture.

**Culture**
Culture of *N. meningitidis* from blood, CSF or other normally sterile sites confirms a diagnosis of IMD. Additionally, cultures provide isolates for strain differentiation and antibiotic susceptibility testing. When meningitis is present CSF offers the best chance of yielding an organism for culture, but sensitivity is reported to decline from 72% to 42% after antibiotic treatment (49). The sensitivity of blood culture is reported to vary from 24-47% (49, 52) but falls to 5% or less if antibiotics have been given before collection (49).

**Nasopharyngeal (throat) swabs**
The collection of throat swabs is not recommended for either cases of IMD or their contacts.

**Serology**
Serum antibody tests for the diagnosis of IMD are not routinely available, but are performed in some laboratories. Serological diagnosis is based on the demonstration of a single elevated level of IgM antibody or seroconversion to outer membrane protein (OMP) antigens. As the OMP antigens amongst the *Neisseria* genus cross-react, the test may be positive in disseminated gonococcal infection.

An assay to detect IgM antibody to serogroup C capsule is also available and will detect an antibody response to recent C capsule vaccination or invasive infection with serogroup C *N. meningitidis*. Serological diagnosis is retrospective but may be useful in circumstances where IMD was suspected clinically and when other tests were negative or not performed.

**Strain differentiation**
Strain differentiation or typing can assist in establishing linkages between cases or cases and carriers that are identified epidemiologically. Laboratory typing results can exclude true relatedness of apparently linked cases if they emerge as being distinct. Also, if the method used is highly discriminating and the prevalence of particular types is taken into account, detection of indistinguishable case isolates can provide quite strong evidence of relatedness.

Isolates and samples for typing are referred to NNN Laboratories (refer to Appendix 4). Historically, phenotyping (serotyping) has been used to separate isolates into serogroups (using capsular polysaccharides), serotypes and subserotypes (using OMP).

Genotyping (molecular) techniques are now used by most state laboratories to type strains in addition to serotyping. Techniques available include pulsed-field gel electrophoresis (PFGE), *porA*/*porB*, or *fetA* sequencing and multi-locus sequence typing (MLST) (53).
Further information is available from the Public Health Laboratory Network (PHLN) case definition website:

9. Case management

Response times
Public health action should commence immediately where the clinical picture is consistent with IMD and either a haemorrhagic rash is present or Gram negative diplococci have been identified in a clinical specimen from a sterile site. Begin investigation and response on the same day of notification of a probable or confirmed case of IMD or of confirmed meningococcal conjunctivitis.

Although meningococcal conjunctivitis is not included in the surveillance case definition for IMD, cases should still be notified in order to enable a public health response as, on occasion, it may precede invasive disease (54) or IMD in a contact (55) (refer to Section 12 Special Situations).

Response procedure

Case investigation
The response to a notification will usually be carried out in collaboration with the case’s medical team. Ensure that action has been taken to:

- Discuss with the treating doctor the need to interview the case or the relevant care-giver in order to provide information and seek a contact history
- Establish what the case or the relevant care-giver has already been told about the diagnosis before beginning the interview
- Confirm the onset date and symptoms/signs of illness and assess whether the clinical evidence is consistent with a diagnosis of IMD
- Confirm results of existing relevant laboratory tests, or recommend that the tests be done
- Review case and contact management undertaken to date. For instance, establish if the treating team has provided clearance antibiotics to household contacts
- Facilitate the support of the case and/or family with a social worker, Aboriginal Liaison Officer or interpreter as required.

Case treatment
Treatment is the responsibility of the treating doctor. For antibiotic treatment recommendations refer to the current edition of Therapeutic Guidelines: Antibiotic. Some antibiotics, including penicillin, do not reliably clear nasopharyngeal carriage of meningococci (1), so appropriate clearance antibiotics must also be used (refer to Table 2).

Isolation and restriction
Droplets and nasopharyngeal secretions are considered to be infectious from the onset of the acute illness until completion of 24 hours treatment with effective systemic antibiotics (8). Hence, during this period both standard and droplet precautions should be practised for suspected, probable or confirmed cases, especially while undertaking airway management during resuscitation.

