



Commonwealth Department of
Health and
Aged Care

Guidelines
for the early clinical and
public health management of
meningococcal
disease
in Australia



Communicable
Diseases
network
AUSTRALIA



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Chapter 1: Introduction

1.1 Public health aims of the *Guidelines on the early clinical and public health management of meningococcal disease in Australia (the Guidelines)*

Invasive infection with *Neisseria meningitidis* (the meningococcus) occurs in endemic and epidemic forms. In Australia epidemic disease has not occurred for many years; endemic disease is at low levels of incidence and cases are generally unrelated to each other. Despite this, invasive meningococcal disease is of public health importance, is frequently a cause of public alarm and receives a high level of media attention. Responding to cases places heavy demands on clinical and public health disease control services. The primary aim of *the Guidelines* is to assist practitioners in meeting these demands.

The Guidelines were developed by consensus by a working party of the Communicable Diseases Network Australia (CDNA) which has reviewed and endorsed the document.

In developing *the Guidelines*, the Working Party considered the literature, practices and published recommendations in Australia and overseas. On many issues there is limited published evidence to guide best practice. Public health interventions for invasive meningococcal disease are frequently required urgently yet the evidence base for many of the interventions that are commonly applied is lacking. Often decisions must be guided by extrapolation from situations where evidence exists.

The Guidelines are intended primarily:

- To assist primary care practitioners with the emergency management of cases of suspected invasive meningococcal disease; and
- To assist public health practitioners with the prevention of further cases after a case of invasive meningococcal disease has been reported.

The Guidelines are not, and cannot be, exhaustive and do not cover every possible eventuality but aim to provide guidance on situations frequently encountered in practice.

Topics covered in *the Guidelines* include:

- Emergency management of suspected invasive meningococcal disease in general practice;
- Early (emergency department) hospital management of suspected invasive meningococcal disease;
- Laboratory tests and their use;

- Public health management of sporadic cases of invasive meningococcal disease;
- Public health management of outbreaks of cases of invasive meningococcal disease; and
- Reporting and public health surveillance of meningococcal disease.

1.2 What's new

This document differs from the *Guidelines for the Control of Meningococcal Disease in Australia*, published by the National Health and Medical Research Council in 1996, in several respects including:

- Separate chapters on early clinical management in general practice and for hospital emergency department situations;
- Recommendations on the importance of re-evaluation of patients where the differential diagnosis may include invasive meningococcal disease;
- Recommendations on management after discharge from hospital;
- New material on laboratory tests and their uses;
- Recommendations for the use of ciprofloxacin and ceftriaxone as alternatives to rifampicin;
- Recommendations that chemoprophylaxis is offered to persons in close contact with a case in the 7 days (previously 10) before onset and that chemoprophylaxis not be offered if more than 14 days have elapsed since contact with the case; and
- An increased emphasis on the importance of information for contacts.

1.3 Linkages with other documents and the World Wide Web

The Guidelines are available on the Department of Health and Aged Care web site at <http://www.health.gov.au>

Other guidelines on the management of invasive meningococcal disease may be found at:

USA <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4907a1.htm>

United Kingdom
<http://www.phls.co.uk/advice/cdrr1395.pdf>

Chapter 2: Management prior to referral to hospital

Key points

- **Meningococcal septicaemia has considerably greater mortality than meningococcal meningitis and is often characterised by a rapidly evolving petechial or purpuric rash that does not blanch under pressure. The rash in its early stages may consist of a few haemorrhagic spots located in a place such as the groin or feet (see Section 2.2).**
- **Meningococcal disease may have clinical features not normally expected in children with acute systemic illnesses (see Section 2.2).**
- **Practitioners should ensure that a patient with a systemic febrile illness, particularly a child, can be promptly reassessed should the need arise (see Section 2.2).**
- **All general practitioners should have benzylpenicillin in their surgeries and emergency bags, and should be ready to administer it immediately to patients with a systemic febrile illness and a petechial or purpuric rash (see Section 2.3). The doses are: children aged < 1 year – 300 mg; children aged 1-9 years – 600 mg; adults or children aged 10 years or over – 1200 mg.**
- **The early administration of benzylpenicillin, followed by urgent transfer to hospital, can be life saving. Ceftriaxone is a suitable alternative if available.**
- **If clinical suspicion exists to warrant a referral for admission to hospital the patient should receive benzylpenicillin prior to transfer.**
- **A history of a rash following penicillin is not a contraindication for benzylpenicillin.**
- **The local public health unit should be notified immediately to enable an appropriate public health response.**

2.1 Introduction

Meningococcal disease usually presents as meningitis or septicaemia, or a combination of the two. Septicaemia, with or without meningitis, can be particularly severe and has considerably greater mortality than meningococcal meningitis^{1,2}. Meningococcal septicaemia (also known as meningococcaemia) can have a fulminant and rapidly fatal course^{1,2} which causes meningococcal disease to be so feared.

2.2 Clinical presentation of invasive meningococcal disease

The most characteristic feature of meningococcal septicaemia is a haemorrhagic (ie. petechial or purpuric) rash that does not blanch under pressure³. However, a rash is not always present, especially in the early stages. In the early stage of development the rash may blanch with pressure thus resembling a viral

exanthem⁴. The rash can appear rapidly on any part of the body including the palms and soles. The petechial rash has discrete 1 to 2 mm in diameter lesions that may proceed to form larger ecchymotic lesions⁴. A petechial or purpuric rash was reported in 16 (70%) of the 23 deaths from meningococcal disease that occurred in New Zealand in 1998⁵. As they commonly appear in clusters in areas where pressure occurs from elastic in underwear and stockings⁴, general practitioners and other primary care practitioners should ensure that an acutely unwell patient with a systemic febrile illness is completely undressed so that a thorough search for a haemorrhagic rash can be undertaken⁶ (see also Section 3.2.2).

Less commonly, the rash has a maculopapular appearance³, the discrete pink macules or papules blanching under pressure. They may progress to become haemorrhagic and non-blanching later or fade away⁴ (see also Section 3.2.2).

Meningococcal disease in children may have clinical features not normally expected in an acute systemic illness⁶. For example, these children may show an unwillingness to interact or make eye contact, an altered mental state, or pallor despite a high temperature⁶.

If a general practitioner decides that a patient with a non-specific febrile illness does not require referral to a hospital, the general practitioner should advise the carer to keep the patient under frequent and regular review. The carer should be told to call the general practitioner again urgently or go immediately to a hospital emergency department if the patient subsequently develops a rash or deteriorates in any way. Rarely, meningococcal disease may present as conjunctivitis. Primary meningococcal conjunctivitis may be associated with invasive disease and should be treated systemically¹⁶.

2.3 Early antibiotic treatment (see also Section 3.3)

It is imperative that antibiotic therapy be commenced early if deaths from meningococcal septicaemia are to be avoided. Immediate administration of benzylpenicillin to suspected cases of meningococcal septicaemia by general practitioners was associated with reduced mortality in three retrospective studies in England^{7,8,9}. When the studies were aggregated (487 patients), it was calculated that those not given parenteral penicillin before hospital admission were 2- times more likely to die than those given penicillin¹⁰. The greatest benefit of parenteral penicillin was seen in those who were most ill, ie. those with a haemorrhagic rash⁸.

For optimal benefit, benzylpenicillin should be given intravenously. However if general practitioners are unable to access the intravenous route, it is appropriate to administer benzylpenicillin by the intramuscular route.

Doses of benzylpenicillin for suspected cases of meningococcal disease:

Children aged < 1 year: 300 mg

Children aged 1– 9 years: 600 mg

Adults or children aged 10 years or over: 1200 mg

The recommendations for empirical therapy prior to hospitalisation with benzylpenicillin are based on UK recommendations¹¹ and are presented in this form for their simplicity in emergency situations. Recommendations in the *Therapeutic Guidelines: Antibiotic*¹², which are based on a dose per body weight, differ from those presented here and are also appropriate.

All general practitioners should have benzylpenicillin in their surgeries and emergency bags, and should be ready to administer it immediately to a patient with an acute systemic febrile illness and a petechial or purpuric rash.

Benzylpenicillin should be withheld *only* if an individual has a clear history of either an anaphylactic or an immediate hypersensitivity reaction (such as difficulty in breathing, angio-oedema, generalised urticarial rash) due to immunoglobulin E(IgE) mediated reactions after a previous dose of penicillin. Most people with a penicillin allergy do not have such a history

and they can safely be given benzylpenicillin¹¹. If there is a history of either an anaphylactic or an immediate hypersensitivity reaction, urgent advice should be sought from the relevant on-call clinician at the referral hospital concerning possible alternatives.

Some general practitioners may have access to ceftriaxone. Ceftriaxone (see Table 1, page 6) is an acceptable alternative to benzylpenicillin for the empirical treatment of suspected meningococcal disease prior to transfer to hospital.

General practitioners need not be concerned that empirical benzylpenicillin will obscure the diagnosis for hospital clinicians. Certainly benzylpenicillin administered before blood and CSF specimens are taken reduces the proportion of positive blood or CSF cultures, but does *not* reduce the likelihood of isolating meningococci from nasopharyngeal swabs^{8,12} or detecting meningococcal DNA using PCR tests.

For this reason and because in virtually all cases an isolate from the nasopharynx will be identical to the invasive organism¹³, hospital clinicians should routinely collect nasopharyngeal swabs from patients suspected of having meningococcal disease. It is particularly important that these swabs be collected if benzylpenicillin, or other antibiotics, have already been administered.

2.4 Transfer to hospital

General practitioners should arrange urgent transfer of the patient to the appropriate hospital and the ambulance service needs to be informed of the urgent and critical nature of the transfer. If the patient exhibits any signs of shock or impaired consciousness an ambulance officer experienced in managing the transfer of critically ill patients should be asked to accompany the patient.

It is strongly recommended that any patient with an acute systemic febrile illness be referred urgently to hospital if *any* of the following are present:

- a haemorrhagic rash;
- an impaired level of consciousness;
- signs of meningeal irritation;
- clinical features not normally expected in children with acute systemic febrile illnesses; or
- the patient is a close contact of someone who was recently diagnosed as having meningococcal disease even if the current patient received chemoprophylaxis.

General practitioners should inform the relevant clinician at the referral hospital of the patient's impending arrival. This is crucial if delays in the emergency department are to be minimised. The hospital clinician should be informed, through the notes accompanying the patient to hospital, that benzylpenicillin has already been given. In addition, the hospital clinician should enquire whether benzylpenicillin, or another antibiotic, has been given.

Practitioners in rural hospital or remote community settings should attempt to take blood cultures whenever possible prior to the administration of the first dose of antibiotic. The blood cultures, and any other clinical samples, should be sent with the patient at the time of transfer to the referral hospital. Blood cultures should not be refrigerated. Taking of cultures should not delay initiation of treatment or transfer to hospital.

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Chapter 3: Management on arrival at hospital

Key points

- **If a patient has clinical signs or symptoms suggestive of invasive meningococcal disease (meningitis or septicaemia) they should be given parenteral antibiotics immediately** (see Section 3.3).
- **Deferral of lumbar puncture may be appropriate** (see Section 3.5.1).
- **Therapy should not be delayed while awaiting results of diagnostic tests, such as a lumbar puncture or computed tomography (CT) scan.**
- **The local public health unit should be notified immediately so that a public health response can be determined.**
- **All patients with suspected meningococcal infection should have blood and a throat/nasopharyngeal swab collected as soon as possible for culture, and blood for neutrophil and platelet counts and serological studies. If petechiae are present or if frank bleeding is evident, formal coagulation studies should be undertaken.**
- **Penicillin treatment alone will not reliably eliminate nasopharyngeal carriage of meningococci and the patient will require treatment to clear organisms from the throat.**

3.1 Introduction

Effective management of meningococcal infection requires early intervention, effective antibiotic therapy and careful attention to associated manifestations such as shock and coagulopathy.

If appropriate antibiotic and supportive therapy is implemented, case fatality rates should be less than 10 per cent when meningitis predominates. If septicaemia predominates, case fatality rates can be higher. Fatality rates of over 50% (and close to 100% in infants) occurred in the era before the introduction of effective therapy^{1,2}.

3.2 Early Assessment

3.2.1 Prior assessment by a general practitioner

If a general practitioner sends a patient to the hospital with a suspicion of invasive meningococcal disease, the patient should be assessed urgently (refer section 3.2.2). If the general practitioner has made a presumptive diagnosis of invasive meningococcal disease then the patient should have received their first dose of benzylpenicillin prior to arrival at hospital. If they have not already received an injection of an antibiotic, then they should be given IV penicillin immediately on arrival at

hospital (preferably after a blood culture is collected if this can be done immediately).

In some cases the general practitioner will have telephoned the on-call hospital clinician for advice but antibiotics may not have been given before transfer of the patient to the hospital (eg. because of drug allergies). In these cases, it is essential that a hospital practitioner immediately assesses the patient and administers IV antibiotics.

3.2.2 Triage in the emergency department

A triage nurse in the emergency department usually assesses patients who present directly to a hospital. If the triage nurse assesses that the patient is a potential case of invasive meningococcal disease (ie. suspected septicaemia or meningitis) then they should be classified as high priority for assessment and review by the medical staff and seen urgently. These patients should always receive their first dose of antibiotics as soon as possible and no later than 30 minutes after arrival at the hospital when a presumptive diagnosis of invasive meningococcal disease has been made.

The most characteristic feature that permits presumptive early diagnosis of meningococcal disease is the appearance of a petechial rash. The rash, which occurs often, typically has progressively enlarging petechial spots that may coalesce into

large ecchymotic lesions. The appearance of a petechial rash in association with fever, vomiting and drowsiness is highly suggestive of meningococcal disease. Alternatively, irrespective of meningeal symptoms, patients presenting with fever and a petechial rash should be evaluated for evidence of actual or incipient shock and a presumptive diagnosis of meningococcaemia should be made. Other prognostic signs include metabolic acidosis, low WBC count, coagulopathy and hypotension.

A less distinctive maculopapular rash has also been associated with the early phase of meningococcal septicaemia. This pink, maculopapular rash has been variously described as rubella-like or as similar to early varicella. Although it may last for as long as two days, it commonly fades rapidly. These lesions may be tender, or may be associated with myalgic pain that may be severe, but in most patients the rash is only recognized as meningococcal following development of more characteristic findings³ (see Section 2.2).

Early recognition of meningococcal infection is most of all dependent on the clinical suspicion of the physician involved and is most difficult with sporadic cases where there has not been heightened community or medical awareness of the problem.

There will be many patients with non-specific symptoms and signs due to other causes but in whom invasive meningococcal disease is considered in the differential diagnosis. These patients need to be kept under frequent observation, especially if they have not received a parenteral dose of penicillin. If they develop while under observation any characteristic skin lesions (petechiae), or other features of invasive meningococcal disease, a presumptive diagnosis of meningococcal disease should be made and parenteral antibiotics should be administered to the patient immediately.

When meningococcal infection is suspected, particularly where actual or incipient shock is evident, immediate empirical therapy in the absence of a formal diagnosis is indicated (see Section 3.3.1). Treatment should commence immediately and not be withheld until *N. meningitidis* or another organism has been identified⁴⁻⁸; this is particularly important in patients with a haemorrhagic rash⁹. If bacterial meningitis is suspected therapy

should be used which covers not only infection with *N. meningitidis* but also other invasive meningeal pathogens such as *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib).

3.3 Introduction of therapy in hospital

There should be no delays in the initiation of treatment before or after hospital admission. In many cases where bacterial meningitis is suspected, the causative organism or susceptibility is not yet known. In this situation empirical therapy which covers the three most common pathogens should be used⁴. Appropriate regimes include ceftriaxone or cefotaxime and/or vancomycin.

For further information consult the *Therapeutic Guidelines: Antibiotic*¹⁰. Antibiotic regimes can be modified as microbiological information becomes available.

After a diagnosis of suspected invasive meningococcal disease has been made it is essential that the patient receive a dose of IV penicillin if antibiotics (parenteral penicillin or ceftriaxone) have not been administered prior to arrival. Invasive meningococcal disease is a medical emergency and therefore the first dose of antibiotic should always be received by the patient as soon as possible, and no later than 30 minutes after a presumptive diagnosis has been made.

The antibiotic of choice for the treatment of all types of invasive disease caused by *N. meningitidis* is benzylpenicillin. Treatment should begin with:

Benzylpenicillin

Child: 60mg/kg (up to 1.8g) IV 4 hourly for 7-10 days

Adult: 1.8g IV 4 hourly for 7 to 10 days

3.3.1 Other empirical antibiotics

If bacterial meningitis is suspected, but the organism is unknown, empirical therapy that covers the three most common pathogens should be instituted. Treatment should begin as shown in Table 1.

Table 1: Early empirical antibiotic treatment for three most common bacterial meningitis pathogens¹⁰

| | |
|--|--|
| Cefotaxime | Child: 50mg/kg (up to 2g) intravenously 6 hourly. Adult: 2g intravenously 6 hourly. |
| | <i>or</i> |
| Ceftriaxone | Child: 100 mg/kg (up to 4g) intravenously daily in one or two divided doses. Adult: 4g intravenously daily in one or two divided doses. |
| | <i>Plus either</i> |
| Benzylpenicillin | Child: 60mg/kg (up to 1.8g) intravenously 4 hourly. Adult: 1.8g intravenously 4 hourly. |
| | <i>or</i> |
| (Amoxy)ampicillin | Child: 50mg/kg (up to 2g) intravenously 4 hourly. Adult: 2g intravenously 4 hourly. |
| <p>If Gram positive cocci are seen on Gram stain, vancomycin should be added to this regime. The appropriate antibiotic regime and duration of therapy should be reviewed and if necessary modified when a diagnosis is confirmed.</p> | |

Table 2: Summary of early antibiotic therapy

| Antibiotic | Empirical therapy prior to hospitalisation or on admission | Early hospital treatment where <i>N. meningitidis</i> is the agent |
|-------------------------------------|---|--|
| Benzylpenicillin^a | <p>Child less than 1 year: 300mg IV or IM single dose</p> <p>Child aged 1-9 years: 600mg IV or IM single dose</p> <p>Adult or child ≥10 years: 1.2g IV or IM single dose</p> | <p>Child: 60mg/kg (up to 1.8g) IV 4 hourly for 7 to 10 days</p> <p>Adult: 1.8g IV 4 hourly for 7 to 10 days</p> |
| Ceftriaxone^b | 50 mg/kg (up to 2g) IV daily (all ages) | <p>Child: 100mg/kg (up to 4g) IV daily in 1 or 2 divided doses for 7 to 10 days</p> <p>Adult: 4g IV daily in 1 or 2 divided doses for 7 to 10 days</p> |
| Cefotaxime^b | | <p>Child: 50mg/kg (up to 2g) IV 6 hourly for 5 to 7 days</p> <p>Adult: 2g IV 6 hourly for 5 to 7 days</p> |

^a The recommendations for empirical therapy prior to hospitalisation with benzylpenicillin are based on UK recommendations and are presented in this form for their simplicity in emergency situations. Recommendations in the *Therapeutic Guidelines: Antibiotic*, which are based on a dose per body weight, differ from those presented here and are also appropriate. The recommendations for early hospital treatment are derived from the *Therapeutic Guidelines: Antibiotic*.

^b These recommendations are derived from the *Therapeutic Guidelines: Antibiotic*.

3.3.2 Local policy for bacterial meningitis

Depending on the prevalence of penicillin resistance (and cephalosporin resistance) individual hospitals may have different protocols for the empirical therapy of bacterial meningitis while culture and sensitivity results are awaited (eg. vancomycin to cover high level penicillin resistance in *Streptococcus pneumoniae*). However, it is essential that either penicillin or a cephalosporin is given to the patient. Both these agents will treat infections caused by the meningococcus. Other antibiotics used in empirical therapy for meningitis may not cover meningococcus (eg. vancomycin). Once the organism has been identified and susceptibility tests are available⁴, then either the penicillin or the cephalosporin should be ceased. A history of skin rash following the administration of penicillin is not a contraindication to the administration of ceftriaxone or cefotaxime at dosages described in Table 1 (page 6). A medical microbiologist, infectious diseases physician or paediatrician should be consulted on appropriate alternative antimicrobial therapy if a history of anaphylactoid reaction following penicillin is elicited.

Empirical therapy must be given parenterally, preferably intravenously. Intramuscular administration of antibiotics is not preferred in this setting as supervening shock and hypotension may lead to failure of absorption of the injected antibiotic from the injection site (see Table 2).

Collection of a blood sample for culture should be attempted prior to administration of antibiotics but should not delay treatment.

3.4 Supportive therapy

As well as antibiotics, other therapy should be used where medically appropriate and patients with meningococcaemic

shock, or with the meningoencephalitic presentation, may require high-level intensive care therapy. Particular attention should be paid to maintenance of blood pressure and tissue perfusion and management of cerebral oedema. Patients may require artificial ventilation and other forms of support for prolonged periods and the complications of the coagulopathy, or intravascular coagulation abnormalities, may be severe.

3.5 Diagnostic studies

Therapy should not be delayed while awaiting results of diagnostic tests such as a lumbar puncture or computed tomography (CT) scan.

All patients with suspected meningococcal infection should have blood and a throat/nasopharyngeal swab collected as soon as possible for culture and blood for neutrophil, platelet counts and serological studies. If petechiae are present, or if frank bleeding is evident, formal coagulation studies should be undertaken and additional investigations such as chest x-rays, electrolyte and acid-base balance studies should be undertaken where the clinical picture warrants. Serological studies should be considered as part of the routine diagnostic work up. Diagnostic studies are discussed in Chapter 4.

3.5.1 Role of lumbar puncture in diagnosis

Diagnostic lumbar puncture for the collection of CSF has been the traditional mainstay in the diagnosis of meningitis. Meningococcal meningitis and other CNS infections may be associated with increased intracranial pressure, cerebral oedema and swelling and possibly with focal swelling or mass lesions such as abscesses. Where evidence exists for increased intracranial pressure (eg. clouded or impaired consciousness, papilloedema, focal neurological signs or vomiting), lumbar

puncture should be deferred until therapy and supportive measures have been established and investigations, such as a CT scan, undertaken to define existing intracranial lesions. The patient's coagulation status should be considered prior to lumbar puncture owing to the potential risk of haemorrhage with concomitant coagulopathy. Deferral of lumbar puncture may be appropriate.

The administration of antibiotics should not be delayed unduly while awaiting the performance of the lumbar puncture. If the lumbar puncture cannot be performed and IV antibiotics given within 30 minutes of the arrival at a hospital of a patient with suspected meningitis or meningococcaemia, then IV antibiotics should be given before the CSF is collected.

3.6 Public health notification

The local public health unit should be notified as soon as practical (within 12 hours) so that contacts can be identified and an appropriate public health response determined. This will include seeking other possibly epidemiologically related cases and the provision of chemoprophylaxis where appropriate.

3.7 Therapy after *Neisseria meningitidis* is identified

After isolation of penicillin sensitive *N. meningitidis*, specific (narrow spectrum) therapy with benzylpenicillin can be continued as sole antibiotic to complete therapy. Ceftriaxone and cefotaxime are appropriate alternatives in patients allergic to penicillin. Primary meningococcal conjunctivitis may be associated with invasive disease and should be treated systemically¹².

3.8 Duration of therapy

Patients with proven or probable meningitis should receive at least five days of therapy following resolution of fever.

3.9 Eradication therapy

Penicillin will not reliably eliminate nasopharyngeal carriage of meningococci^{11,3}. Patients who are treated with benzylpenicillin alone, and do not receive at least one adequate parenteral dose of a third generation cephalosporin, or ciprofloxacin, will therefore require antibiotic treatment on or before discharge to clear any organisms from the throat (doses are given in Section 8.5). It is recommended that this treatment be given early as it will be effective within 24 hours. Patients should not return to any child care facility, school or institution until their treatment is completed.

3.10 Antibiotic susceptibility

Isolates from cases of invasive meningococcal disease have been examined for antibiotic susceptibility in reference

laboratories of the National Neisseria Network (NNN) since 1996 using standardised methods which allow comparison of results.

Meningococci isolated in Australia have remained sensitive to penicillins, but here and overseas a gradual chromosomally mediated decrease in susceptibility to the penicillins has been observed. This has not as yet reached a level where treatment with these agents has been reported to fail and it is not sufficient to compromise treatment with penicillin. This situation is continually monitored. Additionally, there are a few overseas reports of beta-lactamase production in meningococci. These are rare events and have not been detected in Australia. There are no reports of resistance in meningococci to third generation cephalosporins.

Rifampicin is the most widely used agent in Australia for prophylaxis. Sporadic cases of rifampicin resistance occur in Australia and resistance may develop quickly. Resistance is accelerated by poor compliance with the recommended multiple dose regimen. Rifampicin-resistant "clones" of meningococci have been reported overseas.

Ciprofloxacin is also used for prophylaxis. Quinolone-resistant meningococci have been reported in Australia.

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Chapter 4: Laboratory Diagnosis

Key points

- **Antibiotic therapy should not be delayed while initiating or awaiting results of diagnostic tests.**
- **Meningococcal septicaemia often occurs without meningitis. In these cases the cerebrospinal fluid (CSF) may be normal.**
- **Negative findings on initial microscopy and biochemical examination of CSF do not exclude meningococcal meningitis. Positive cultures may be obtained in the following days.**
- **Culture of *Neisseria meningitidis* from a normally sterile site confirms the diagnosis. However, with early use of antibiotics and the likelihood of a negative culture, non-culture methods for diagnosis become more important.**
- **PCR tests to detect meningococcal DNA can be performed on blood and CSF, and have high sensitivity and specificity, even when prior antibiotics have been given (see Section 4.4).**
- **Serology can confirm the diagnosis in a clinically compatible case with a single positive IgM antibody result or by seroconversion in acute and convalescent sera (see Section 4.5).**
- **Strain differentiation by phenotyping, molecular typing, and gene sequencing is performed in National Neisseria Network laboratories to identify possibly related cases and for longer-term population studies.**

4.1 Introduction

In situations where there is clinical suspicion of invasive meningococcal disease (IMD), antibiotic therapy must not be delayed while initiating or awaiting results of diagnostic tests.

All patients with suspected meningococcal infection should have blood and a throat/pharyngeal swab collected as soon as possible for culture, and blood for neutrophil, platelet counts and serological studies. The latter (anticoagulated blood) sample may be also used for polymerase chain reaction (PCR) testing for meningococcal DNA (see below). Serological studies should be considered as part of the routine diagnostic work up. It may be appropriate to take a sample of CSF.

Diagnosis is confirmed by the isolation of *N. meningitidis* from CSF, blood, other normally sterile sites or skin lesions, or by the demonstration of Gram negative intracellular diplococci in blood or CSF (refer to Table 3, page 9). Demonstration of meningococcal polysaccharide antigen in CSF may add confirmatory evidence in patients with clinically compatible diseases when

positive, and in the presence of other indicative laboratory parameters. However diagnosis and especially exclusion of invasive meningococcal disease by means of antigen tests *alone* is not reliable.

Table 3: Specimens used for the diagnosis of meningococcal infection

- Blood for culture, PCR, serology
- Throat/pharyngeal swab
- Aspirate from skin lesions, other sterile sites, for microscopy, culture, PCR
- CSF for microscopy, culture, PCR

(See also Table 4, page 11)

Early administration of antibiotics may prevent the confirmation of a clinical diagnosis by traditional culture methods. However, nucleic acid amplification assays such as PCR tests are now available in a number of centres in Australia for confirmation of invasive meningococcal disease. This examination requires the availability of uncentrifuged CSF or anticoagulated blood. For further details of specimen requirements, collection, handling and availability of testing which may vary between centres, contact the relevant laboratories (See Appendix 5 – National Neisseria Network Laboratories, page 45).

Additionally, serum antibody tests are available for the diagnosis of invasive meningococcal disease. These are based on the demonstration of a single high IgM titre, or a rising IgM and/or IgG antibody titres to outer membrane protein antigens. Acute phase serum (5-7 days after onset of symptoms) or paired acute and convalescent sera are required. Diagnosis is retrospective but of public health relevance.

Urinary antigen tests are of doubtful clinical use in invasive meningococcal disease because of low sensitivity and specificity, and should not be performed.

4.2 Microscopy

Microscopy, if positive for Gram negative intracellular diplococci from sites such as CSF or smears from skin lesions, provides a highly specific confirmatory test. The adequacy of specimen collection, stage of the disease, intercurrent use of antibiotics and experience of the microscopist affect the sensitivity and specificity.

4.2.1 Cerebrospinal fluid (CSF)

Classically the CSF from a case of meningococcal meningitis reveals a high neutrophil count, low glucose and high protein content. Gram negative diplococci, if observed within neutrophils, provide evidence of meningococcal meningitis.

There are numerous exceptions to this classical picture so that low or absent white cells do not exclude meningitis. In meningococcal disease with high white cell counts in CSF the number of organisms may be so low as to be undetectable. Initial CSF parameters may be normal in approximately 5% of cases where subsequent CSF specimens reveal characteristic changes of meningococcal meningitis.

Prior administration of antibiotics will remove or distort the appearance of the diplococci.

The sensitivity of the Gram stain in CSF is estimated to be of the order of 65%. This is affected by the stage of disease, number of organisms present (which may vary considerably between patients) and timing of lumbar puncture in relation to antibiotic administration.

4.2.2 Aspirates of skin lesions and joint fluid

In the presence of a clinically compatible illness, Gram stains of aspirates from sterile sites provide confirmation of invasive meningococcal disease (ie. they are highly specific) but are not sufficiently sensitive so that a negative result does not exclude invasive meningococcal disease.

Gram stains of skin lesion aspirates or biopsy specimens have a reported sensitivity of 30% to 70% but this varies with the form

of meningococcal disease and type of skin lesion, being highest in haemorrhagic lesions of meningococcal septicaemia¹.

Gram stains of skin biopsies may remain positive for long periods (about 48 hours) after antibiotic administration (thought to be due to poor penetration of antibiotics into poorly perfused lesions) but the sensitivity at this time is not known. False positive Gram stain results may occur but the frequency is undefined.

4.3 Culture

Culture of *N. meningitidis* from blood, CSF or other normally sterile sites provides unequivocal confirmation of invasive meningococcal disease. Additionally, cultures provide isolates for strain differentiation and susceptibility testing.

In cases where meningococcal disease is suspected clinically, it is imperative that antibiotics be given before transfer to hospital and not withheld pending collection of diagnostic specimens. This decreases the likelihood of a positive culture but not to the same extent from all sampling sites. Collection of diagnostic samples should nevertheless still proceed even after administration of antibiotics as these samples may not only still occasionally yield a positive culture, but also may be used for non-culture diagnosis such as PCR.

4.3.1 Blood culture

Blood for culture should be obtained whenever possible. Several variables affect the sensitivity of blood cultures in invasive meningococcal disease: the number of blood cultures collected; the volume of the sample; and the prior use of antibiotics.