Active case finding
Contacts (refer below) who develop symptoms consistent with IMD should be advised to seek medical advice urgently and to inform the PHU.
A single case of serogroup A meningococcal disease in an Indigenous case may be the sentinel event of a community outbreak and requires appropriate action (refer to Section 12 Special situations).

10. Control of environment

None routinely required (refer to Section 12 Special situations).

11. Contact management

Identification of contacts

The aim of identifying contacts is to:

- Clarify their degree of contact with the case
- Provide them with information about meningococcal infection and their level of risk aimed at both allaying unnecessary anxiety and advising them of what action to take if they develop symptoms
- Recommend clearance antibiotics and vaccination where indicated as defined below and in Table 1.

Contact definition

Public health follow-up focuses on identifying the subset of ‘higher-risk’ contacts who require information and clearance antibiotics and vaccination in some instances. Other lower-risk contacts groups may be given information only. Higher-risk contacts fall into the following groups:

1. Household contacts of a case are those who lived in the same house (or dormitory-type room) or were having an equivalent degree of contact with the case in the 7 days prior to the onset of the case’s symptoms
2. Intimate kissing and sexual contacts in the 7 days prior to the onset of the case’s symptoms
3. Child-care: Children and staff in childcare should have an equivalent degree of contact with the case as a household contact. As a guide, this should mean at least 4 hours/day on average or 20 hours in total in the 7 days prior to the onset of the case’s illness. Child-care includes any situation where children under 5 years of age are cared for with other children away from home. This setting includes kindergartens and pre-schools (pre-primary)
4. Passengers seated immediately adjacent to the case during long distance travel (>8 hours duration) by aeroplane, train, bus or other vehicle (61).

Healthcare workers are rarely at risk, and only those who have come into direct contact with the nasopharyngeal secretions of a case during a procedure such as intubation without wearing a surgical mask or mouth-to-mouth resuscitation should be regarded as higher-risk contacts (32)(54)
Table 1: Public health responses in defined settings in which a single case of invasive meningococcal disease has occurred

<table>
<thead>
<tr>
<th>Settings</th>
<th>Clearance antibiotics⁴</th>
<th>Vaccination⁵</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Household and other higher-risk contacts of a case (refer above)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Childcare facilities (children and staff not high-risk contacts of a case: refer to point 3 above)</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Schools and universities</td>
<td>Only students who are household-like contacts of a case</td>
<td>Only students who are household-like contacts of a case</td>
<td>All other students in the same classroom (schools) or tutorial groups (universities).</td>
</tr>
<tr>
<td>Those exposed to a case after the onset of symptoms</td>
<td>No, unless meet other criteria for higher risk contacts</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Those in seats directly beside a case during long duration travel (&gt;8 hours)</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Healthcare workers who have performed airway management (e.g. suctioning, intubation) of a case wearing a mask.</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Sporting team and work contacts (including both shared office or open air settings)</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

⁴ Only those in close and prolonged contact with a case in the 7 days prior to the onset of symptoms, and only very close contacts after the onset of the case's symptoms, and prior to completion of 24 hours of appropriate treatment, require clearance antibiotics.

⁵ Vaccination recommendations only apply when IMD is caused by serogroups A, C, W135 and Y, but not to B. See Vaccination section below.
Clearance antibiotics
The main rationale for provision of clearance antibiotics is to eliminate meningococci from any carrier within the network of contacts close to each case, thereby reducing the risk of further transmission of what may be a more virulent strain of the organism within the social network and preventing further cases of invasive disease. Clearance antibiotics given to household contacts was estimated to be 89% effective in preventing secondary cases (56).

Clearance antibiotics should also be provided for contacts of meningococcal conjunctivitis because secondary cases of IMD have occurred (55).

Wider provision of clearance antibiotics outside the recommended groups should be avoided due to the risk of doing more harm than good, including elimination of protective flora, risk of side effects and development of antibiotic resistance. Following even a single case of IMD there may be considerable demands and pressure from parents or others for clearance antibiotics to be administered more widely than is recommended. It is important that public health personnel do not acquiesce to these demands, but rather provide reassurance on the low risk of IMD in contacts and carefully explain the purpose for clearance antibiotics.