The sensitivity of blood culture is reported to be only about 50% in untreated cases of invasive meningococcal disease, falling to about 5% or less if antibiotics have been used.

4.3.2 CSF culture

The sensitivity of CSF culture is about 95% in cases of untreated meningococcal meningitis. This percentage falls rapidly after treatment as viable meningococci are quickly cleared from CSF.

It is again emphasized that a negative CSF culture does not exclude meningococcal septicaemia without meningitis.

4.3.3 Skin rash aspirate or biopsy

Culture of skin aspirates/biopsies is similar in sensitivity to Gram stain of the same lesion. Combined Gram stain/culture of skin lesions has a sensitivity of about 60%-65%.

4.3.4 Throat swabs

These may yield meningococci in about 50% of cases of invasive meningococcal disease and are less affected by prior antibiotic therapy². A positive culture provides corroborative, but not definitive, evidence of invasive meningococcal disease because there is a reasonable correlation between a nasopharyngeal isolate and an invasive isolate in a patient with invasive meningococcal disease. In addition, results of the phenotype of a nasopharyngeal isolate from a patient with suspected invasive meningococcal disease but negative systemic cultures may be helpful to public health staff in identifying possibly related cases. Routine swabbing of close contacts is not recommended.

4.4 Non culture diagnostic tests – polymerase chain reaction (PCR)

More rapid treatment of suspected cases of meningococcal disease with effective antibiotics and reluctance to lumbar puncture mean that PCR tests are becoming more important in the laboratory diagnosis of invasive meningococcal disease. PCR tests may increase the laboratory diagnosis of cases of meningococcal disease by more than 30%³ and meningococcal DNA in CSF samples has been detected up to 72 hours after commencement of antibiotic treatment⁴. A number of PCR-based assays for specific DNA sequences of *N. meningitidis* have been developed and primarily applied to CSF and blood/plasma/serum specimens. The sensitivity of PCR in CSF was 89% with a specificity of 100% in one Australian study⁵. For blood samples, PCR testing on EDTA blood (buffy coat) specimens had a sensitivity of 81% and a specificity of 97% in a recent Australian evaluation (Rob Porritt, personal communication).

There are no definitive studies on the sensitivity and specificity of PCR assays from skin lesions.

PCR tests for serogroup determination should be performed both from a confirmatory and epidemiological point of view. PCR can detect and amplify genes specific for serogroups B, C, W135 and Y^{4,6}. Positive meningococcal DNA preparations should be stored (preferably at –70°C) for subsequent sequencing of outer membrane protein genes and multi locus sequence typing for epidemiological surveillance, if required.

4.5 Serodiagnosis

Serological testing, based on an enzyme immunoassay using outer membrane proteins as the antigen, was developed by the UK PHLS Meningococcal Reference Unit⁷. The test has a sensitivity in excess of 97% in adults and older children (4 years or older) and reactions compatible with a recent meningococcal infection are a positive IgM test in a single sample or seroconversion if paired sera are available. Test specificity has been calculated at 95% (John Tapsall, personal communication). IgM reaches diagnostic levels about 5–7 days after onset, although the precise onset of invasive meningococcal disease is often difficult to determine. At present in Australia the serogroup cannot be determined by serological testing and the test lacks sensitivity in very young children; only adult test parameters are currently available for the interpretation of results.

4.6 Polysaccharide antigen testing

In the presence of other indicative laboratory parameters the demonstration of meningococcal polysaccharide antigen in CSF may add confirmatory evidence when positive. However diagnosis or exclusion of invasive meningococcal disease by means of antigen tests *alone* is not reliable as the test has poor sensitivity and specificity. The test is no longer performed by many laboratories.

Newer test methodologies such as ultrasound-enhanced polysaccharide antigen detection on CSF samples are undergoing evaluation overseas but are not currently available in Australia. Refer to Table 4.

Table 4: Summary of tests available to diagnose meningococcal disease

| Test | Specimen | Utility |
|---------------------|--|--|
| Gram stain | CSF, skin lesion, joint fluid or other normally sterile site. | <ul style="list-style-type: none"> ● Rapid, readily available. ● Confirms diagnosis if positive from a sterile site in a clinically compatible case. ● Sensitivity in CSF: 65%. ● Sensitivity from skin lesions: 30%-70%. |
| Culture | a) CSF, blood, skin lesion, joint fluid or other normally sterile site b) Throat swab | <ul style="list-style-type: none"> ● Results in 24-48 hours. Positive result confirms diagnosis. ● Sensitivity in CSF 95% if no prior antibiotics. ● Sensitivity in blood 50% if no prior antibiotics, 5% if prior antibiotics ● Positive result supports diagnosis in a clinically compatible case. |
| PCR test | CSF, blood | <ul style="list-style-type: none"> ● Positive result confirms diagnosis in a clinically compatible case. Can determine serogroup without a positive culture. ● Sensitivity in CSF 89%, specificity up to 100%. ● Sensitivity in blood (buffy coat) 81%, specificity 97%. |
| Serology | Blood | <ul style="list-style-type: none"> ● Single positive IgM or rising convalescent titre confirms diagnosis in a clinically compatible case. ● Sensitivity in adults and older children >97%. |
| Antigen test | CSF | <ul style="list-style-type: none"> ● Unreliable in its present form by itself. ● Corroborates diagnosis if other laboratory parameters positive eg. positive Gram stain. |

4.7 Strain differentiation of *N. meningitidis*

Differentiation of meningococci from cases of invasive meningococcal disease is undertaken for public health reasons, eg. 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 confirm or exclude such a link, not establish one.

A variety of typing techniques is available and is employed for different purposes at different times. One of the most widely used involves characterisation of surface structures in the capsule and outer cell membrane. Capsular polysaccharide antigens can be used to differentiate meningococci into 13 serogroups, with A, B, and C accounting for the majority of invasive infections worldwide. Further strain differentiation within the serogroups can be made by identification of outer membrane or porin proteins (OMPs). There are five different classes of OMPs, some of which are sufficiently antigenically variable to make them useful for typing. All meningococci have either class 2 or 3 OMPs. Using monoclonal antibodies the class 2/3 OMPs can be characterised in a system called serotyping, while the class 1 OMP is similarly characterised by a subtyping system. The serogroup, serotype, and subtype describe the phenotype of an organism. A commonly encountered phenotype in Australia is C:2a:P1.5,2. The organism has the serogroup C capsular polysaccharide, the 2a class 2/3 OMP serotype, and the P1.5,2 class 1 OMP subtype.

Currently all isolates are typed by National Neisseria Network laboratories (see Appendix 5, page 45) by determining the serogroup as soon as practicable after receipt and then the serotype and serosubtype using standard monoclonal reagents.

Serotyping and serosubtyping are performed by batching of isolates and testing at regular intervals; less frequently in low incidence periods and more frequently in the winter/spring. These techniques can however be rapidly employed if an epidemiological link between cases is established or suspected and can quickly exclude the presence of clustering of cases. However, many serogroup B strains are non-typable and reagent stocks are finite.

Genotyping (molecular) procedures are now supplanting phenotyping (serological typing) methods. Those available include pulsed field gel electrophoresis (PFGE), *porA/porB* sequencing and multi-locus sequence typing (MLST).

These techniques are used for different purposes, eg. PFGE and *porA* sequencing are used for short term studies of strain

relatedness and MLST for longer term population studies of meningococci. PFGE methods are not uniform, there are significant variations in choice of cutting enzymes, pulse and ramp times, but PFGE patterns are usually considered of short-term use for differentiating suspected outbreaks under local conditions. The non-clonal nature of serogroup B meningococci, for example, means that comparisons of PFGE patterns are not suitable for distinguishing invasive meningococci separated temporally and/or geographically across Australia.

Similarly *porA/porB* typing is increasingly available and can also be applied for short term examination of possible outbreaks but is not suited to longitudinal genotyping studies. A global standard nomenclature for *porA* sequencing is being developed, meaning that greater comparability of strains can be achieved by this means.

MLST is currently a technique more appropriately used for studies of meningococcal populations as it examines more stable parts of the genome.

The application and development of these techniques in Australia is under constant review by the National Neisseria Network (NNN).

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Chapter 5: Discharge and post discharge planning

Key points

- In most cases, with early diagnosis and prompt treatment, outcomes of meningococcal disease are good.
- Complications of meningococcal disease require appropriate discharge planning and specialised follow-up arrangements.
- Counselling and support for the patient, family members and health professionals involved in the care of the patient should be considered.

5.1 Outcomes of meningococcal disease

In most cases, with early diagnosis and prompt treatment, outcomes of meningococcal disease are good. On discharge from hospital the patient's general practitioner should be sent a discharge summary containing details of the follow-up required and the prognosis. If the patient makes an uncomplicated recovery then they can be discharged to the care of the general practitioner. Symptoms such as fatigue and headache may persist for months after the acute illness. Patients may need reassurance that this is common and that the outlook is good¹.

Complications of meningococcal disease such as brain injury, hearing loss, seizures and amputation will require appropriate discharge planning and specialised follow-up arrangements. At least one outpatient review with neurological examination is mandatory if a patient had lateralised neurological signs or an impaired conscious level at any stage of the illness¹. Deafness is the single most common permanent deficit in survivors of meningococcal meningitis. It occurs in 4%-6% of survivors, in half of whom it is severe and bilateral². Deafness is more common in children than adults. All cases of meningitis require a formal hearing assessment.

Permanent motor deficits, retardation and hydrocephalus occur in less than 1% of survivors³. A significant proportion of survivors will have tissue damage that requires surgical treatment, such as skin grafts, or partial or full amputation of limbs. Where amputation has been required, assessment and follow-up physiotherapy and occupational therapy should be arranged.

The patient and/or members of the affected family are likely to seek explanation and support from health professionals for several months after the illness. Family members will require this especially if the patient died or has permanent disability. Appropriate counselling and support for the patient and family members should be arranged. Public health professionals should be aware of the distress that media attention can cause to patients and/or their families. The counselling needs of health professionals involved in the care of the patient should also be considered. There are a number of groups (see Appendix 6,

page 46) that can provide support for people who have complications of meningococcal disease in particular for those who have hearing loss, epilepsy or other brain injuries.

Driving can recommence after clinical recovery is complete if the patient had no seizures. The current recommendation is that driving is discontinued for at least three months from the date of the seizures if they occurred during the acute illness. If seizures occurred during or after convalescence the patient is subject to the Medical Standards for Epilepsy for Australian drivers⁴. Stricter criteria apply for drivers of commercial vehicles⁵.

5.2 Infection risk and cadavers

The most recent data indicate a mortality rate of 9.1% (see Section 7.4). While cadavers with meningococcal disease have traditionally been considered a possible infection risk⁶, in cases where the deceased has been treated with an effective antibiotic for at least 24 hours prior to death, any risk is likely to be very low. If the deceased has not been treated with an effective antibiotic prior to death, then it would be prudent to judge the case on its merits and, if appropriate, take a precautionary approach.

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Chapter 6: Surveillance

Key points

- **Clinicians and laboratories should notify all cases (see Section 6.4) of suspected meningococcal disease to the local public health unit without waiting for microbiological confirmation.**
- **Public health authorities should ensure that comprehensive information on all confirmed and probable cases is collected to enable prompt public health interventions, to allow the monitoring of epidemiological changes and to evaluate public health strategies.**
- **Data on invasive meningococcal disease should be reviewed on a regular basis at local, state and national levels to identify outbreaks of cases and epidemiological trends.**

6.1 Surveillance of meningococcal disease

Surveillance is based on notification of cases by clinicians and laboratories and has two broad objectives:

- to ensure prompt identification of cases so as to enable early intervention from a public health point of view in relation to contacts and the wider community; and
- to improve understanding of the epidemiology of meningococcal disease and provide an evidence base for control measures.

The objectives of surveillance, and therefore the level of detail in the information collected, are different at State, Territory and National levels. There are also differences in the speed of notification and sensitivity/specificity in the diagnostic criteria applied. The systems adopted will have to be able to accommodate these varying needs.

6.2 Objectives of surveillance

The objectives of disease surveillance are:

- To ensure prompt identification and appropriate management of cases;
- To ensure prompt identification of all relevant contacts to enable the institution of appropriate public health responses;
- To ensure the prompt identification of outbreaks of invasive meningococcal disease to enable the rapid institution of control measures;
- To enable the monitoring of changes in the epidemiology of the disease across the country in relation to serogroup, serotype and antibiotic susceptibility; and
- To monitor the effectiveness of current control measures and to provide an evidence base for further review of national guidelines.

Notification of cases of invasive meningococcal disease to the relevant State/Territory health authority is the trigger for the public health responses. The public health system requirements are for timeliness and sensitivity. All clinicians and laboratories should immediately notify cases of suspected meningococcal infection by telephone. This should not be delayed until microbiological confirmation is obtained.

6.3 Surveillance case definitions

For surveillance purposes cases should be classified as 'probable' or 'confirmed'. These are defined as follows:

Probable case

A probable case of invasive meningococcal disease is defined as a case with at least one of the following:

- haemorrhagic rash in a patient with clinically compatible disease^a;
- isolation of *N. meningitidis* from the throat in a patient with clinically compatible disease^a; or
- close contact with a confirmed case within the previous 60 days in a patient with clinically compatible disease^a.

Confirmed case

A confirmed case of invasive meningococcal disease is defined as laboratory confirmation by one or more of the following methods:

- Isolation of *N. meningitidis* from a normally sterile site;
- Positive test for meningococcal DNA in a specimen from a normally sterile site from a patient with clinically compatible disease^a;
- Detection of Gram negative intracellular diplococci in Gram stain of specimen from a normally sterile site in a patient with clinically compatible disease^a;

- High titre IgM and/or significant rise in IgM and/or IgG titres to outer membrane protein antigens of *N. meningitidis* in a patient with clinically compatible disease^a;
 - Positive polysaccharide antigen test in CSF with other laboratory parameters consistent with meningitis and in a patient with clinically compatible disease^a; or
 - Isolation of *N. meningitidis* from the conjunctiva in a patient with conjunctivitis^b.
- a. Clinically compatible disease refers to disease which in the opinion of the treating clinician is compatible with invasive disease.
 - b. Primary meningococcal conjunctivitis is not, strictly speaking, invasive but is included in surveillance because it is associated with invasive disease in the patient and with secondary invasive disease.

6.4 Notification of suspected cases

It should be noted that these case definitions are for use by health authorities in reporting cases to the National Notifiable Disease Surveillance System (NNDSS). The responsibility of the treating clinician (GP or hospital doctor) and laboratory is to notify all cases in which a diagnosis of meningococcal infection is being considered. This will enable discussion of the case with staff in the communicable diseases control unit in the State or Territory health authority. Decisions can be taken at this stage in relation to appropriate action concerning contacts of the case. Immediate notification by telephone will also enable discussion with clinicians about further measures to confirm the diagnosis.

6.5 Surveillance Data

For meaningful surveillance of meningococcal disease it is essential to have a data set which includes epidemiological, laboratory and clinical information. These data should be reviewed and analysed on a regular and frequent basis. Identification of outbreaks in time and place with the same risk factors or phenotypes is a particular cause for concern, as they may require the implementation of specific control measures.

The requirements for data are different at State, Territory and National levels. For example at the State or Territory level information may be collected on the numbers of contacts provided with prophylactic antibiotics and the type of antibiotic used, while this information may not be routinely required at the National level.