All identified contacts, regardless of whether or not they are eligible to receive clearance antibiotics, should be advised to remain alert for symptoms and to seek medical review if appropriate.

As of November 2012 Therapeutic Guidelines: Antibiotic lists ceftriaxone, ciprofloxacin and rifampicin as suitable agents. Characteristics of these agents are shown below in Table 2. Clearance antibiotics should be given as soon as possible after the contact is identified. However, there is no purpose in administering antibiotics if more than four weeks have elapsed since the most recent contact with the case.

Table 2: Characteristics of agents used for nasopharyngeal clearance of meningococci

<table>
<thead>
<tr>
<th>Agent</th>
<th>Certriaxone</th>
<th>Ciprofloxacin</th>
<th>Rifampicin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred agent for</td>
<td>Pregnant women Situations where access to and/or compliance with rifampicin and ciprofloxacin may be poor, such as in remote indigenous communities</td>
<td>Adults and children of all ages6 Women taking the oral contraceptive pill (OCP)</td>
<td>Young children</td>
</tr>
<tr>
<td>Dosage</td>
<td>Child under 12 years: 125 mg IM as 1 dose Adult: 250 mg IM, as 1 dose</td>
<td>Adult or child ≥12 yrs: 500 mg orally, as 1 dose 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</td>
<td>Child7: Neonate &lt;1 month: 5 mg/kg orally, 12-hourly for 2 days. Child ³ 1 month: 10 mg/kg up to 600 mg orally, 12-hourly for 2 days. Adult: 600 mg orally, 12-hourly for 2 days</td>
</tr>
</tbody>
</table>
Advantages
- 97-98% effective in elimination of nasopharyngeal carriage (57)
- Well tolerated
- Single dose
- No adverse reactions or drug interactions of importance

Disadvantages
- IM Administration
  - Painful and may require concomitant local anaesthetic
- Contraindications:
  - Not for use in infants less than 4 weeks old.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>91-100% effective in elimination of nasopharyngeal carriage (57)</th>
<th>81-98% effective in elimination of nasopharyngeal carriage (57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well tolerated</td>
<td>Single dose</td>
<td>Oral, available in syrup</td>
</tr>
<tr>
<td>Single dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No adverse reactions or drug interactions of</td>
<td></td>
<td></td>
</tr>
<tr>
<td>importance</td>
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**Contraindications:**

- Previous allergy
- Pregnancy/breast feeding
- Drug interactions
  - Allergic reactions, including anaphylaxis
  - Safety and effectiveness in prepubertal children have not been established

- 2-day course – compliance
- Side effects
  - orange discolouration of soft contact lenses, tears and urine
  - gastrointestinal disturbance, dizziness, drowsiness, headache
- Contraindications:
  - Severe liver impairment
  - Alcohol abuse
  - Pregnancy
- Drug interactions including hormonal contraceptives, anticoagulants and anticonvulsants.

**Vaccination**

Due to the prolonged risk of secondary cases in household settings, even following provision of clearance antibiotics, vaccination with an appropriate vaccine is indicated for unimmunised household and other higher risk contacts of cases of IMD and meningococcal conjunctivitis confirmed to be caused by serogroup C, A, W135 or Y.

Vaccination with 4CMenB vaccine, however, is not recommended for higher risk contacts after a single case of IMD caused by serogroup B, due to lack of adequate evidence of benefit in such situations. This includes lesser strain coverage and lack of evidence that adequate protection is achieved rapidly enough following a single dose. Vaccination of household contacts with 4CMenB vaccine should, however, be considered if a second serogroup B case occurs in the same household (even if >30 days later), as this may indicate increased susceptibility of family members to IMD and/or ongoing transmission within the household.

Eligible contacts of cases of vaccine-preventable strains should be provided with a letter advising that they should receive vaccination and that they should visit their usual health care provider at the earliest opportunity to receive this. PHUs provide free vaccine for this purpose.

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6 Quinolones damage the joints of immature animals and therefore should be used with caution in children less than 14 years of age and pregnant or breastfeeding women.