6.6 The National Notifiable Diseases Surveillance System (NNDSS)

The following data items are to be collected by State and Territory Health Departments on all probable and confirmed cases of invasive meningococcal disease and will be used for national surveillance:

- State/Territory
- Notification ID
- Disease code
- Organism name
- Serogroup
- Serotype and serosubtype
- Confirmation status (ie. confirmed or probable)
- Laboratory Diagnosis Method
- Resident postcode
- Resident location
- Clinical onset date

- Specimen date
- Notification date
- Report date
- Outbreak reference
- Date of Birth
- Age
- Gender
- Indigenous status
- Occupation
- Clinical outcome (died/survived)
- Travel (interstate or overseas) in the 60 days prior to onset
- Contact with another case in the 60 days prior to onset
- Attendance at an institution (childcare, preschool, school, university or other tertiary institution, military barracks, prison)
- Clinical features:
 - meningitis
 - septicaemia
 - other invasive illness

It should be noted that the majority of the data items given above are required in all notifiable infections while a few of these are specific to meningococcal infection.

6.7 Information for program management

Apart from the data items given above there will be other information on cases and contacts that may be required at the State or Territory level for program management purposes. It is not intended that this information will become part of NNDSS.

This additional information may include the following:

- Notifier details – name and address
- Patient details – name and address
- Case seen by GP immediately prior to hospital admission – yes, no, unknown (If yes, date and time seen by GP)
- Date and time hospitalised – name of hospital
- Blood culture taken before first dose of antibiotics (yes/no/not known)
- Antibiotics given prior to hospital admission – yes, no, unknown (if yes, date and time antibiotic given)
- Contacts
 - number of contacts identified (names, addresses, phone numbers)
 - number offered antibiotic prophylaxis
 - number accepted prophylactic antibiotics
 - number offered vaccine
 - number given surveillance letter only

6.8 Reports on meningococcal disease

When the proposed surveillance system is established Australia will have a database at a national level that will include both clinical and laboratory data on meningococcal disease. It will be extremely important to ensure that changes in the epidemiology of the condition are closely monitored through regular reports based on analysis of NNDSS data.

A comprehensive annual report will be produced. In addition, there may be a need to produce more frequent reports such as quarterly reports during the winter and spring when the incidence of meningococcal infection is highest.

Chapter 7: Epidemiology of meningococcal disease

Key points

- Meningococcal disease is an endemic infection with cyclical peaks of incidence in Australia.
- Meningococcal infections have a seasonal peak in winter-spring.
- The age groups 0-4 years and 15-25 years have the highest incidence.
- The availability of strain differentiation data nationally in the 1990s has greatly improved our understanding of the epidemiology and allowed comparison with other countries.
- Diverse serogroup B phenotypes have predominated in all States over the decade with no reports of outbreaks or hyperendemic disease.
- An increase of serogroup C disease occurred during the 1990s, particularly in New South Wales and, in 1999, in Victoria. Cases of serogroup C infection were more common in adolescents and young adults.
- The phenotype C:2a:P1.5 was associated with outbreaks of cases in urban New South Wales affecting adolescents and young adults disproportionately. The increase in Victoria in 1999-2000 is associated with a new phenotype C:2a:P1.4, 7.
- Non-culture diagnosis by PCR techniques and serology are making an important contribution to laboratory confirmation of the diagnosis of invasive meningococcal disease.

7.1 National surveillance of meningococcal disease

The National Notifiable Diseases Surveillance System (NNDSS) was established in its current form in 1991 under the direction of the Communicable Diseases Network Australia (CDNA). The NNDSS compiles annual reports on notifications of meningococcal disease made to State and Territory health authorities. There is also a national program of laboratory-based surveillance of meningococcal isolates from invasive disease, which began in 1994 as a component of the National Neisseria Network. This program is designed to supplement data from the NNDSS by adding information on strain type and subtype as well as antibiotic sensitivity data. Table 5 indicates the number of reports of meningococcal infection collated by the NNDSS from 1994-1999 and the number of invasive isolates received by laboratories of the National Neisseria Network during that time^{1,2,3,4,5}. Positive cultures have been received and typed from over 60% of notified cases since 1995.

While meningococcal disease may affect all age groups, there has been a bimodal age distribution during the 1990s, with the highest rates in the 0-4 year age group and a second peak in the 15-25 year age group. The male to female ratio has consistently shown a slight male preponderance.

Table 5: National Notifiable Diseases Surveillance System invasive isolates – 1994-1999

| | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 |
|----------------------------|------|------|------|------|------|------|
| Total NNDSS notifications | 382 | 391 | 425 | 499 | 455 | 571 |
| NNN Invasive notifications | 216 | 250 | 297 | 343 | 323 | 368 |

The overall notification rates per 100,000 population in the 1990s ranged from a minimum of 1.7 per 100,000 in 1992 to a maximum of 2.7 per 100,000 in 1997⁴. The highest State or Territory rate was 8.9 per 100,000 in the Northern Territory (in 1998). Rates in other States ranged from 1.0-3.1 per 100,000 population.

Figure 1:
Notification rate of invasive meningococcal disease, Australia 1991-1999

Data source:
National Notifiable Diseases Surveillance System

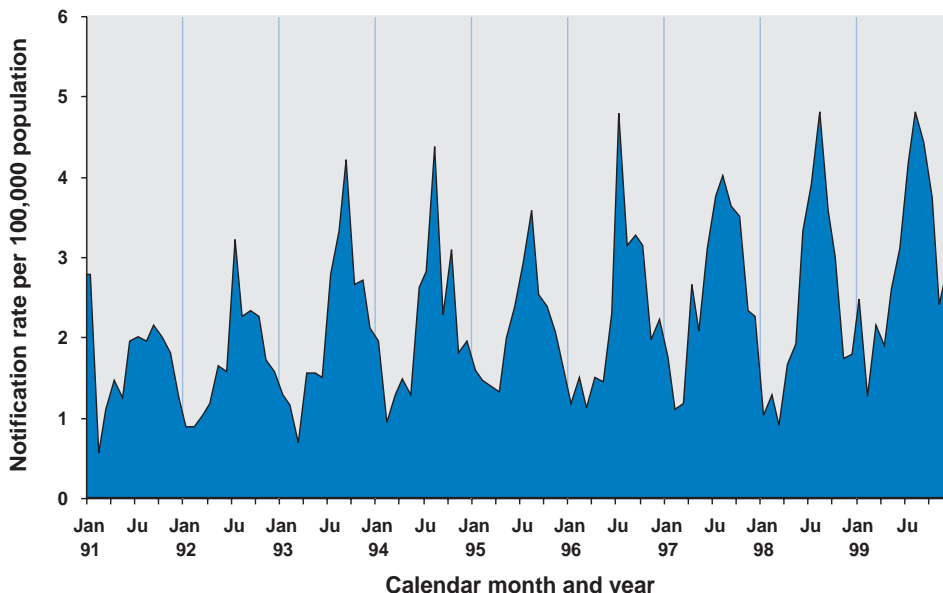


Figure 2:
Age-specific notification rates of invasive meningococcal disease, Australia 1991-1999

Data source:
National Notifiable Diseases Surveillance System

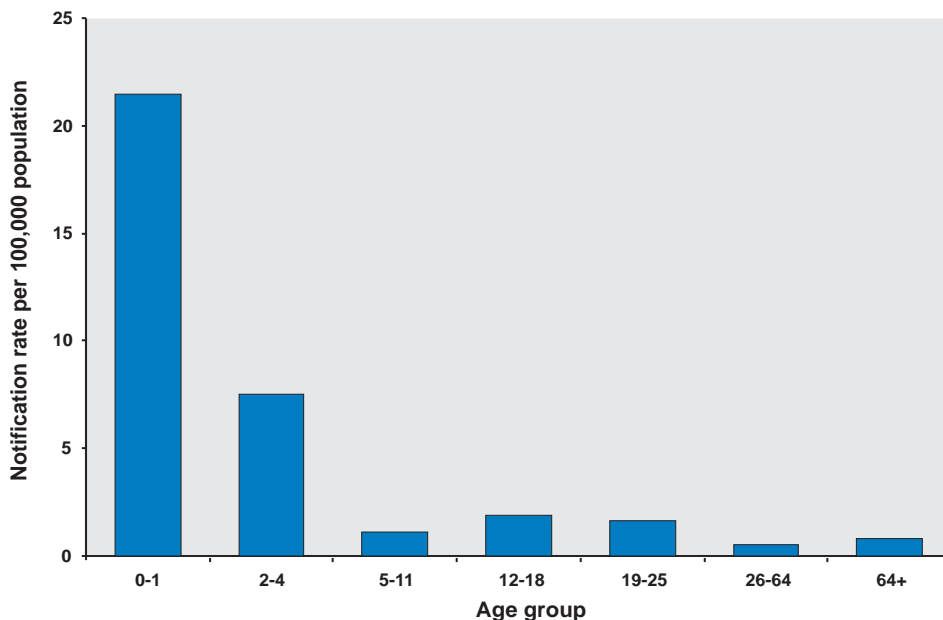


Table 6:
Neisseria meningitidis isolates, 1999, by serogroup (NNN)

*NG = non-groupable

| B | | C | | A | | Y | | W135 | | NG* | | TOTAL | |
|-----|----|-----|----|---|---|---|-----|------|-----|-----|-----|-------|-----|
| N | % | N | % | N | % | N | % | N | % | N | % | N | % |
| 232 | 63 | 120 | 33 | 0 | 0 | 9 | 2.5 | 6 | 1.5 | 2 | 0.5 | 369 | 100 |

Meningococcal disease characteristically has a seasonal pattern with a peak of incidence in the winter and spring months (see Figure 1). Although the reasons for this seasonality are not clear, there is evidence that influenza virus or *Mycoplasma pneumoniae* infections may predispose to invasive disease⁶ and closer personal contact or lack of ventilation may facilitate transmission of meningococci⁷. In adolescents and young adults, social gatherings in crowded conditions, smoking, sharing of drinks and other close personal contact may be risk factors for acquisition of meningococci⁸.

The three major serogroups of meningococci cause different patterns of disease. Table 6 (above) shows the serogroup distribution found in 1999. Serogroup A meningococci cause outbreaks of infection in areas such as the meningitis belt of

Africa where the incidence of meningococcal infection rises sharply towards the end of the dry season and declines rapidly with the onset of rains. The epidemics occur in 8-14 year cycles⁹. Similar epidemic patterns occurred in many countries during World War II, including Australia, as part of a serogroup A pandemic. In 1987 a large outbreak of serogroup A meningococcal disease occurred in Aboriginal central Australians¹⁰. Similarly, there was an outbreak of serogroup A disease in New Zealand in the late 1980s¹¹.

Since 1990 New Zealand has been experiencing an epidemic of serogroup B meningococcal disease. In 2000 there were 480 cases of meningococcal disease reported giving a rate of 13.3 per 100,000. Of these cases 348 (72.5%) were confirmed giving a confirmed rate of 9.6 per 100,000 population. Age-standardised

rates for Maori and Pacific Island people were three and six times higher respectively than for the European population. Meningococcal disease is more common in the upper North Island with a rate of 21.3 occurring in the Northern region. Meningococcal disease resulted in 17 deaths in 2000 giving a case fatality rate of 3.5%. In 2000 serogroup B meningococci accounted for 94.1% (241/256) of viable organisms from cases. As a proportion of serogroup B, isolates with the P1.4 subtype represented 90.4 (217/240) of cases.

In developed countries the pattern of meningococcal infection is one of sporadic cases with irregular peaks of incidence associated with small or large outbreaks of cases. Serogroup B meningococci are the major cause of sporadic disease or outbreaks with lower attack rates than seen with serogroup A infections. Serogroup C meningococci are usually associated with sporadic disease but can cause small or large outbreaks, with attack rates between those seen with serogroups A and B.

7.2 Trends in Australia

An understanding of the epidemiology of meningococcal disease in Australia has been greatly facilitated in the 1990s by the development of the NNDSS and the availability of standardised national data on serogroup, serotype, serosubtype and antibiotic susceptibility patterns of invasive meningococcal isolates through the National Neisseria Network of laboratories. Prior to this, there was little information about strains of meningococci causing invasive disease.

Meningococcal disease has been an infection with cyclical peaks of incidence. Notification of "meningitis" reached a peak of 33.1 cases per 100,000 in 1942 (2,371 cases) as part of a pandemic of serogroup A disease during World War II¹². Apart from another peak of activity in the early 1950s, there was a steady decline of notifications to < 0.5 cases per 100,000 in 1987, when, in addition to the outbreak of serogroup A meningococcal disease amongst the Aboriginal populations of central Australia, there was a rise in the number of notifications of both serogroups B and C isolates¹³. In the early 1990s outbreaks caused by serogroup C were reported in urban areas of NSW and in Aboriginal communities in Queensland and the Northern Territory. These serogroup C isolates had the phenotype C:2b:P1.2 and showed close genetic relatedness on DNA fingerprinting¹⁴. The phenotype C:2b:P1.2 was also a common cause of sporadic disease in 1990-1994 in NSW¹⁵. Serogroup C isolates also accounted for 70% of cases of invasive meningococcal disease in north Queensland between 1990-1994 during which time five outbreaks were identified¹⁶.

7.3 Meningococcal strain differentiation data post 1994

From 1994 strain differentiation data for invasive meningococcal isolates were available nationally¹⁷. In 1994 serogroup C strains predominated in NSW, but serogroup B meningococci were more common in all other States. In 1995 serogroup B strains predominated in all States¹⁸. In 1996, the largest community outbreak of meningococcal disease reported in urban Australia to date occurred in western Sydney, with an initial association with attendance at a nightclub⁸. The phenotype involved was C:2a:P1.5. Although strains of this phenotype had caused sporadic disease in NSW in the 1990s, there were no outbreaks identified until 1996. In Canada and Europe in the 1990s this

phenotype had caused multiple outbreaks of infection with high attack and case fatality rates in young adults^{19,20}, followed by hyperendemic disease for several years thereafter¹⁹. Rates of meningococcal disease in north western Sydney following the outbreak in 1996-1998 were up to 11.2 per 100,000 representing the largest, sustained, hyperendemicity recorded in urban Australia since the 1950s (J Brown, personal communication). The majority of isolates involved were phenotype C:2a:P1.5. The Australian C:2a:P1.5 isolates are closely related genetically to strains from Canada and Europe, belonging to the ET15 clone of the ET37 complex²¹.

Phenotype data were available nationally for the first time in 1996²². Serogroup B strains predominated in all States and Territories, although serogroup C strains accounted for 41% of isolates from NSW. The phenotype C:2a:P1.5 was most commonly isolated from NSW. In eastern States, the phenotype B:4:P1.4 was the commonest serogroup B strain. This phenotype caused an ongoing epidemic of serogroup B meningococcal disease in New Zealand in the 1990s, and has close genetic similarities to Australian strains²³, although in Australia the strains have only caused sporadic cases of meningococcal disease.

In 1997, while serogroup B again predominated in all States except NSW, there was a substantial change in NSW, both in terms of phenotype and age distribution of cases². Most serogroup C isolates now came from NSW and caused disease especially in adolescents and young adults. The phenotype C:2a:P1.5 had become the most frequently encountered phenotype and caused further outbreaks of cases of serogroup C in urban areas. Amongst serogroup B strains, which predominated in the less than 4 year age group, the phenotype B:4:P1.4 remained prominent.

In 1998, while serogroup B organisms predominated in all states and Territories, New South Wales continued to have a preponderance of the C:2a:P1.5 phenotype, especially in adolescents and young adults²⁴. No outbreaks were identified in 1998.

In 1999, the number of serogroup C organisms increased significantly in Victoria and remained prominent in New South Wales, although diverse serogroup B isolates predominated in all States and Territories again. A number of serogroup C infections with a phenotype new to Australia, C:2a:P1.4⁴ were noted in Victoria and, to a lesser extent, in New South Wales. Non-culture based diagnosis using nucleic acid amplification techniques and serology, made a significant contribution to laboratory-confirmed diagnosis, for the first time in 1999⁴.

7.4 Mortality from invasive meningococcal disease

Outcome data have been collected nationally by NNN laboratories since 1994 for patients from whom an invasive isolate was obtained. The data are most comprehensive for 1999, when outcome data were obtained for 320 (87%) patients⁴. The reported overall mortality was 9.1%. There was a significantly higher mortality in serogroup C infections (14.9%) than in serogroup B infections (6.4%). No fatalities were recorded for the few serogroup Y or W135 infections that occurred. Although serogroup C strains have been associated with an increased mortality overseas, other factors such as age, and time from onset to presentation and treatment, for which data are not available, may explain this difference.

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Chapter 8: Management of sporadic cases of meningococcal disease

Key points

- **Nasopharyngeal carriage of meningococci is common; about 10% of the population carry meningococci at any given time.**
- **There is a definite increased risk of further cases among the household contacts of a case of meningococcal disease. There *may* be an increased risk in child-care facilities, schools or universities attended by a case, among those who have shared saliva with a case and among those in very close contact with a case after the onset of symptoms.**
- **The public health response to meningococcal disease includes: providing contacts of a case with information about the disease; the provision of chemoprophylaxis to selected contacts with advice on the possibility, albeit small, of disease occurring; explaining that there are no particular quarantine or behaviour requirements of the contacts; and the maintenance of surveillance for further cases.**
(See Section 8.3 for definitions of ‘contacts’).
- **The public health response should only include those who were in contact with a case in the 7 days preceding onset of the illness, and those in *very* close contact after the onset of symptoms.**
- **The rationale for chemoprophylaxis is to eliminate meningococci from any carrier within the network of contacts close to each index case thereby reducing the risk to other susceptible individuals in the network.**
- **There are three antibiotics currently used for chemoprophylaxis of meningococcal disease; each agent has advantages and disadvantages and each is the preferred agent in specific circumstances. Ciprofloxacin is the preferred chemoprophylactic agent for women taking an oral contraceptive as rifampicin can affect the efficacy of oral contraceptives. Ceftriaxone is the preferred chemoprophylactic agent for pregnant women, and in rural and remote Indigenous communities. Rifampicin is the antibiotic of choice for chemoprophylaxis for young children.**
- **Throat swabs have no role in the public health management of contacts of invasive meningococcal disease.**
- **A single case of serogroup A in an Indigenous patient demands further attention; it may be the sentinel event of a community outbreak.**

8.1 Transmission and carriage of meningococci

Respiratory droplets shed from the upper respiratory tract transmit meningococci from one person to another. Humans are the only natural hosts for meningococci and the organism dies quickly outside the human host. It is not able to be isolated from environmental surfaces or samples.

Nasopharyngeal carriage of meningococci is common; about 10% of the population carry meningococci at any given time¹, not all of which are virulent strains. In North American and European populations the average duration of meningococcal carriage is about nine months; it is an immunising process with protective antibodies developing soon after acquisition. Factors associated with an increased risk of carriage include smoking and living in crowded conditions.

8.2 Rationale for chemoprophylaxis

Contrary to popular belief, a patient with meningococcal disease is not an efficient transmitter of the meningococcus that is causing their illness. Even in the pre-antibiotic era, hospital-acquired meningococcal disease in medical and nursing staff was very rare². Instead it is the carrier, who transmitted the organism to the patient in the first instance, who is much more likely to transmit the meningococcus again and cause further cases³.

The rationale for chemoprophylaxis is to eliminate meningococci from any carrier within the network of contacts close to each index case thereby reducing the risk to other susceptible individuals in the network.

8.3 Defining close contacts for chemoprophylaxis

Throat swabs are of no value in determining who, among a case's close contacts, is the carrier of the implicated meningococcus. A single negative throat swab is unreliable for predicting the absence of meningococcal carriage¹.

Pragmatic decisions, based upon the known risks of further cases, have to be made in defining the network of contacts (of a case) that is likely to include the meningococcal carrier. The risk of further cases of meningococcal disease may be increased in certain discrete settings where close and prolonged contact with a carrier can occur.

8.3.1 Settings with a definite increased risk of secondary cases

8.3.1.1 Households of a case

Studies carried out in Europe and America before the routine use of chemoprophylaxis showed that people who lived in the same household as a case with meningococcal disease were at a 500- to 1200-fold greater risk of meningococcal disease than the general population^{4,5}. The risk was highest in the first week after a case and fell rapidly thereafter⁴.

A recent retrospective survey in England and Wales, has confirmed the markedly increased risk in household contacts, even in the 'chemoprophylaxis era'⁶. The absolute risk of further cases in the month following the index case was 210/100,000 household contacts. The survey also documented that the risk of further cases in household contacts is much greater in the first week than in subsequent weeks, but the increased risk remains for many weeks, even after the administration of chemoprophylaxis. Another important point: approximately half of the further cases were co-primary, occurring within 24 hours of the diagnosis of the index case⁶.

8.3.2 Settings where there *may* be an increased risk of secondary cases

8.3.2.1 Child-care facilities attended by a case

Only two studies, one from Belgium published in 1981², and the other from Russia published in 1975⁶, have prospectively examined the risk of secondary cases occurring in day-care contact children. In the former study, the subsequent disease risk for children under three years of age was similar to that for household contacts (of a similar age) of an index case, and in the latter study a substantial subsequent disease risk was also documented.

However, because of the small number of further cases in the Belgian study (four cases in two day-care centres²) authorities in England believe that the study provides, at best, 'weak evidence'³ that there is an increased risk of further cases in such settings.

A retrospective survey in England and Wales did not demonstrate any increased risk of further cases among contacts in nurseries (which cater for, on average, 41 children aged 2-3 years), even in the first week after the index case⁶. A previous survey from the pre-chemoprophylaxis era^{5,7} was also unable to demonstrate an increased risk among nursery contacts.

8.3.2.2 Schools attended by a case

A study from Brazil, published in 1976, showed no increased risk of further cases among classroom contacts of cases during an epidemic of meningococcal disease⁷.

However, recent surveys in both the United States⁸ and England and Wales⁶ have demonstrated a modestly increased risk of further cases in schools attended by index cases, particularly secondary schools. Subsequent cases are not necessarily in the same classroom as the index cases with others occurring, for example, in contacts sharing extracurricular activities (such as sporting events) with index cases⁸.

In the United States the relative risk of further cases among school students was about twice that of sporadic disease among children 5-18 years of age⁸, whereas in England and Wales the absolute risk of secondary school students subsequently developing meningococcal disease was about 20 times less than that in household contacts⁶. The authors of the former study concluded 'mass chemoprophylaxis following a *single* case of meningococcal disease in a school would therefore be an extremely inefficient way to reduce the burden of meningococcal disease among children'⁸.

8.3.2.3 Universities (or other tertiary education facilities) attended by a case

Although the incidence of meningococcal disease in college students in the United States does not seem to be greater than that in the general population of the same age⁹, this is not the situation in the United Kingdom where the incidence is certainly greater in university students¹⁰. In the latter study, disease rates were shown to be highest in students, often in their first year, living on campus¹⁰.

Regardless of the increased incidence of sporadic cases, the absolute risk of a university or college student in England and Wales becoming a case in the month after the diagnosis of an index case in the same university or college is very low⁶.

8.3.2.4 Among those who have shared saliva with a case

Saliva contains other bacteria that are able to inhibit the growth of meningococci, and consequently meningococci are not easily isolated from saliva¹. Although there is an anecdotal report of transmission of meningococci from saliva¹¹, there are no estimates of the risk, if any, among those who have shared saliva with a case. 'Kissing' contacts are often included among household contacts^{3,12}, but it is unclear whether they are more likely to transmit meningococci to others via saliva rather than via droplets shed during household-like (ie. close and prolonged) contact.

Despite a lack of strong evidence that invasive meningococcal disease may result from sharing drink bottles, it is prudent to recommend against the practice.

8.3.2.5 Among those in very close contact with a case after the onset of symptoms but prior to the commencement of antibiotics (see Table 7, page 23)

Although, as stated above, a case is not an efficient transmitter, on rare occasion cases have been documented to transmit the implicated meningococcus to very close contacts after the onset of the illness¹³.

8.3.3 Risk of disease over time

Finally, a network of close contacts has to be defined in time as well as place. Because most patients with meningococcal disease acquired the invading meningococcus within the seven days preceding the onset of the illness³, the network need only include people who have been in close and prolonged contact with the case during that time.

8.3.4 Close contacts

The extent of the response is determined by the likely whereabouts of the putative meningococcal carrier who could have transmitted the meningococcus to the index case in the 7 days prior to the onset of the illness. The public health response should be implemented as soon as possible, targeting the following groups of people who are defined as 'close contacts':

- The household contacts of a case, including recent visitors who have stayed overnight in the 7 days preceding the onset of the case's illness. It is not unusual for up to 20 such contacts to be identified in an Indigenous family. Those who share the same dormitory, military barrack or hostel bunkroom as a case are, in effect, household contacts as are those passengers in seats adjacent to a case (eg. in an aeroplane or bus) during travel of 8 hours or longer duration. Persons sitting in the rows in front of and behind the case should be considered for chemoprophylaxis depending on the nature of their contact with the case. It should be quickly determined whether any of these contacts are acutely unwell with a febrile illness. If so, they could be co-primary cases and therefore require urgent medical assessment.
- The children and staff in the same room group at a child-care facility attended by the index case. Only those who were in the same room group for any one period of 4 hours or longer in the 7 days preceding the onset of the case's illness require chemoprophylaxis. Although there may have been some intermingling of all the children at the facility at the beginning and end of the day, this is usually of a short duration only and not enough to justify extending the chemoprophylaxis as this may be counter-productive (see Section 8.4).
- Those school or university (or other tertiary education facility) colleagues who have been, in effect, household contacts of a case. For example children who have undertaken a 'sleep over' at the house of the case, or dormitory contacts at a boarding school.
- Those who have shared saliva with the case, including those who have shared either bongs used for smoking marijuana, or cigarettes or drink-bottles. Only those

kissing contacts who kissed the index case on the mouth need to be included. Those who have kissed the case in a simple greeting on the cheek do not.

- Those who had very close contact with a case after the onset of symptoms but before the commencement of antibiotics. For practical purposes these very close contacts should *only* include any further household contacts and medical personnel who are directly exposed to a case's nasopharyngeal secretions (ie. the person who either intubated the case, but only if a facemask was not worn, or performed mouth-to-mouth resuscitation on the case). Except for those who have been directly exposed to a case's nasopharyngeal secretions, healthcare staff managing the patient do not require chemoprophylaxis².

8.4 The public health response

A public health response is required following the diagnosis of either a probable or confirmed case of invasive meningococcal disease or of meningococcal conjunctivitis. The latter is included because on occasion it may be associated with invasive disease¹⁴, or with invasive meningococcal disease in a contact¹⁵.

Meningococci coincidentally isolated from superficial sites (eg. from oropharyngeal, genital or anal swabs) are of no public health consequence, and therefore do not require any public health responses.

The public health response includes:

- Providing information to the network of contacts, or to the responsible guardians of young children 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.
- Providing chemoprophylaxis (ie. a specific antibiotic) in appropriate dosages to each person in the network. The rationale for chemoprophylaxis must be explained, and the possible adverse reactions and interactions with other medications (see below) need to be discussed. Ideally, chemoprophylaxis should be given as soon as possible (within 24 hours) after the diagnosis of the index case. Although either diagnosis or notification may occasionally be delayed, there is no purpose in administering chemoprophylaxis if more than 2 weeks have lapsed following the most recent contact with the index¹⁶.
- Emphasising that chemoprophylaxis does not exclude the possibility, although small, of a person developing meningococcal disease despite perfect compliance with chemoprophylaxis. Because the early recognition and treatment of someone with meningococcal disease can be life-saving, the symptoms and signs of the disease must be explained (see Appendices 2A, 2B & 2C on pages 35-37), and the need to seek urgent medical advice should they become unwell, needs to be stressed to each contact or their guardian.
- Explaining that there is no need for an asymptomatic person who is taking chemoprophylaxis to be 'quarantined' in any way (eg. a child can continue to attend day-care). Similarly there is no need to change practices or behaviours: family members (not taking chemoprophylaxis) can still nurse/handle a child (on chemoprophylaxis) in the normal manner, and couples (at least one of whom is taking chemoprophylaxis) need not

modify any aspect of their physical (kissing, sexual intercourse) relationship.

- Maintaining surveillance for any subsequent cases. A single case of serogroup A meningococcal disease in an Indigenous patient demands further attention as it may be the sentinel event of a pending community outbreak.

The broader public health response to meningococcal disease includes: the provision of information about the disease; the provision of chemoprophylaxis to selected contacts with an emphasis on the possibility of disease occurring despite chemoprophylaxis; explaining that there are no particular quarantine or behaviour requirements of the contacts; and, the maintenance of surveillance for further cases.

It is important that public health personnel do not acquiesce to demands from concerned members of the public for the more liberal use of chemoprophylaxis. The further one goes outside the household or immediate network of contacts the lower the chance of finding the carrier of the virulent meningococcus, and the greater the potential for inadvertently doing harm³ because:

- all antibiotics have side effects, adverse reactions and drug interactions;
- the liberal use of antibiotics encourages the emergence of resistant bacteria; rifampicin resistance can emerge rapidly¹⁷ and rifampicin-resistant meningococci¹⁸ and other organisms can subsequently cause invasive disease; and
- the prevalence of carriage of *Neisseria lactamica*, a non-pathogenic but closely related bacterium, is very high among infants and young children¹. *N. lactamica* is able to

induce natural immunity to invasive meningococcal disease¹⁹ and therefore the unnecessary use of antibiotics, which can eliminate this important organism, is to be avoided.

Following even a single case of meningococcal disease there may be considerable demands from parents or others for public health authorities to administer chemoprophylaxis, and sometimes even meningococcal vaccine, in a liberal manner¹⁹. These demands are likely to be intense, and parents understandably agitated, if the case dies.

It is recommended that when a case of meningococcal disease occurs in a child who attends a day care centre, public health personnel make an on-site visit to meet with parents and staff. The messages that should be communicated to the parents of children who have had brief and inconsequential contact with a case, and are therefore outside the case's immediate network of contacts, are¹⁹

- secondary cases of meningococcal disease are rare in Australia;
- chemoprophylaxis is not guaranteed to either prevent colonisation or abort incubating disease in your child;
- your child is unlikely to have been the carrier who was the source of infection in the index case or to subsequently have become a carrier;
- chemoprophylaxis is given to prevent those children who may be carriers from passing the infection on to other children; and
- therefore chemoprophylaxis is not recommended for your child.

Table 7: Public health responses in defined settings in which a case of invasive meningococcal disease has occurred

| Settings | Information ^a and chemoprophylaxis ^b | Information ^a only |
|---|---|--|
| Household ^c of a case | All | N/A |
| Child-care facilities | Children and staff in the same room for 4 or more hours at one time in the 7 days prior to the onset of the case's illness | All other children and staff at the facility |
| Education facilities | Very close contacts (essentially those who have been 'household-like' contacts) | All other students in the same classroom (schools) or tutorial groups (universities) |
| Those who have shared saliva with case (via mouth kissing, drink-bottles, bongs, etc) | All | Even though they may not have shared saliva with a case, other members of any sporting team which include a case should be given information |
| Those exposed to a case after the onset of symptoms | Very close household-like contacts; health carers who have either intubated the case without a face mask or done mouth-to-mouth resuscitation | All others concerned that they may have had contact with the case after the onset of symptoms |

^a The disease, including the common signs and symptoms, must be described and the mode of transmission explained (see Appendices 2A, 2B and 2C, pages 35-37) and appropriate action if symptoms suggestive of meningococcal infection occur should be detailed.