7 Note; Rifampicin is compatible with breastfeeding but may cause diarrhoea in infants. Monitoring of infants for jaundice is recommended.
Education
Provide information to the network of contacts (or to the responsible guardians of in the network) about the disease and how it is spread. A fact sheet, appropriate to the cultural and literacy needs of recipients, should be provided (refer to example at Appendix 2). This information should include the message that contacts, or anyone close to them, who develop symptoms consistent with meningococcal disease, should seek urgent medical attention.

Isolation and restriction
None required

12. Special situations

Outbreaks
Outbreaks of meningococcal disease can be particularly challenging for public health authorities due to the intense public concern and media interest they generate (22), the potential for significant morbidity and mortality and the limited published evidence to guide best practice (60).

The term ‘outbreak’ is taken to mean the occurrence of more cases than expected for the population or group under consideration. The objective of public health management of outbreaks of IMD is to interrupt transmission and prevent further cases. Once an outbreak is either suspected or recognised there is an immediate need to initiate a coordinated response. Elements of this response include:

- A situation review to determine if there is an outbreak and its extent;
- The establishment of a response team(s) and, if appropriate, a site visit;
- Establishment of heightened surveillance;
- Determination of the population at risk and calculation of age-specific and region-specific attack rates where indicated;
- Decisions on what action is to be taken, tailored to the setting;
- Provision of adequate information to all contacts and other people as indicated, including healthcare providers, affected communities or groups, the media and the wider public;
- Ensuring the provision of clearance antibiotics (and immunisation where indicated) as required for the setting; and
- Review of all actions taken and the preparation and dissemination of final documentation and a report.

Definitions
Sporadic case - a single case in the absence of previous known close contact with another case (refer to contact definition above).

Primary (index) case - a case that occurs in the absence of previous known close contact with another case and is subsequently associated with a co-primary or secondary case.

Co-primary case - a close contact who develops disease within 24 hours of onset of illness in a primary case.

Secondary case - a close contact who develops disease more than 24 hours after onset of illness in a primary case where the available microbiological characterisation of the organisms is the same.
Organisation-based outbreak - two or more probable or confirmed (where the available microbiological characterisation of the organisms is the same) cases with onset in a four week interval, among people who have a common organization-based affiliation (such as attending the same high school) but no close contact with each other, in a grouping which makes epidemiological sense.

Community outbreak - three or more confirmed or probable cases of IMD where there is no direct epidemiologic link between the cases, with onset in a 3 month interval among persons residing in the same area and the primary attack rate is at least 10 per 100,000 (61). Rate calculations should not be annualised. This is not an absolute threshold and should be considered in the context of other factors, e.g. completeness of case reporting, whether there is continuing occurrence of cases after recognition of a suspected outbreak and population vaccination coverage where relevant.

**Identification of outbreaks**
The following changes in epidemiology of meningococcal disease are suggestive of an outbreak (62):

- An increased rate of disease. In small populations it may be more useful to focus on the number of cases rather than the rate;
- Clustering of cases in an age group or a shift in the age distribution of cases; and
- Phenotypic and/or genetic similarity among strains causing disease in the population.

Suspected outbreaks should be reviewed in order to identify the microbiological features of the cases and any epidemiologic links between cases. Microbiological investigation should focus on confirmation of the diagnosis and rapid characterisation of organisms in as much detail as locally possible. Cases that occur closely in time and place, but are infected with different serogroups (or serotypes, serosubtypes or genotypes if known), should be managed as sporadic cases (63). The identification of possible epidemiological links should include a search for contacts in common, particularly in childcare, educational institutions or other groupings or organisations (29, 64-67). Examples include attendance at nightclubs or parties (68).

**Organisation-based outbreaks**
In settings such as childcare centres and aged care facilities, the population at risk is a natural grouping that makes epidemiological sense. Identification of populations at risk in other organisational settings, such as schools, universities and workplaces, may be more difficult.

Clearance antibiotics should be considered for a wider group than household-like contacts, even though the evidence for preventing further cases is not strong (28, 69). Co-primary or secondary cases should not be counted when determining whether criteria for provision of organisation-based clearance antibiotics have been met. This is because they are the household-like contacts.