^b 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, require chemoprophylaxis. The possible adverse reactions and drug interactions should be described. It must be emphasised that meningococcal disease can occur (rarely) despite chemoprophylaxis. It should be explained that those taking chemoprophylaxis need neither to be quarantined nor to adopt any specific behaviours.

^c 'Households' include those in the same dormitory, military barracks or hostel bunkroom in the seven days prior to the onset of the case's symptoms. It also includes those in adjacent seats to the case during long distance (≥ 8 hours duration) travel. Sexual contacts should be managed as household contacts.

As an extra precaution these parents and staff should nevertheless be informed about the symptoms and signs of the disease.

The tetravalent (A,C,W135,Y) polysaccharide meningococcal vaccine has no role in the management of sporadic cases of meningococcal disease. This is because²⁰:

- it does not cover serogroup B which is the predominant serogroup causing sporadic disease in Australia;
- as with all polysaccharide vaccines, it does not induce an optimal immune response in young children (<2 years of age) who comprise the highest risk age-group for meningococcal disease. Serogroup C in particular is poorly immunogenic in young children;
- it takes at least 2 weeks to induce an optimal immune response even in those older than 2 years of age; and
- it does not induce long-term immunity.

When a sporadic case of invasive meningococcal disease occurs in a school student, public health personnel should liaise with the school principal to explain the circumstances. The parents of the student's classroom colleagues must be informed of the symptoms and signs of the disease. The principal may request information to either send to other parents or to include in the school newsletter.

When a sporadic case occurs in a university student, public health personnel should liaise with the university's health service. The service should be provided with the appropriate fact sheets to distribute to relevant contacts. Similarly, those who are in the same sporting team as a case, but who have not shared saliva with the case, should also be given information about meningococcal disease. Team officials should be asked to distribute the information.

8.5 Chemoprophylaxis

There is a lack of evidence concerning the efficacy of chemoprophylaxis in preventing further cases of meningococcal disease. The only published study²¹ to support the use of chemoprophylaxis as a control measure was an unblinded, observational study that demonstrated a lower secondary attack rate among household contacts of meningococcal disease who were given rifampicin, minocycline or sulpha prophylaxis, when compared with households where prophylaxis was not given. The difference in attack rates between the two groups failed (just) to reach statistical significance. There are no published studies assessing the efficacy of chemoprophylaxis in preventing secondary cases among non-household contacts. It would be virtually impossible to conduct such studies now, given the very low secondary attack rates in non-household settings and the ethical objections that would be raised by the need to withhold prophylaxis from a control group²².

Although evidence from randomised trials is lacking, there is evidence from cohort studies on the microbiological clearance of meningococci following the administration of chemoprophylaxis²². There are three antibiotics currently used for chemoprophylaxis of meningococcal disease; each agent had advantages and disadvantages, and each is the preferred agent in specific circumstances.

8.5.1 Ceftriaxone

A study has shown that not only was a single dose of intramuscular ceftriaxone very effective (97%) in eradicating

pharyngeal meningococci from carriers but also that it appeared to be more effective than rifampicin (75-81%)²³.

Ceftriaxone is very well tolerated²³ and there are no adverse reactions or drug interactions of particular importance. It should be dissolved in 1% lignocaine to reduce pain at the injection site. The recommended doses for chemoprophylaxis are 250 mg IM for adults and 125 mg IM for children younger than 12 years of age, as a single dose. Ceftriaxone should not be used for chemoprophylaxis in infants in the first 4 weeks of life.

Ceftriaxone is the preferred chemoprophylaxis for pregnant women. Because compliance is likely to be good and because it is readily available, it should also be considered as the preferred agent when chemoprophylaxis is required in rural and remote communities, especially in Indigenous communities. Although ceftriaxone is not registered for chemoprophylaxis of meningococcal disease in Australia, it is recommended by the Meningococcal Disease Guidelines Working Party for that purpose.

8.5.2 Ciprofloxacin (see also Appendix 2D, page 38)

A single oral dose of 500mg of ciprofloxacin was shown to be 97% effective in eradicating pharyngeal meningococci from 336 adult carriers²³.

Iron, sucralfate, highly buffered drugs (eg. antiretrovirals) and antacids containing magnesium, aluminium and calcium interfere with the absorption of ciprofloxacin. Interactions may occur with probenecid, anticoagulants, cyclosporin, glibenclamide, NSAIDs and theophylline. The stimulatory effects of caffeine may be increased. Ciprofloxacin is contraindicated in pregnancy and in prepubescent children. Allergic reactions, although very uncommon, have been reported in about one in one thousand people following single-dose ciprofloxacin²⁴. Therefore, if possible, recipients should be able to be observed for 30 minutes post-ingestion.

Ciprofloxacin is the preferred chemoprophylaxis for women on the contraceptive pill. Because it is easy to administer it should also be considered when a large number of adult contacts, some of whom are likely to be taking an oral contraceptive (eg. university students), require chemoprophylaxis.

Public health personnel administering ciprofloxacin to a large group should have, on site, an anaphylaxis management protocol, tuberculin syringes and adrenaline.

Although ciprofloxacin is not registered for chemoprophylaxis of meningococcal disease in Australia, it is recommended by the Meningococcal Disease Guidelines Working Party for that purpose. The recommended dose for chemoprophylaxis for adults and children aged 12 years or more is a single oral dose of 500mg. Ciprofloxacin is not recommended for use in children under 12 years of age.

8.5.3 Rifampicin (see also Appendix 2E, page 39)

A two day course of rifampicin given orally eradicates nasopharyngeal meningococci in 75%-95% of carriers^{25,26}. Side effects include headache, dizziness and gastrointestinal symptoms²⁸. It can cause orange colouration of urine, orange staining of contact lenses and, because it induces liver microsomal enzymes, it can reduce the efficacy of the oral contraceptive pill²⁶. Rifampicin can also reduce the efficacy of phenytoin, warfarin, corticosteroids, cyclosporin, dapsons, diltiazem, quinidine, sulfonylureas, theophylline, tricyclic

antidepressants, verapamil, beta-blockers, and methadone. It may interact with antiviral agents. Antacids reduce the bioavailability of rifampicin. Interactions with other drugs should be considered. Rifampicin is contraindicated in pregnancy, alcoholism and severe liver disease.

Women taking an oral contraceptive should continue to take it, omitting any pill free interval while taking rifampicin and for the seven days after the last dose of rifampicin. They should also use additional barrier contraception while taking rifampicin and for four weeks after the last dose of rifampicin. Rifampicin is the antibiotic of choice for young children (eg. in child day-care settings), but other alternatives should be considered for women taking an oral contraceptive.

The recommended schedule for rifampicin for chemoprophylaxis for meningococcal disease is 600 mg every 12 hours for 2 days for adults; 10 mg/kg/dose for children one month of age and over; and 5 mg/kg/dose for children aged less than one month (neonates). This is simplified in the following table that has been taken from the *Control of meningococcal disease: guidance for consultants in communicable disease control* developed by the PHLS³.

| Age | Dose | |
|---|---------------|--------------------------|
| 0-2 months | 1ml syrup* | } Twice daily for 2 days |
| 3-11 months | 2ml syrup* | |
| 1-5 years | 7.5ml syrup* | |
| 6-12 years | 300mg capsule | |
| > 12 years | 600mg capsule | |
| * Rifampicin syrup contains 100mg / 5ml | | |

Note: The Product Information recommends a once-daily four-day regimen of rifampicin for chemoprophylaxis of meningococcal disease. The two-day regimen above is recommended by the Meningococcal Disease Guidelines Working Party for chemoprophylaxis.

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Chapter 9: Management of outbreaks of meningococcal disease

Key Points

- An organisation based outbreak is the occurrence of two or more cases of meningococcal disease with an onset within a 4-week interval in a grouping that makes epidemiological sense, and where the available microbiological characterisation of the organisms is the same. Groupings can occur in schools, universities, classmates, yearmates, members of the same workgroup and community.
- A community based outbreak is the occurrence of three or more cases of confirmed meningococcal disease within a 3-month interval, which brings the rate of invasive disease in the community to 10 or more/100,000 total population in a 3 month period, in a geographical area that makes epidemiological sense and where available microbiological characterisation of the organisms is the same.
- The objective of public health management of outbreaks is to interrupt the transmission of disease and prevent further cases occurring. This can be achieved by establishing a response team, making a site visit if appropriate, undertaking intensified surveillance, providing adequate information and initiating appropriate responses via chemoprophylaxis or vaccination.
- In responding to organisation based outbreaks of cases, chemoprophylaxis should be considered for a wider group than solely close contacts.
- Those who receive chemoprophylaxis or vaccination should receive written information on meningococcal disease, the efficacy and adverse events associated with chemoprophylaxis and vaccination, and procedures (including after hours contact phone numbers) for answering questions or resolving problems. It is important to emphasise that further cases may occur even if chemoprophylaxis or vaccination has been given. Where outbreaks occur in institutions or organisations, written information on meningococcal disease should also be given to those who do not require chemoprophylaxis or vaccination. This is to inform them of the low level of risk, and to advise what actions to take should they develop symptoms suggestive of meningococcal infection.
- Meningococcal vaccination, in addition to the use of chemoprophylaxis, should be considered if an outbreak is due to a vaccine preventable strain. In Australia tetravalent polysaccharide vaccines against A, C, Y and W135 serogroups of *N. meningitidis* are available.

9.1 Introduction

Outbreaks of cases of meningococcal infection are some of the most challenging situations for public health authorities due to the intense public concern and media interest they generate^{1,2}, the potential for severe morbidity and mortality among cases

and the limited published evidence to guide best practice^{2,3,4,5}. Outbreaks may occur in the general community or in institutional settings such as schools and universities. The public health actions for each of these settings may vary and will depend on the identification (or otherwise) of epidemiological links between cases.

The term 'outbreak' is taken to mean the occurrence of more cases than expected for the population or group under consideration. Outbreaks of invasive meningococcal disease need to be distinguished from increases of sporadic and epidemiologically unlinked cases. Such increases may occur in the general community⁶ or within institutions such as schools and child care centres.

The objective of public health management of such outbreaks of invasive meningococcal disease 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 possible, a site visit;
- Ensuring the institution of chemoprophylaxis and/or immunisation as required for the setting, and the provision of information to all contacts and other persons involved;
- Establishment of heightened surveillance;
- Determination of the population at risk and calculation of age-specific and region-specific attack rates;
- Decisions on what action is to be taken;
- Provision of adequate information to health care providers, affected communities, the media and the general public; and
- Review of all actions taken and the preparation and dissemination of final documentation and a report.

Actions should be tailored to the setting. It is generally accepted that outbreaks of cases require more intensive and extensive management than sporadic cases, however the evidence base for many of the interventions that are commonly applied is lacking²⁻⁵ and decisions must be guided by extrapolation from situations where evidence exists.

9.2 Definitions

Sporadic case – A single case in the absence of previous known close contact* with another case.

Primary case – A case that occurs in the absence of previous known close contact* with another 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 cases with onset in a four week interval in a grouping which makes epidemiological sense; or two or more confirmed cases with onset in a four week interval where the available microbiological characterisation of the organisms is the same in a grouping which makes epidemiological sense.

Community outbreak – Three or more confirmed cases with onset in a 3 month interval, where the available microbiological characterisation of the organisms is the same, *and* incidence at least 10 per 100,000 total community population in a 3 month interval.

* See Section 8.3.4 for a definition of close contact.

9.3 Identification of outbreaks

Surveillance data on invasive meningococcal disease should be reviewed on a continuous basis to identify cases and to identify outbreaks of cases. The following changes in the epidemiology of meningococcal disease are suggestive of an outbreak⁷:

- 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 patients in an age group or a shift in the age distribution of cases;
- Phenotypic and genetic similarity among strains causing disease in the population. For serogroups B and C, the likelihood that two strains are related increases as one goes from serogroup in common to serotype and serosubtype in common, to nucleic acid and enzyme electrophoretic types in common. Investigation of subtype and serosubtype may help in the identification of outbreaks.

Serogroup A *N. meningitidis* was associated with large outbreaks of meningococcal disease in central Australian Indigenous communities during 1987-91. A single patient with group A meningococcal infection in an Aboriginal community should therefore alert health workers to the potential for a large outbreak⁸.

Suspected outbreaks should be reviewed in order to identify the microbiological features of the cases and any epidemiological links between cases. Microbiological investigation should focus on confirmation of the diagnosis (see Table 3, page 15) and rapid characterisation of organisms in as much detail as locally possible. Cases close in time and place, but infected with different serogroups (or serotypes or serosubtypes if known), should be managed as sporadic cases (see Chapter 8)³. The identification of possible epidemiological links³ should include a search for contacts in common, particularly in childcare, educational institutions⁹ or other groupings or organizations. Examples include attendance at nightclubs^{10,11} or parties.

9.4 Management of outbreaks

Following the identification of an outbreak of cases as defined above, the public health actions that follow include: the establishment of a response team; making a site visit if appropriate; intensified surveillance; communication with all involved parties.

9.4.1 Establishment of a response team

Setting up a small response team or planning committee is useful^{4,7}. Depending on the circumstances such a group might include a public health physician, a medical microbiologist, an infectious diseases clinician, a paediatrician, a public health nurse and a media liaison adviser.

A reporting system must be established to ensure that key individuals, including those from other organisations (eg. local government, educational and medical organisations), are kept informed.

The size of the response team and the frequency of meetings will vary according to the nature and extent of the outbreak.

9.4.2 Site visit

A site visit is useful:

- to gather first hand information on the outbreak;
- to assess the capability of local infrastructure and the availability of resources for implementation of strategies such as vaccination, should they be required;
- to meet local doctors and other health workers to give accurate advice;
- if necessary, to hold a public meeting to discuss community concerns; and
- to establish a list of health workers, school officials, environmental health officers, reporters and others who might play a part in local management of the outbreak.

9.4.3 Intensified surveillance

Surveillance should be intensified to identify further cases, and to collect relevant data on cases^{3,7,12}.

The following steps should be considered:

- active laboratory surveillance through daily contact with laboratories;
- active clinical surveillance through daily contact with hospital emergency departments, clinicians and admission offices;
- intensified passive surveillance through communication with laboratories, clinicians and hospitals to emphasize the need for immediate notification by a rapid reliable means (ie. telephone) on suspicion of the diagnosis;
- collection and rapid analysis of epidemiological data on patients as for sporadic cases (the case definitions for routine surveillance from Section 6.3 should be used; cases should be classified as 'probable' or 'confirmed' on the basis of diagnostic information to hand^{9,7,12});
- collection of information for contact tracing;
- collection of microbiological data on cases. Serogrouping and antibiotic sensitivity test results should be collected for all *N. meningitidis* isolates; microscopy and PCR results should be compiled for patients for whom an isolation was not made^{7,13,14}. Testing should include a full range of specimens – blood culture, throat swabs for culture and plasma for PCR;
- development of a feedback mechanism for the timely dissemination of information, initially to persons participating in surveillance and control, and later more widely; and
- maintenance of intensified surveillance until incidence rates have returned to pre-outbreak levels.

9.4.4 Communication

Communication with the public, health care professions and affected communities is of utmost importance⁴. A communication strategy should be considered at the initial meetings of the response team. Communication should be targeted to:

- individuals at risk, such as contacts or organisation members in organisation based outbreaks;
- health care professionals;
- the general community; and
- the media.

The communication requirements of these groups differ.

9.4.4.1 Individuals at risk

It is important to give information on meningococcal infection to people identified as being at risk.

9.4.4.2 Health care professionals

The health care community needs to be informed of the likely existence of an outbreak of cases, and that further cases could occur. Consideration should be given to direct communication with health professionals in the area. A letter to emergency departments and medical practitioners would emphasize the need for early diagnosis, empirical treatment and prompt notification of suspect cases. General practitioners should be aware of the treatment guidelines (for cases of invasive meningococcal disease) and have the appropriate drug available (see Section 2.3). General practitioners, emergency department clinicians and other primary health care providers diagnosing cases should be encouraged to collect blood cultures and throat swabs before administration of the first dose of antibiotics³. Specimens should be sent at the same time as the patient is sent to hospital. Treatment and evacuation should, however, never be delayed if specimen collection is problematic. Hospital clinicians should be encouraged to take throat swabs as well as blood cultures from persons suspected of having meningococcal disease as prior antibiotic therapy may render blood and CSF cultures sterile.

Several communication methods should be considered for disseminating information including websites, faxes, hotlines, mail or deliveries conducted by pathology companies.

9.4.4.3 The community at large

Consideration should be given to the establishment of information systems for the general community. In addition to communication through the mass media, websites, community meetings and help lines may be helpful¹⁵.

9.4.4.4 The media

Outbreaks of cases of meningococcal disease generate intense media interest and a professional approach to communication through the media is required¹⁶. It is usually better to have a single spokesperson who is experienced in dealing with the media, is authoritative, and is able to present the facts clearly. Where several institutions (hospitals, public health units etc) are involved, there should be agreement on the messages to be given. It is often helpful to hold press conferences when there is major media interest, both to reduce the time given to dealing with media enquiries (thus maximising the time available for the response team to do their work) and to ensure a consistent message is given to the media¹⁷.

9.5 Response related to specific settings

9.5.1 Organisation based outbreaks

In organisations such as schools and child care centres it is usually relatively easy to determine the population at risk as a natural grouping that makes epidemiological sense, and has meaning for the people concerned. Identification of populations at risk in other settings such as universities and workplaces is more difficult.

If cases are of different serogroups (or serotypes or serosubtypes where this information is available) they should be regarded as

Table 8: Recommended public health actions for organisation-based outbreaks

| Setting | Clustering ^a of cases | Public health action | | |
|--|---|--|--|--|
| | | Information | Chemoprophylaxis | Vaccination |
| Child care | 2 or more ^b probable cases ^c (or confirmed cases ^c of the same sero- group) in 4 weeks | All students and staff ^{3,12,18} | Children and staff of the same group(s) ^a as the cases. ^{3,9,12} | If confirmed cases ^c are of serogroups A, C, W, Y: all children and staff 2 years ^d and older. ^{3,7,18} |
| Pre-school, primary school, secondary school or university | 2 or more ^b probable cases ^c (or confirmed cases ^c of the same sero- group) in 4 weeks | All students and staff. ^{3,12,18} | Members of the same group(s) ^a as the cases | If confirmed cases ^c are of serogroups A, C, W, Y: members of the same group(s) ^a as the cases. |
| Other organizations (workplaces etc) | 2 or more ^b probable cases ^c (or confirmed cases ^c of the same sero- group) in 4 weeks | All members | Members of the same group(s) ^a as the cases | If confirmed cases of serogroups A, C, W, Y: Members of the same group(s) as the cases ¹² |

^a Groups should be defined according to the most specific groupings available (groupings within childcare centres, teammates, classmates, yearmates, members of the same workgroup etc). If cases occur in a single class in a school, chemoprophylaxis is indicated for classmates, *not* for yearmates.

^b Co-primary or secondary cases (as defined in Section 9.2) should not be included in this count since it is assumed that transmission will have occurred in the setting of close contact.

^c See definition, Section 6.3.

^d Vaccine efficacy is minimal in children under 18 months for serogroup C, and under 3 months for serogroup A^{3,12,14,28, 20} (See section 9.5.1.2).

sporadic cases and managed accordingly^{3,4,7} (see Chapter 8). The specific actions to be considered for organisation based outbreaks are chemoprophylaxis and vaccination.

9.5.1.1 Chemoprophylaxis

In responding to organisation based outbreaks of cases chemoprophylaxis is considered for a wider group than solely close contacts even though the evidence to support the use of chemoprophylaxis to prevent further cases is not strong^{2,3}. Close contacts should be provided chemoprophylaxis as for sporadic cases^{3,7,12} (refer to Chapter 8).

Unless microbiological evidence is to the contrary, co-primary or secondary cases (as defined in Section 9.2) are assumed to have acquired their disease in settings of close contact with primary cases. Other than in child care settings these cases should not be counted when deciding whether to offer organisation based chemoprophylaxis. For example, two probable cases in university students in the same class who share accommodation do not define a university based outbreak since the risk is assumed to be in the household like setting of the shared accommodation. Conversely, two probable cases in children attending the same child care centre define a centre based outbreak since the risk is assumed to be in the child care setting.

Conventional doses of antibiotics should be used for chemoprophylaxis (see Section 8.2). When mass chemoprophylaxis is given in institutions, it should be given whenever possible on the same day and only with written parental, caregiver or patient consent. Adequate information should be provided on the possible adverse effects of the agent selected with contact numbers of persons to ring in case such adverse events occur.

9.5.1.2 Vaccination for organisation based outbreaks

The use of meningococcal vaccine in addition to the use of chemoprophylaxis should be considered if the outbreak is due

to a vaccine preventable strain.^{3,12,14,19} Vaccination is not recommended for contacts of sporadic cases (see Section 8.5).

Tetravalent polysaccharide vaccines against serogroups groups A, C, Y and W135 of *N. meningitidis* are available in Australia. The vaccine induces antibodies in 10 to 14 days in 90 percent of recipients over the age of two years.

Meningococcal vaccines have limitations that include:

- poor immunogenicity of serogroup C polysaccharide vaccine in young children²⁰;
- short duration of antibody response to both serogroup A or C vaccines (typically up to three years, but less in children under two years of age)²⁰;
- significantly lower protective efficacy of immunisation for children immunised before the age of four years, compared with that for older children²⁰;
- failure of vaccines to reduce carriage rates²⁰ and;
- the lag time between vaccination and the time when adequate levels of protective antibodies are produced (10 to 14 days)^{14,19,20}.

Conjugate serogroup C vaccines are now in routine use in the UK after trials showed immunogenicity in young children²¹. These vaccines are not currently available in Australia. Vaccines against serogroup B disease are not currently available.

Children may be immunised against serogroup A using the tetravalent meningococcal vaccine from three months of age but, in those less than 18 months of age, a second dose of vaccine should be given three months later if there is continuing risk of disease. In children 18 months and older, a single dose of vaccine is sufficient^{14,20}. In practice, outbreaks of group A meningococcal disease are rare in Australia and, in recent times, have only occurred in remote Aboriginal communities.

For serogroup C, fewer data are available; efficacy has been shown for children older than 2 years and the vaccine may be

protective from 6 months of age¹⁴. The following should be noted in relation to vaccination of children with polysaccharide vaccine:

- vaccination against serogroup C is not advised for children less than six months of age because of the lack of response to vaccine in this age group; and
- if patients are only in the school aged population, persons aged between 5 and 19 years should be offered the vaccine. The need to vaccinate adults will depend on the age distribution of the patients in a given outbreak.

There are no data to evaluate the efficacy of vaccination against serogroups W or Y.¹⁴

The recommended procedure for obtaining consent prior to vaccination, as outlined in *The Australian Immunisation Handbook (7th edition Section 1.3)*, should be used. Prior to vaccination, the person being vaccinated or, in the case of a child, the child's parent or care giver should be given adequate information about the risks and benefits so as to be able to make an informed decision. It is preferable that printed information is available to supplement any oral explanations.

Vaccination of children in schools or similar venues should proceed only after written consent from the parent or guardian has been obtained. Such consent should be based on information adequate to enable the person to make an informed decision. If a child is old enough to adequately understand the benefits and risks of the proposed vaccination and refuses the vaccination in spite of such understanding, their wish should be respected. In such situations this should be discussed further with the parents.

In preparing for a vaccination program at a school or university the response team should ensure that, prior to the day selected for vaccination: the consent forms and information have been distributed and arrangements made for their collection; adequate supplies of vaccines ordered and arrangements made for cold chain maintenance; adequate consumables (syringes, needles, swabs, etc) ordered with arrangements for disposal; a suitable venue with sufficient space for staff, volunteers, groups awaiting vaccination etc; sufficient staff for the numbers expected; and, arrangements made for handling members of the media who may attend.

Immediately prior to vaccination the health professional should assess the health status of the person to ensure the appropriate vaccine can be given.

Whenever mass vaccination is implemented the target population must be carefully defined and a conscious effort made to adhere to that definition. If the defined target population includes children and adolescents schools can be used as a venue for efficient and rapid mass vaccination. The criteria for vaccination should be clearly defined and firmly stated, for example, "*all those born after 1 January 1980*".

9.5.2 Community outbreaks

These outbreaks are difficult to define and manage and have to be distinguished from a general increase in incidence caused by more than one serogroup. Table 9 (over page) lists public health actions for a community outbreak.

A community outbreak is defined as:

- the occurrence of three or more confirmed cases of invasive meningococcal disease due to a single serogroup (and serotype and serosubtype if

characterisation to this level is available) in a three month period; and

- there is an incidence of this type of at least 10 per 100,000 total community population in the same three month period.

At risk populations are usually defined geographically by using natural or political boundaries that most closely fit the residence data for the majority of the outbreak patients. School districts or town borders have been used to demarcate populations for preventive measures. However, physical or political boundary lines obviously 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.

Vaccination should be offered to selected age groups within the community population depending on the age-specific incidence. The affected age groups should be clearly defined. Vaccination should be offered if the incidence in the affected age group(s) is high²².

9.5.2.1 Chemoprophylaxis

Community wide chemoprophylaxis should not be used. The widespread use of chemoprophylaxis in community outbreaks has not been shown to be of value and may result in:

- the eradication of benign strains of *Neisseria* that provide protective antibodies;
- the generation of drug resistant strains; and
- an increase in the prevalence of drug-related adverse events¹⁹.

9.5.2.2 Vaccination for community outbreaks

The decision to vaccinate a large population for serogroup C disease is a difficult one for several reasons:

- there are usually a small number of patients with a relatively low attack rate in the population;
- the cases are often widely dispersed in time and space, and this makes it difficult to distinguish them from fluctuations expected of sporadic disease; and
- the cost of the vaccine and other resources required to vaccinate the group are considerable.

A community wide vaccination program should be considered if there are three or more confirmed cases.

The steps in preparing for mass vaccination are:⁷

- nominate a person to be responsible for coordinating the vaccination campaign;
- arrange adequate supplies of vaccine;
- arrange transport, cold chain and storage facilities for large quantities of vaccine;
- deploy adequately trained personnel to assist with the mass vaccination campaign;
- arrange venues for vaccination clinics;
- prepare a schedule for a phased campaign so that the clinics are not overwhelmed, including 'catch-up' clinics for those who missed out on the first round of vaccination;
- set up an adequate communication network (telephone, facsimile) linking the coordinating office, the supervisory public health office and the vaccination clinics;

Table 9: Recommended public health action for community outbreaks

| Setting | Clustering | Public health action | | |
|--------------------------------|---|--------------------------|--|--|
| | | Information | Chemoprophylaxis | Vaccination |
| General community ^a | 3 or more ^b confirmed cases ^c of serogroup A, C, W, or Y in 3 months <i>and</i> incidence ^c at least 10 per 100,000 total community population in 3 months | Mass media communication | Not indicated for the community (only for close contacts, as for sporadic cases) | Community members in specific age groups where age-specific incidence is high ^d . |

^a A general community should be defined using boundaries that make epidemiological sense, make sense to community members and are as unambiguous as possible.

^b Exclude secondary and co-primary cases (as defined in Section 9.2) in incidence calculations since it is assumed transmission will have occurred in settings of close contact.

^c See definition, Section 6.3.

^d Suggested age groups for calculation of age-specific rates are: 0-1 years, 2-4 years, 5-11 years, 12-18 years, 19-25 years and 26+ years (approximating babies, preschoolers, primary school, secondary school, tertiary student age groups, and other adults).

- establish a system to record relevant details of those receiving the vaccine (names, sex, address, date of birth, date of vaccination, vaccine batch number, address of vaccination clinic) so that vaccine uptake and perhaps ultimately vaccine efficacy can be determined;
- prepare the necessary information and consent material, translated into several languages if necessary; and
- plan for maintenance of routine immunisation programs and clinic services while the vaccination program is in progress.

Whenever mass vaccination is implemented, the target population must be carefully defined and a conscious effort made to adhere to that definition. For a community wide program, the criteria for vaccination should be clearly defined and firmly stated, for example, “*all those born after 1 January 1980 and at least 12 months of age by the date of meningococcal vaccination, and a resident, employee or school pupil within the Shire administrative boundary*”.

If public statements about eligibility for vaccination are unclear there is a risk that individuals at minimal risk will also demand vaccination and people may become confused, angry, or even aggressive. Persons whose children fall outside the announced criteria will often seek vaccination for their children, or for themselves. It is preferable that a single official, normally the coordinator of the vaccination program, be responsible for all decisions to grant or not to grant exemptions in such cases.

9.5.3 Indigenous communities

The risk of sustained transmission of invasive meningococcal disease in Indigenous communities, especially remote Aboriginal communities, is high. For this reason, a low threshold should be used to determine the necessity for control measures. Interventions targeted to all community members should be implemented if there are 2 or more cases in a remote Aboriginal community in a 4-week period.

Interventions aimed to prevent further cases should include:

- educational materials and information for all community members. Such information should be in a form which is appropriate to the community and should include contact

procedures (including after hours procedures) for people with queries;

- chemoprophylaxis for close contacts, as for sporadic cases;
- where cases are confirmed as serogroup A, C, Y or W135, vaccination is indicated for all community members in the age groups designated by the local public health unit; and
- monitoring resistance patterns in sustained outbreaks in Indigenous communities.

9.6 Documentation and review

It is important to adequately document outbreaks and the actions taken. A structured review should always be undertaken of each outbreak and its management with a view to improving performance. Documentation and reviews provide an evidence base for refining policy.

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Appendices

Appendix 1

Public health responses in defined settings in which a case of invasive meningococcal disease has occurred

| Setting | Information ^a and chemoprophylaxis ^b | Information ^a only |
|---|---|--|
| Household ^c of a case | All | N/A |
| Child care facilities | Children and staff in the same room for 4 hours at one time in the 7 days prior to the onset of the case's illness | All other children and staff at the facility |
| Education facilities | Very close contacts (essentially those who have been 'household like' contacts) | All other students in the same classroom (schools) or tutorial groups (universities) |
| Those who have shared saliva with case (via mouth kissing, drink-bottles, bongs, etc) | All | Even though they may not have shared saliva with a case, other members of any sporting team which include a case should be given information |
| Those exposed to a case after the onset of symptoms | Very close household like contacts; health carers who have either intubated the case without a face mask or done mouth-to-mouth resuscitation | All others concerned that they may have had contact with the case after the onset of symptoms |

- The disease, including the common signs and symptoms, must be described and the mode of transmission explained (see Appendices 2A, 2B and 2C, pages 35-36). Appropriate action if symptoms suggestive of meningococcal infection occur should be detailed.
- 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, require chemoprophylaxis. The possible adverse reactions and drug interactions should be described. It must be emphasised that meningococcal disease can occur (rarely) despite chemoprophylaxis. It should be explained that those taking chemoprophylaxis need neither to be quarantined nor to adopt any specific behaviours.
- 'Households' include those in the same dormitory, military barracks or hostel bunkroom in the seven days prior to the onset of the case's symptoms. It also includes those in adjacent seats to the case during long distance (≥ 8 hours duration) travel. Sexual contacts should be managed as household contacts.