If cases have occurred in a household-like setting, then this may not meet criteria for an organisational outbreak. For example, two cases in university students in the same class who share accommodation do not define a university-based outbreak, since the risk is assumed to arise from the household-like setting of the shared accommodation.

The use of meningococcal vaccine in addition to clearance antibiotics should be considered if the outbreak is due to a vaccine-preventable serogroup (63, 68, 70-72).
**Community outbreaks**

These outbreaks are difficult to define and manage. At-risk populations are usually defined geographically by using natural or administrative boundaries that most closely fit the residence data for the majority of the outbreak cases. However, physical or administrative boundaries do not limit factors that contribute to the increasing risk of meningococcal disease and accurate identification of the at-risk population should not be inappropriately constrained by them.

Assess carefully all available epidemiological information, including both confirmed and probable cases, serotyping and/or genotyping data, dates of onset, direct and indirect links between cases, the size of the population or identifiable sub-population containing the cases and meningococcal C conjugate-containing vaccine uptake rates (where relevant) (51).

From an epidemiologic perspective, when determining if the criteria for an outbreak are met, secondary and co-primary cases should be counted as one case (61) for the purpose of calculating community attack rates.

Vaccination of the population at risk should be considered if an outbreak of a vaccine preventable serogroup is identified, as defined above. Other factors should be taken into account, including logistic and financial considerations. The decision to vaccinate a large population is a difficult one for several reasons:

- when the issue is first raised, there is usually a small number of cases with a relatively low attack rate in the total population;
- cases may be widely dispersed in time and space, making it difficult to determine whether this is an outbreak or a fluctuation within expected limits for sporadic disease; and
- the costs of the vaccine and other resources required to vaccinate the group are considerable.

Community-wide clearance antibiotics should not be used. The widespread use of clearance antibiotics in community outbreaks has not been shown to be of value. It may result in:

- the eradication of benign strains of *N. meningitidis* and bacteria of other species that induce protective antibodies;
- the generation of drug resistant strains; and
- an increase in the prevalence of drug-related adverse events.

**Aboriginal and Torres Strait Islander communities**

Based on outbreaks reported in the 1980s and early 1990s, the risk of sustained transmission of IMD in Aboriginal and Torres Strait Islander communities, especially remote communities, is probably higher than in the general community (73). For this reason a low threshold should be used to initiate disease control measures. Action targeted to all community members should be considered if there are 2 or more cases in a remote Aboriginal or Torres Strait Islander community within a 4 week period and where available characterisation indicates they are the same strain. The nature of any action will depend on factors including the size of the community and the serogroup of the organism.

**Meningococcal Conjunctivitis**
Primary meningococcal conjunctivitis may also precede invasive disease in a case or in a close contact (54, 55). Hence, it is recommended that contacts of individuals with meningococcal conjunctivitis receive information and clearance antibiotics as for contacts of IMD cases.

Conjunctival swabs should be collected from suspect cases of meningococcal conjunctivitis as soon as possible for microscopy and culture. Gram staining of conjunctival exudate or scrapings from suspect cases of meningococcal conjunctivitis consistently reveals Gram-negative diplococci and abundant polymorphonuclear leukocytes. This provides a preliminary diagnosis of meningococcal conjunctivitis (with *N. gonorrhoeae* and *M. catarrhalis* considered in differential diagnosis), but culture is essential for diagnostic confirmation, strain characterization and antibiotic susceptibility testing (55).

**13. References**


35. Anon. Updated recommendation from the Advisory Committee on Immunization Practices (ACIP) for revaccination of persons at prolonged increased risk for meningococcal disease. MMWR. 2009;58(37):1042-3.


64. Davison RP, Lovegrove DR, Selvey LA, Smith HV. Using the national guidelines to manage a meningococcal group C outbreak in a Brisbane boarding school--some discretionary judgements are needed. Commun Dis Intell. 2003;27(4):520-3.


14. Appendices

Appendix 1: PHU checklist for meningococcal cases

Appendix 2: Meningococcal disease factsheet

Appendix 3: Data collection form

Appendix 4: National Neisseria Network (NNN) laboratories