Appendix 2

| Sample Documentation | Page |
|---|-------------|
| Meningococcal disease information | |
| 2A Information for the public | 35 |
| 2B Meningococcal symptom chart – older children and adult | 36 |
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Appendix 2a

MENINGOCOCCAL DISEASE:

Information for the public

(This information sheet can be adapted to different settings)

What is the 'meningococcus'?

The meningococcus is a bacterium that can be found at the back of the throat or in the nose in about 10% of the community at any given time. Although most people who 'carry' this germ in their throat or nose remain quite well, they are able to spread it to others, a few of whom may subsequently become very ill. It is spread in the fine droplets that are shed through coughing, sneezing and spluttering.

What is meningococcal disease?

Meningococcal disease is a severe infection that occurs when the meningococcal germ 'invades' the body from the throat or nose. It does not occur in people who carry the germ but rather occurs in people who have very recently (within the previous 7 days) acquired the germ from a healthy 'carrier'.

Meningococcal disease occurs in two main forms or it can occur as a combination of these two forms. Meningococcal septicaemia occurs when the germ invades the bloodstream and causes blood poisoning. Meningococcal meningitis occurs when the germ infects the outer lining around the brain and spinal cord.

Meningococcal septicaemia, also known as meningococcaemia, can be very serious and cause death after even a very short illness. The patient usually is obviously sick, has a fever and may have marked joint or muscle pains; and there is often a rash. The rash may start anywhere on the body as tiny red or purple spots but they soon spread and enlarge to look like fresh bruises; the rash does not fade when pressure is applied to it, eg. with the thumb.

The rash must be taken seriously as the person requires urgent medical attention.

The typical symptoms of meningococcal meningitis include fever, a stiff neck, severe headache, dislike of bright lights, vomiting, joint or muscle pains, drowsiness and even coma; there may also be a rash with the same features as those described above. The symptoms of meningococcal meningitis in young babies may differ from those detailed above and include: refusing feeds, vomiting, a high pitched moaning cry, irritability and a dislike of being handled, a blank staring expression, lethargy or drowsiness and a pale blotchy complexion.

How easy is it to catch meningococcal disease?

Although the germ is spread in droplets that are shed from the nose or throat it is not, fortunately, easy to catch the disease. This is because the meningococcal germ does not survive for long outside the body. Close and prolonged contact with a carrier is usually required for the germ to spread to other people.

Because the germ is not easily spread, meningococcal disease is uncommon. Young children under 5 years of age, and young

adults (15-24 years of age) are at highest risk of acquiring meningococcal disease, and there is usually a seasonal increase in the winter to early spring months.

Even though it is hard to catch and uncommon, meningococcal disease is a feared infection that is often featured in the media. This is because it can be fatal, even in healthy young adults, and because outbreaks of meningococcal disease, although very infrequent, can occur.

How can meningococcal disease be prevented?

Cigarette smoking, both active and passive, appears to increase the risk of a person developing meningococcal disease. This is yet another reason to stop smoking and to stop adults smoking near young children.

There is a small, but real, risk for those who live in the same house as a person with meningococcal disease to also develop the disease. This is because the carrier who infected the patient is able to spread the germ to others. There is no accurate and quick test to identify the carrier so all of the 'household contacts' of the patient are regarded as potential carriers.

Instead, public health authorities attempt to contact these household contacts to explain to them the nature of the disease and to dispense a short course of an antibiotic. The purpose of the antibiotic is to eliminate the germ from the nose or throat of the carrier. Cases of disease may occur despite taking the antibiotic so the contacts must also be told to be aware for the symptoms of the disease.

Sometimes other contacts are also identified by public health authorities and given the above-mentioned advice and antibiotic. However it is very important that the public health authorities are involved in the identification of other contacts because the antibiotic should be used very carefully.

Is there a vaccine against meningococcal disease?

Yes, but is not suitable for routine use in Australia. This is because it does not protect against the commonest strain of the meningococcal germ, known as the group B strain, which commonly occurs in Australia. Another problem with the current vaccine is that it does not protect children under two years of age who are more prone to develop the disease than older people. Research is in progress to develop vaccines that protect even young children against all the common strains of the meningococcal germ.

For further information contact your local public health authority:

Phone: () _____

Fax: () _____

e-mail: _____

Appendix 2B

How can you tell if someone has meningococcal disease?

Not all these symptoms may show at once



Fever



Headache



Drowsiness or confusion-coma



Neck stiffness, joint pains



Rash of red-purple spots or bruises



Dislike of bright lights



Vomiting

Appendix 2C

How can you tell if a baby has meningococcal disease?

Not all these symptoms may show at once



Fever



Fretfulness



Child is difficult to wake



Pale or blotchy skin



Rash of red-purple spots or bruises



High pitched moaning cry



Refusing feeds or vomiting

Appendix 2D

CIPROFLOXACIN: an antibiotic for contacts of a person with a meningococcal infection

Ciprofloxacin is an antibiotic that is sometimes given to those in close contact with a person who has developed a meningococcal infection. The purpose of this antibiotic is to get rid of any meningococcal germs being 'carried' in the throat of contacts so that they cannot lead to further infections. The antibiotic cannot treat someone who is already developing the infection: you need to know what signs (of meningococcal infections) to look out for regardless of taking ciprofloxacin.

The dose of ciprofloxacin is a **single dose** of 500mg taken in tablet form.

You should **not** take this medicine if:

- You have had a previous allergic reaction to ciprofloxacin.
- You are pregnant or breast-feeding.

Before taking this medicine, you should check with your doctor if you are taking any other medications. It is quite safe to take ciprofloxacin if you are taking the oral contraceptive pill. Ciprofloxacin is not recommended for use in children under 12 years of age.

It is important that you take your tablet as follows:

- The tablet should be swallowed whole with a full glass of water.
- Do not take the tablet if you have taken antacid/indigestion medicines or medicines containing iron or mineral supplements within the previous 4 hours.

You may also feel tired or develop a stomach ache but these effects usually settle quickly and are not cause for concern.

A **very** uncommon side effect is an allergic reaction with facial swelling. This might happen soon after taking the tablet; if it happens, you should seek medical attention **immediately** (see the doctor if you are at a hospital, or ring 000).

Appendix 2E

RIFAMPICIN: an antibiotic for contacts of a person with meningococcal disease

Rifampicin is an antibiotic drug that is sometimes given to those in close contact with a person who has developed a meningococcal infection. The purpose of this antibiotic is to get rid of any meningococcal germs being 'carried' in the throat of contacts so that they cannot lead to further infections. The antibiotic cannot treat someone who is already developing the infection: you need to know what signs (of meningococcal infections) to look out for regardless of taking rifampicin.

Rifampicin should **not** be taken by a person who

- has severe liver impairment (including yellow jaundice);
- is an alcoholic; or
- is pregnant

Rifampicin is taken twice a day for 2 days (a total of four doses). It should be taken on an empty stomach: half an hour before or two hours after food. A few people feel 'off' after taking rifampicin: stomach upset, headache and dizziness can occur.

Rifampicin can also make urine and tears a pink-orange colour. This discolouration is harmless and stops when the medication is discontinued. Rifampicin can permanently stain soft contact lenses so use during treatment should be avoided.

Interactions with other medicines

If you are taking any of the following prescription drugs: anticoagulants such as warfarin, steroids, several drugs for heart disease, tablets to control diabetes, tablets for epilepsy, tablets for asthma, methadone, antiviral agents, antidepressants and cyclosporin – **notify** your doctor that you will be taking rifampicin as the dosage of your other medication may need adjustment.

Rifampicin can reduce the effectiveness of oral contraceptives. Women taking the oral contraceptive pill should continue to take it, omitting any pill-free or sugar pill interval, while taking rifampicin **and** for the seven days after the last dose of rifampicin. They should **also** use additional barrier contraception, such as condoms, while taking rifampicin and for four weeks after the last dose of rifampicin.

Appendix 2F

Chemoprophylaxis letter to close contacts

NOTE FOR PHU – Please copy this text onto PHU letterhead, or otherwise provide contact details.

Dear

I believe you have recently been in close contact with a person who has meningococcal infection.

Meningococcal infection is caused by a bacterium that is carried, usually harmlessly, in the nose and throat by up to 10% of people. However, occasionally carriers may pass it on to others who have been in close contact with them. Only a very small number of people in contact with carriers develop meningococcal disease. Once exposed to the bacterium it may take up to ten days for the infection to develop.

As you have been in contact with a person who has this infection you may be a carrier of meningococcal bacteria. For this reason you should take a short course of antibiotics. This is intended to eliminate the bacteria you may be carrying and to prevent further infections. The antibiotic may not always prevent disease in a person who is already developing the infection. Whilst on the medication it is not necessary for you to avoid contact with family members and children and you do not need to be isolated or excluded from school, or work.

It is important that you should seek medical advice immediately if you develop any of the following symptoms listed below, or if you are unwell. **Please take this letter with you if you need to see your doctor or the emergency department of a hospital.**

Symptoms in infants include

- Fever
- Refusing to take feeds
- Fretfulness
- Child difficult to wake
- Rash of redish-purple spots or bruises
- High pitched or moaning cry
- Pale or blotchy skin

Symptoms in older children and adults include

- Headache
- Fever
- Vomiting
- Neck stiffness and joint pains
- Drowsiness or confusion
- Rash of redish-purple spots or bruises
- Discomfort when looking at bright lights

Yours sincerely,

Director
Public Health Unit

Appendix 2G

Information letter to contacts

NOTE FOR PHU – Please copy this text onto PHU letterhead, or otherwise provide contact details.

Dear

I believe you have recently been in contact with a person who has meningococcal infection.

Meningococcal infection is caused by a bacterium that is carried, usually harmlessly, in the nose and throat by up to 10% of people. However, occasionally carriers may pass it on to others who have been in close contact with them. Only a very small number of people in contact with those that carry the infection develop meningococcal disease. If a carrier passes the bacterium to another person it may take up to 10 days for the infection to develop.

It is not necessary for you to take any antibiotic medication, or avoid contact with family members or children, and you do not need to be isolated or excluded from school or work. While your risk of developing infection is very low, it is important that you seek medical advice immediately if you develop any of the symptoms listed below, or if you become unwell. **Please take this letter with you if you need to see your doctor or the emergency department of a hospital.**

Symptoms in infants include

- Fever
- Refusing to take feeds
- Fretfulness
- Child difficult to wake
- Rash of redish-purple spots or bruises
- High pitched or moaning cry
- Pale or blotchy skin

Symptoms in older children and adults include

- Headache
- Fever
- Vomiting
- Neck stiffness and joint pains
- Drowsiness or confusion
- Rash of redish-purple spots or bruises
- Discomfort when looking at bright lights

Yours sincerely,

Director
Public Health Unit

Appendix 3

Case report form

MENINGOCOCCAL DISEASE CASE REPORT

PUBLIC HEALTH UNIT:

FAX:

Date notified: / /

Time notified: am/pm

Hospital:

Notified by:

Phone:

Date initial response: / /

Time initial response: am/pm

PATIENT DETAILS

Patient's name:

Phone:

Current address:

DOB: / /

Age: years months

Sex: Male

Female

Occupation:

Aboriginal

TSI

Place of work/school:

Non-Indigenous

Unknown

Preschool/child care:

Phone:

CLINICAL PRESENTATION

Meningitis: Yes

No

Unknown

Septicaemia: Yes

No

Unknown

Petechial or purpuric rash: Yes

No

Unknown

Other invasive illness (specify):

LABORATORY CRITERIA

Isolation of *N.meningitidis* :

Yes, Site:

No

Not done

Awaiting results

Detection *N.meningitidis* DNA by PCR:

Yes, Site:

No

Not done

Awaiting results

Gram neg. diplococci in CSF/blood:

Yes, Site:

No

Not done

Awaiting results

N.meningitidis IgM+ve

Yes

Rise in *N.meningitidis* IgM and/or IgG titres

Yes

Detection of *N.meningitidis* antigen in CSF

Yes

No

Not done

Awaiting results

Isolation of *N.meningitidis* from nasopharynx

Yes

No

Not done

Awaiting results

STATUS

Under investigation

Probable

Confirmed

ADDITIONAL LABORATORY DETAILS

Serogroup: A

B

C

W135

Y

Other (specify):

Serotype:

Subtype:

Other lab details:

CLINICAL COURSE AND OUTCOME

Date of onset: / /

Time of onset:

Died Yes

No

Unknown

Was case referred to hospital by a GP?

Yes

No

Unknown

If yes, did GP consider meningitis/meningococcal disease?

Yes

No

Unknown

Date: / /

time seen by GP:

Date of arrival at hospital ED: / / Time seen hospital ED:

Hospital:

Were parenteral antibiotics given prior to hospital admission? Yes No Unknown

IV/IM antibiotics: Date: / / Time: am/pm

CASE MANAGEMENT

Were blood cultures taken before first dose antibiotics? Yes No Unknown

Was throat swab taken at the time of first dose? Yes No Unknown

Antibiotics used in hospital:

Chemoprophylaxis given to patient? Not required Yes No Unknown

RISK FACTORS

Contact with presumptive meningococcal case in 60 days before onset Yes No Unknown

If yes, was prophylaxis offered? Yes No Unknown

If yes, was prophylaxis taken? Yes No Unknown

If yes, specify type of prophylaxis Antibiotic Vaccine

Name of presumptive case:

Type of contact with presumptive case: (see contact management categories below)

Attends child care / preschool / school / university (circle as appropriate) Yes No Unknown

Returned or arrived from overseas country in past 60 days Yes No Unknown

Other risk factor for meningococcal disease (specify):

OUTBREAK DETAILS

Is this case known to be linked to other cases of the same disease? Yes No

Details:

CONTACTS

| Type of contact | Number of contacts identified | Number offered antibiotics | Number offered vaccine | Comments |
|--------------------------------|-------------------------------|----------------------------|------------------------|----------|
| Household | | | | |
| Child-care or Preschool | | | | |
| Close institutional | | | | |
| Exposed to oral secretions | | | | |
| Other close contacts (specify) | | | | |

Appendix 4

The Meningococcal Disease Guidelines Working Party

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Appendix 5

National *Neisseria* Network Laboratories

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Appendix 6

Information and Support Groups

Information and support is available from the following groups

Australia

The Meningitis Centre

<http://www.ichr.uwa.edu.au/affiliations/meningitis/>
TVW Telethon Institute for Child Health Research
PO Box 855, West Perth WA 6872

Phone: (08) 9489 7791

Fax: (08) 9489 7705 or (08) 9489 7700.

Freecall: 1800 250 223

E-mail: rozanne@ichr.uwa.edu.au

The Meningococcal Foundation of Australia

1 Dekalb Street, Tamworth NSW 2340

Phone: (02) 6766 4224. **Fax:** (02) 6766 4107.

Mobile: 0413 356 242.

E-mail: eire@optusnet.com.au

Better Hearing Australia Inc.

Offices in each capital city.

International

Meningitis Research Foundation (United Kingdom)

<http://www.meningitis.org.uk/>

National Meningitis Trust (United Kingdom)

<http://www.meningitis-trust.org.uk/frame.htm>

Meningitis Research Foundation of Canada

<http://www.meningitis.ca/>

Meningitis Foundation of America (USA)

<http://www.musa.org/>